Consolidated guidance on tuberculosis data generation and use
Module 3

National tuberculosis prevalence surveys

World Health Organization

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Abbreviations

AFB	acid-fast bacilli
AI	artificial intelligence
ALARA	as low as reasonably achievable
ART	antiretroviral therapy
ASSIST	Alcohol, Smoking and Substance Involvement Screening Test
BMI	body mass index
BSC	biosafety cabinets
CAD	computer-aided detection
CATA	Cambodia Anti-Tuberculosis Association
CHiP	community HIV care providers
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CR	computed radiography
CXR	chest X-ray
DDR	direct digital radiography
DEFF	design effect
DHS	demographic and health surveys
DM	diabetes mellitus
DMP	data management plan
DMS	data management system
DMU	data management unit
DOTS	directly observed treatment, short course
DR	digital radiography
DR-TB	drug-resistant TB
DST	drug-susceptibility testing
EA	enumeration area
ERC	ethics review committee
FDA	Food and Drug Administration (United States)
FIND	Foundation for Innovative New Diagnostics
GCP	good clinical practice
GDMP	good data management practice
GDP	gross domestic product
GIS	geographical information system
GNI	gross national income
GPS	global positioning system
HCT	HIV counselling and testing
HIV	human immunodeficiency virus
HSRC	Human Sciences Research Council
HTS	HIV testing services
IT	information technology
LAN	local area network
LGA	local government areas
LJ	Löwenstein–Jensen
LIMS	laboratory information and data management system
LIS	laboratory information system
MAR	missing at random
MCAR	missing completely at random
MDG	Millennium Development Goal
MGIT	mycobacterial growth indicator tube
MNAR	missing not at random
MUAC	mid-upper arm circumference
NALC	*N*-acetyl-l-cysteine
NCD	noncommunicable disease
NICD	National Institute for Communicable Diseases
NTCP	national TB control programme
NTM	non-tuberculous mycobacteria
NTP	national TB programme
PACS	picture archiving and communication system
PCR	polymerase chain reaction
PD	prevalence difference
PIN	personal identification number
PPE	personal protective equipment
PPS	probability-proportional-to-size
PR	prevalence ratio
PSU	primary sampling unit
QA	quality assurance
QC	quality control
RBS	random blood sugar
REC	research ethics committee
RS	random start
SAMRC	South African Medical Research Council
SD	standard deviation
SE	standard error
SI	sampling interval
SLIPTA	Stepwise Laboratory Improvement Process Towards Accreditation
SOP	standard operating procedure
SSU	secondary sampling unit
TAG	technical advisory group

TB	tuberculosis
TPT	TB preventive treatment
TREATS	TB Reduction through Expanded Antiretroviral Treatment and Screening
TST	tuberculin skin test
UHC	universal health coverage
UI	uncertainty interval
UN	United Nations
UNICEF	United Nations Children's Fund
UNOPS	United Nations Office for Project Services
USAID	United States Agency for International Development
VR	vital registration
WHO	World Health Organization

CHAPTER 1

Introduction

The main purpose of a national tuberculosis (TB) prevalence survey is to measure the burden of TB disease in the population at a given point in time; repeat surveys (usually after an interval of about 10 years) allow assessment of trends. Survey data also provide important insights that can help national TB programmes (NTPs) to identify ways to improve TB diagnosis and treatment, and to quantify and correct any underreporting of people diagnosed with TB through national disease surveillance systems *(1–4)*.

In recognition of the limitations of available diagnostics, the realities of field operations and relatively low rates of TB disease (per 100 000 population) in children, national TB prevalence surveys typically focus on measuring the number of people aged 15 years and older who have bacteriologically confirmed pulmonary TB disease *(3, 4)*.[1,2] Results can then be used to estimate the overall prevalence of TB disease in the whole population (for all ages and including extrapulmonary TB disease). To identify people with bacteriologically confirmed pulmonary TB disease, the first step is to randomly select geographical areas in the country (referred to as clusters). The number of clusters is defined according to the overall sample size and cluster size required to provide a precise estimate of the national prevalence of TB disease (typically, an overall sample size of about 30 000–100 000 people and a cluster size of 400–800 people).[3] In the selected clusters, the eligible population (based on age and residency criteria) is identified through a household census; people are then screened for TB disease using a combination of a questionnaire about TB-related symptoms and a chest X-ray (CXR); those who screen positive are tested for TB disease.

National TB prevalence surveys are not required to reliably measure the burden of TB disease and assess trends in all countries. Ideally, all countries should be able to reliably track their TB disease burden using national disease notification systems (to count the number of people developing TB disease each year) and national vital registration (VR) systems that include coding of causes of death according to international standards (to count the number of people who die from TB). Many countries already have high-quality disease notification and VR systems that cover a high percentage of the population and can be used for this purpose *(5, 6)*. However, there are many countries in which this is not yet possible.

In about 70 countries, including most of those with a high burden of TB disease, national disease notification systems do not yet provide reliable data about the number of people developing TB disease each year *(5, 7)*. This is for two reasons:

- underreporting of people diagnosed with TB, especially in countries with a large private sector or in which people with TB seek care in public facilities that are not linked to the NTP, and where notification of TB cases to national authorities is not mandatory; and
- underdiagnosis, especially in countries where there are geographical or financial barriers to accessing health care, or where there are health system gaps in terms of infrastructure, human resources and diagnostic facilities *(5, 8)*.

Similarly, many countries (about 90), including most of those with a high burden of TB disease, do not yet have national (or sample) VR systems in which there is high coverage and quality of cause-of-death registration *(6, 9)*.

In the absence of national disease notification and VR systems of high quality and coverage, national TB prevalence surveys provide an alternative way to directly measure the burden of TB disease in the population.

The first national TB prevalence surveys were implemented in various countries in Africa and Asia in the 1950s, when there was a lack of evidence about the burden of TB disease in the population (*1, 3, 10)*. Between the 1960s and the end of the 1990s, further surveys were done in Asia, both to assess the burden of TB disease in the population and (in countries where a series of surveys was done) to assess trends *(3)*.

[1] A definitive diagnosis of extrapulmonary TB often requires a biopsy or on-the-spot clinical expertise (or both). This is difficult to provide in the context of a population-based survey. Chest X-rays (CXRs) are not suitable for use in healthy children with a low risk of TB disease; it is difficult for children to produce sputum samples and the collection of other specimens (i.e. gastric aspirate or faecal samples) requires specific expertise and infrastructure; a precise estimate of the prevalence of TB disease in children would require a very large sample size.

[2] The diagnosis of TB in people with negative bacteriological test results typically requires follow-up investigations that are not logistically feasible in the context of a national TB prevalence survey.

[3] Most other health-related surveys are of diseases and conditions with a much higher prevalence; hence, sample sizes can be much smaller.

Fig. 1.1

Countries in which national TB prevalence surveys were implemented, 2000–2023[a]

2000	China				
2001					
2002	Cambodia				
2003	Malaysia				
2004	Indonesia [b]				
2005	Eritrea [c]				
2006	Thailand				
2007	Philippines	Viet Nam			
2008	Bangladesh [c]				
2009	Myanmar				
2010	China				
2011	Cambodia	Ethiopia	Lao People's Democractic Republic	Pakistan	
2012	Gambia	Nigeria	Rwanda	United Republic of Tanzania	Thailand
2013	Malawi	Ghana	Sudan		
2014	Indonesia	Zambia	Zimbabwe		
2015	Bangladesh	Kenya	Mongolia	Uganda	
2016	Democratic People's Republic of Korea	Philippines			
2017	Mozambique	Myanmar	Namibia	South Africa	Viet Nam
2018	Eswatini	Nepal			
2019	Lesotho				
2020	India				
2021					
2022	Timor-Leste				
2023	Cambodia				

CXR: chest X-ray; TB: tuberculosis.

[a] The year in which most field operations were implemented is shown. African countries are shown in **purple** and Asian countries in **green**.

[b] The survey in Indonesia (2004) did not use CXRs to screen individuals for sputum submission.

[c] The surveys in Bangladesh (2008) and Eritrea (2005) collected sputum samples from all individuals (aged ≥15 years), and did not use CXR or a symptom questionnaire to screen individuals for sputum submission.

Following a period in which only a small number of surveys were done, there was an unprecedented national and global effort to implement national TB prevalence surveys between 2007 and 2017 (**Fig. 1.1**). These surveys were required to provide more robust evidence about the burden of TB disease and to inform assessment of whether global targets for reductions in TB disease burden set for 2015 as part of the United Nations (UN) Millennium Development Goals and the World Health Organization (WHO) Stop TB Strategy were achieved *(3, 4)*. Subsequently, six countries implemented a national TB prevalence survey between 2018 and 2023 (**Fig. 1.1**).

In total, between 2007 and the end of 2023, 37 national surveys in 32 countries were implemented. These included surveys in 20 of the 22 "global focus countries" that were identified as top global priorities for a survey in 2007 *(4)* and in 12 other countries. Of the 37 surveys, 20 were in Asia and 17 in Africa. Five countries – Cambodia, China, Myanmar, the Philippines and Viet Nam – undertook repeat surveys.[1] These surveys now provide a baseline that can inform assessment of national and global progress towards the milestones (for 2025) and targets (for 2030 and 2035) for reductions in TB disease burden set in the WHO End TB Strategy and the UN Sustainable Development Goals *(11, 12)*, and ultimately, assessment of whether these milestones and targets are achieved.

Among the subset of countries that do not yet have national disease notification and VR systems of high

[1] Bangladesh in not included because the first survey (in 2008) used methods that were different from those recommended in WHO guidance issued in 2011 *(4)*, with no use of CXR or symptom screening (see also **Fig. 1.1**). The survey in 2015 was the first to use methods recommended in this guidance.

Table 1.1

Epidemiological criteria to assess whether a country should consider implementing a national TB prevalence survey

CRITERIA	EXPLANATION OF CRITERIA
Countries that completed a national TB prevalence survey, 2007–2023	
1. Estimated prevalence of bacteriologically confirmed pulmonary TB ≥250 per 100 000 population aged ≥15 years during the previous survey[a]	• Sample size small enough (<70 000 individuals) to make a survey feasible in terms of cost and logistics
and	
2. About 10 years since the last survey[b]	• Time between surveys is sufficient to allow a statistically meaningful comparison of prevalence
Countries that did not implement a national TB prevalence survey, 2007–2023	
1. Estimated TB incidence ≥150 per 100 000 population per year (all forms, all ages)[c]	• Sample size small enough (<70 000 individuals) to make a survey feasible in terms of cost and logistics
and	
2. No national or sample VR system of high coverage and quality that includes coding of causes of deaths according to international standards	• No reliable direct measurement of TB disease burden
and	
3. UHC service coverage index score is <80 (SDG Indicator 3.8.1) *(14)*	• This is an indirect indicator of insufficient access to quality health services, as defined in the WHO TB surveillance checklist of standards and benchmarks (second edition) *(15)*

SDG: Sustainable Development Goal; TB: tuberculosis; UHC: universal health coverage; VR: vital registration; WHO: World Health Organization.

[a] The best estimate was below this threshold in five of the 32 countries that implemented a survey between 2007 and 2023. Of these, Thailand (with a best estimate of 242 and 95% confidence interval of 176–322) could be considered to meet the threshold, especially after adjustment for the lower sensitivity of the diagnostic algorithm (relying on solid culture) compared with that recommended in this guidance.

[b] An interval of about 10 years between two surveys is recommended to allow assessment of trends.

[c] For survey sample size calculations, prevalence in those aged ≥15 years can be estimated from incidence.

quality and coverage, a national TB prevalence survey is not a viable option for assessment of the burden of TB disease in all of them. If the level of TB disease burden is low (relative to population), the sample size required to obtain a reliable estimate of the number of people with TB disease in the population becomes prohibitively large. This means that national TB prevalence surveys should only be considered in countries in which the estimated level of TB disease burden is above a certain threshold. The epidemiological criteria that can be used to assess whether a country should consider implementing a national TB prevalence survey are shown in **Table 1.1**.[1]

Based on WHO estimates of the TB incidence rate (new cases of TB disease per 100 000 population per year) published in 2023, and the current capacity of national disease notification and VR systems to provide reliable data on TB disease burden (in terms of cases and deaths), the 52 countries that met these epidemiological criteria at the end of 2023 are listed in **Table 1.2** and shown in **Fig. 1.2**. The table and figure distinguish between countries that have already implemented at least one national TB prevalence survey,[2] and those that have never implemented a survey.

For countries that meet the epidemiological criteria for considering implementation of a national TB prevalence survey, there are various nonepidemiological requirements that must also be satisfied, both before a survey can be embarked upon and throughout its implementation. These were clearly identified in 2011 *(4)* and are summarized in **Box 1.1**.[3] Among these factors, one that is fundamental is that the security situation in the country allows for both a nationally representative survey (without exclusion of large parts of the country), and the safety of field teams and survey participants during survey operations.

During the period of unprecedented national and global efforts to implement national TB prevalence surveys between 2007 and 2017, WHO published two editions of guidance on the design, implementation, analysis and reporting of national TB prevalence surveys, first in 2007 and then in 2011 *(4, 16)*. The second edition became widely known as the "lime book" *(4)*.

It is a strong testament to the comprehensiveness and quality of the *lime book* that it was very widely used over a period of more than 10 years. Nonetheless, in the years since its publication, major technological developments have occurred, and important lessons have been learned from surveys implemented in 2007–2023 *(3, 17)*. These include:

[1] This is updated and adapted from the criteria agreed at a WHO meeting in 2016 *(13)*.

[2] Five countries that implemented a survey between 2007 and 2015 do not meet the epidemiological criteria for implementing further surveys: China, Gambia, Rwanda, Sudan and Thailand.

[3] The list has been updated where appropriate; for example, in terms of the type of tests for which laboratory capacity is needed.

Table 1.2

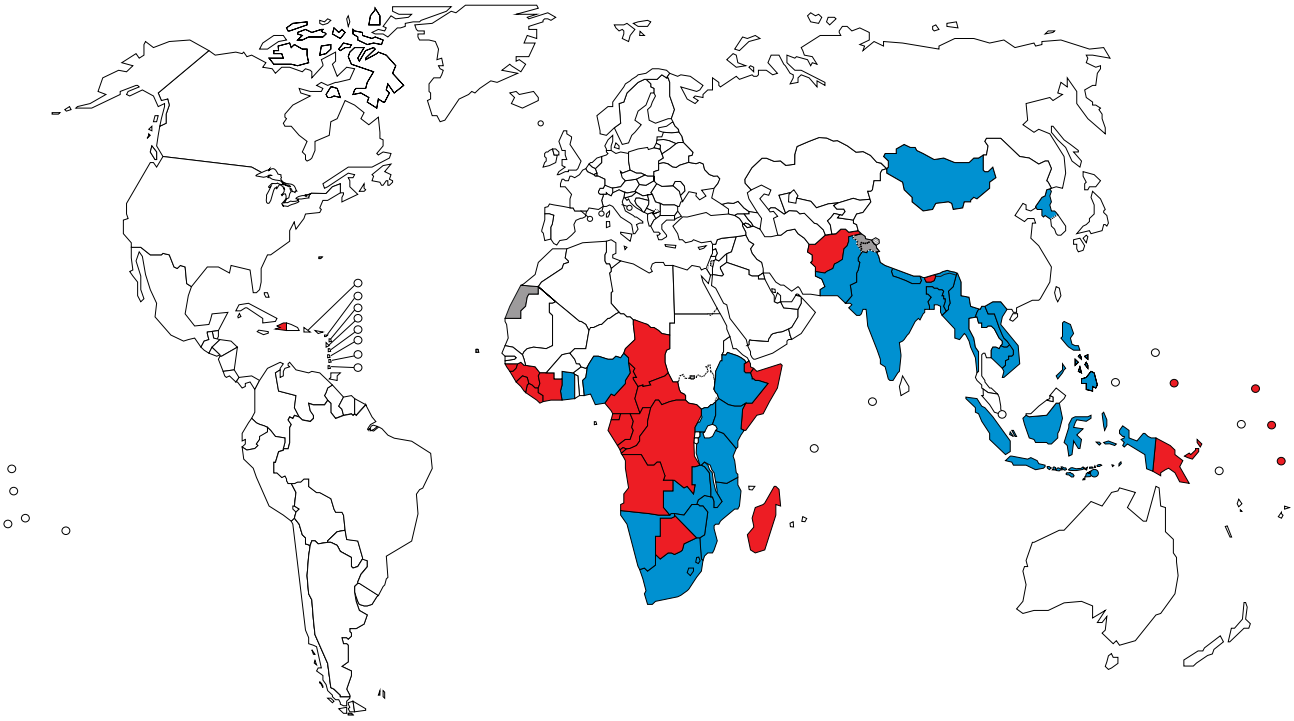
Countries that met epidemiological criteria (Table 1.1) for considering implementation of a national TB prevalence survey, at the end of 2023

COUNTRIES THAT HAVE ALREADY IMPLEMENTED AT LEAST ONE NATIONAL TB PREVALENCE SURVEY (N=27)	COUNTRIES THAT HAVE NEVER IMPLEMENTED A NATIONAL TB PREVALENCE SURVEY (N=25)
Bangladesh, Cambodia, the Democratic People's Republic of Korea, Eswatini, Ethiopia, Ghana, India, Indonesia, Kenya, the Lao People's Democratic Republic, Lesotho, Malawi, Mongolia, Mozambique, Myanmar, Namibia, Nepal, Nigeria, Pakistan, the Philippines, South Africa, Timor-Leste, Uganda, the United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe	Afghanistan, Angola, Bhutan, Botswana, Cameroon, the Central African Republic, Chad, the Congo, Côte d'Ivoire, the Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Gabon, Guinea, Guinea-Bissau, Haiti, Kiribati, Liberia, Madagascar, Marshall Islands, Micronesia, Papua New Guinea, Sierra Leone, Somalia and Tuvalu

TB: tuberculosis.

Fig. 1.2

Countries that met epidemiological criteria for considering the implementation of a national TB prevalence survey at the end of 2023[a]



TB: tuberculosis.

[a] Countries that had already implemented at least one survey by the end of 2023 are shown in **blue** and those that had not implemented a survey by the end of 2023 are shown in **red**.

- **New TB diagnostics.** WHO-recommended rapid molecular tests for TB diagnosis are now widely available and used. Among these, the Xpert Ultra assay (first recommended by WHO in 2017) has higher sensitivity than the solid culture methods previously relied upon in most national TB prevalence surveys *(17)*. The availability of rapid tests also means that all survey participants who meet screening criteria and are tested for TB disease should be provided with a rapid diagnostic test result.
- **Digital technology and tools for chest radiography**. There have been major advances in digital CXRs and computer-aided detection (CAD) software, which can improve the speed and efficiency with which CXRs are done and read, and the consistency and reliability of results. In addition, digital formats mean that the external readers required for quality assurance do not have to be physically present in survey field sites, or even in the country where the survey is being done.
- **Digital tools for data management**. Over time, there has been a shift away from paper-based forms to the digitalization of many aspects of survey data collection (including with real-time dashboards and automated reporting). This can substantially improve data accuracy, and the speed and efficiency

with which data are collected, cleaned, analysed and used. It can also facilitate monitoring of the flow of participants and associated specimen collection during field operations.

- **Culture testing is challenging in the context of a survey**. Ensuring a high quality of culture testing was the main challenge reported in surveys implemented during 2007–2016 *(3, 17)*.
- **Data management was a major challenge in recent surveys**. Data management ranked second only to culture testing as the main challenge faced in countries implementing surveys during 2007–2016 *(4)*.
- **Testing for HIV and other comorbidities**. Recent surveys have shown widespread acceptability of testing for HIV in the context of a survey, and there is growing interest in testing for other comorbidities.

These developments and lessons learned necessitated a comprehensive update of WHO guidance on national TB prevalence surveys. The process used for the update is summarized in **Box 1.2**.

This new edition is intended to support the design, implementation, analysis and reporting of national TB prevalence surveys in the period up to about 2030. Compared with the *lime book (4)*, it includes:

- major revisions to the diagnostic algorithms that are recommended for use in national TB prevalence surveys, and in turn the case definitions used to count the number of survey participants who have TB disease;
- updated guidance on sampling design and the analysis and reporting of data, based on the new diagnostic algorithms and case definitions;
- updated and considerably expanded guidance on data management;
- updated guidance on chest radiography, clinical management, survey management and field operations; and
- new chapters on testing for HIV and comorbidities, survey monitoring, comparisons with previous surveys, reporting and dissemination of survey results, and use of survey data.

Updated country examples to illustrate the guidance are provided throughout.

The guidance is structured in four major parts:

- **Part I** covers **Design and methods**. It includes 10 chapters: protocol development and standard operating procedures; screening and diagnostic algorithms; survey case definitions – classifying who is, and who is not, a survey TB case; sampling design; interviews and data collection tools; chest radiography; diagnostic investigations; clinical management related to TB treatment and other interventions; testing for HIV and other comorbidities; and ethical considerations and good clinical practice.

BOX 1.1
NONEPIDEMIOLOGICAL REQUIREMENTS THAT MUST BE SATISFIED BEFORE A NATIONAL TB PREVALENCE SURVEY CAN BE EMBARKED UPON

For countries that meet epidemiological criteria for implementing a national TB prevalence survey, there are other requirements that must be satisfied, both before a survey can be embarked upon and throughout its implementation. These include:

- strong commitment and leadership from the NTP, the ministry of health and a core group of professionals;
- availability of a suitable institute, organization or agency to lead and manage the survey;
- the national security situation being such that a nationally representative survey is feasible, and the safety of survey field teams and participants can be assured throughout the survey;
- availability of the funding required to implement a survey;
- confidence that a sufficiently high participation rate among the eligible population can be achieved, based on either a previous national TB prevalence survey or a comparable type of survey – community engagement, starting with the preparatory phase of the survey and continuing throughout, is crucial to help ensure high participation;
- availability of adequate laboratory capacity (or confidence that such availability can be established before the survey), for both Xpert® MTB/RIF Ultra (Xpert Ultra) and liquid culture testing;
- capacity to undertake CXR examinations in the field in compliance with the regulations of the national radiation authority (or confidence that such capacity can be established before the survey);
- capacity to adhere to good clinical practice and good data management practices;
- feasibility of reliable and timely procurement of equipment (especially X-ray equipment);
- survey protocols having undergone expert review and clearance (including ethical clearance); and
- availability of external support and technical assistance, if required (this is particularly relevant for countries implementing a national TB prevalence survey for the first time).

- **Part II** covers **Survey management and organization**. It includes four chapters: survey organization and training; field operations; survey monitoring; and budgeting and financing.
- **Part III** covers **Data management and analysis**. It includes three chapters: documents and data management; analysis and reporting; and comparisons with previous surveys.
- **Part IV** covers **Report writing, and dissemination and use of survey results**. It includes two chapters: report writing and dissemination; and use of survey results.

BOX 1.2
GUIDANCE DEVELOPMENT PROCESS

The guidance was developed between 2022 and 2024. It was built on the foundation provided by the *lime book (4)*, and an extensive period of data analysis and discussions between 2018 and 2022 related to diagnostic algorithms to recommend in future surveys *(17)*.

A core group of authors was identified and convened by the WHO Global Programme for Tuberculosis & Lung Health. These authors were selected based on their high level of technical expertise, and their extensive expertise and experience related to national TB prevalence surveys. They included people from NTPs, national institutes and other national entities who had lead roles in their country's national TB prevalence survey; and globally recognized experts from technical agencies, universities, research institutes or independent consulting firms who have provided guidance and support to multiple surveys over a period of several years (often for more than a decade).[a]

Each chapter was drafted by a group of experts, many of whom were previously lead or co-lead authors of chapters in the *lime book*. WHO convened two meetings (in September 2022 and June 2023) that brought together all those who were leading or co-leading chapter development, to review and discuss advanced drafts.[b] Final versions were produced after the second meeting, based on a final round of feedback.

[a] The **Acknowledgements** provides details of individuals and their affiliations, and the chapters to which they contributed.

[b] Declarations of interest were obtained from all meeting participants in advance, in accordance with WHO policy. No relevant conflicts of interest were identified.

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CHAPTER 2

Protocol development and standard operating procedures

A good protocol is fundamental to a high-quality national tuberculosis (TB) prevalence survey. A thoughtful and technically sound protocol demonstrates preparedness to national authorities and external partners. This should help to secure funding, facilitate advocacy, foster collaboration and create momentum to implement a survey. The protocol then provides the basis for all aspects of survey design, implementation, analysis and reporting.

This chapter describes the process of protocol development for a national TB prevalence survey, the essential elements that should be included in a survey protocol and the standard operating procedures (SOPs) that need to be developed alongside the protocol. It also provides a checklist that can be used to review a protocol (**Annex 2.1**), to check that all essential elements are properly covered. This checklist is an updated version of one that was widely used by country survey teams and their technical partners between 2011 and 2019.

2.1 Protocol development process

A protocol is a document that thoroughly describes a research study. This includes the objective or objectives, design, methods, organization (including the roles and responsibilities of the entities and individuals involved, and timelines), the required budget and ethical considerations. In addition, it usually includes a description of the background to and reason(s) for the study being conducted, as well as how the results will be used and disseminated.

Before a TB prevalence survey is conducted, a clear, detailed and to-the-point protocol is required. All survey protocols must be approved by an appropriate ethical review committee before implementation. Review of the protocol by members of the WHO Global Task Force on TB Impact Measurement *(1)* before its submission to in-country ethics committees (and, where applicable, other such committees) is highly recommended to ensure that the survey is conducted in line with global guidance.

During the initial stages of protocol development, obtaining political commitment by involving national authorities and external partners is essential. As the protocol develops, it can also be used for advocacy purposes, and to apply for and secure funding.

The development of a protocol and associated SOPs is an iterative process that involves multiple partners. Steering committees and technical advisory groups comprising both national and international partners should be formed and engaged early in the protocol development process. The best way to start developing a protocol is to convene a protocol development workshop. Ideally, this workshop would be facilitated by a partner or technical agency with experience in conducting prevalence surveys, with the participation of all key partners. In the case of a repeat survey, those with key roles in the previous survey should be involved, where possible, to make the best use of in-country knowledge.

Ideally, the following people should be part of the core team developing the protocol:

- The **survey coordinator** who will be responsible for overseeing day-to-day survey activities; if such a person has already been identified, they should be encouraged to participate in survey protocol development, whenever possible.
- An **epidemiologist** to support the design of the survey, data collection tools, case definitions, inclusion and exclusion criteria, and interpretation and application of survey results.
- A **statistician** to provide advice on sampling design (including calculation of the sample size) and to develop the data analysis plan. In several countries, the sampling frame was designed in close collaboration with the national statistics agency (e.g. in Eswatini, Mozambique and Rwanda). In Eswatini, the Central Statistics Office was an active member of the steering committee and led the sampling of the survey. A similar arrangement was used in Mozambique, where the Instituto Nacional de Estatistica provided oversight to the drawing of the survey sample and the household census, and conducted field training for census enumerators.
- A **data management expert** to provide advice on the design of the data management systems to be used in the field, radiology sites and laboratories. Input from data management teams experienced in conducting national surveys for other diseases is useful in this regard.
- A **radiologist** to provide guidance on chest X-ray (CXR) procedures, equipment selection and radiation board approval and guidelines for the use of equipment in community settings, and guidelines for standardizing the interpretation and reporting of radiographic images.

- A **medical officer with expertise in TB** (e.g. respiratory physician) to develop procedures for the management of participants diagnosed with TB, those with serious non-TB-related pathology and those with comorbidities (e.g. HIV and diabetes).
- A **laboratory expert** to support the development of procedures for the collection, transportation and processing of clinical specimens.
- A **monitoring and evaluation (M&E) officer** (or a quality assurance officer) to provide advice about monitoring aspects of the survey.
- A person with experience in **field logistics, and financial and administrative procedures** to provide advice on the planning of fieldwork, the procurement of equipment and consumables required, and the development of human resource contracts.

During the initial process of developing the SOPs and training manuals, input from epidemiologists, laboratory experts, radiologists and the data manager will be essential. External technical assistance – provided by key staff from a national TB prevalence survey conducted elsewhere or international organizations – is an asset, especially in countries planning a first-ever survey. It is important to discuss and define the different roles and responsibilities of the partners from the beginning of the process, and to agree on procedures and data ownership. The protocol should be a joint product of the team that will be involved in carrying out the survey.

Protocol development can be time consuming, often lasting for a year or more from the initial discussions through to identifying key partners and approval of the protocol by the appropriate ethical committee. Investing time and effort in the planning and development stages to create a good study design and well-standardized procedures will help to avoid challenges when the survey is implemented.

2.2 Essential components of the protocol

Table 2.1 provides a list of the minimal recommended elements to be included in the protocol. Each topic area is discussed below and a protocol checklist is provided in **Annex 2.1**.

Topic 1. Summary

This should provide an overview of the most important elements of the survey, including:

- The rationale for and main objective(s) of the survey.
- Key elements of the survey design and methods.
- The required budget.
- Anticipated outcomes and potential use of the survey results.
- How results will be published and disseminated.

Table 2.1

General structure of the survey protocol

	TOPIC AREA
1	Summary
2	Background and rationale
3	Objectives
4	Survey design and methods
5	Survey procedures and organization
6	Piloting of survey procedures
7	Monitoring and quality assurance
8	Training
9	Data collection and management
10	Data analysis and reporting
11	Survey management
12	Ethical considerations
13	Timeline of the survey
14	Technical assistance
15	Reporting and dissemination
16	Budget
17	References

Topic 2. Background and rationale

This should provide background information and explain the rationale for the survey, including:

- The population size of the country.
- The TB epidemiological situation in the country, based on available surveillance and survey data (including results from previous national TB prevalence surveys, if available).
- A description of how TB services are organized and delivered, including the composition of the national TB programme (NTP), the number of health facilities where TB diagnostic and treatment services are provided, the diagnostic tests used in routine health services (e.g. molecular tests) and the number of facilities able to perform culture.
- The main reasons why a national TB prevalence survey is required (see **Chapter 1**).
- If studies on risk factors or other embedded studies are to be undertaken, a short description of these and the rationale for embedding them in the TB prevalence survey (see also **Chapter 10**).

Topic 3. Objectives

The main objective or objectives of the survey should be clearly defined (see also **Chapter 1**).

Topic 4. Survey design and methods

The main components of survey design and methods should be described and explained, including sampling design, the screening and diagnostic algorithm to be used, and case definitions. Detailed guidance is provided in **Chapters 3**, **4**, **5**, **6**, **7** and **8**.

4.1 Survey design, including the sampling frame and survey population

- Description of the survey design that will be used i.e. a cluster randomized survey.
- Description of the geographical or political structure of the country and definition of the lowest administrative level (enumeration area or "village") that will be the basis for the sampling of clusters.
- Population data (typically from national censuses) that form the basis for the sampling frame (e.g. data source, accurateness of available data and assumptions made for population projections).
- Description and explanation of the parameters used to calculate the sample size and the assumptions underlying the estimation of the sample size:
  - a prior guess of the true population prevalence of bacteriologically confirmed pulmonary TB;
  - the relative precision required around the estimate of the true population prevalence of TB drawn from the survey;
  - the estimated design effect (i.e. the multiple by which a sample size must be increased, relative to the sample size required for a simple random sample survey, due to a cluster sample survey design);
  - the number and size of clusters, and the justification for the choices made.
  - the target participation rate (i.e. the percentage – or proportion – of the eligible population that will participate in the survey); and
  - the proportion of the national adult population included.
- Sampling strategy, with justification for choices made:
  - description of stratified sampling, if used;
  - procedures used for sampling of units (e.g. primary and secondary), where applicable;
  - the process that will be used to replace clusters (e.g. due to natural disasters or insecurity), if needed.
- Definition of the eligible population, including the inclusion and exclusion criteria that will be applied at four stages:
  - **Sampling frame stage**. Description of the sampling frame and whether it includes all populations in the country (e.g. mobile populations). Description of areas where survey operations are considered not to be feasible (e.g. regions of insecurity and military zones) that will not be included in the sampling frame, if applicable.
  - **Household level**. Description of how the mobile population will be included, if applicable, and description of how people in institutions (e.g. prisons, refugee camps, schools or dormitories, military or police barracks, and hospitals) will be included.
  - **Individual level**. Definition of members of the household, and description of enrolment procedures for inclusion of seriously sick individuals or others who are unable to attend for CXR at the central site.
  - **Examination level.** Inclusion criteria for CXR, eligibility for sputum examination of those not able to undergo CXR and procedures to be followed for participants who are not able to produce sputum.

4.2 Screening and diagnostic algorithm

- Description and justification of the screening strategy that will be used to identify individuals at highest risk of having TB, and identification of any limitations (e.g. the type of people with TB who could be missed).
- Description and justification of the diagnostic algorithm that will be used to test all those who screen positive.

4.3 Case definitions

- The following terms should be defined in the protocol:
  - eligible to participate in the survey;
  - screen positive (i.e. by symptom questionnaire or by CXR, or both);
  - participants with a normal CXR and those with an abnormal CXR;
  - previous history of TB;
  - current history of TB;
  - eligible for sputum examination (as defined in the survey);
  - eligible for an HIV test;
  - HIV status;
  - bacteriologically confirmed pulmonary TB case;
  - smear-positive pulmonary TB case (only if used in repeat surveys);
  - Xpert® MTB/RIF (Ultra) positive TB case (for programmatic comparisons only); and
  - rifampicin-resistant TB case.

Topic 5. Survey procedures and organization

The main components of survey procedures and organization should be described and explained. Detailed guidance on the topics to be covered is provided in **Chapters 12**, **13** and **14**, as well as **Chapters 3**, **6**, **7**, **8**, **9** and **10**.

5.1 Outline

- Brief overview of steps that will be performed during the survey:
  - reference to subsequent sections in the protocol for more detailed information; and
  - a note that the protocol outlines the key procedures, but that specific SOPs will be developed to describe all procedures in detail (see **Section 2.3**).

5.2 Informing authorities

- Activities to be undertaken after ethical approval (**Chapter 11**), to inform all respective authorities about the survey.
- Information and sensitization activities to take place at central, regional or local levels.

5.3 Presurvey visit, cluster sensitization and community mobilization

- Activities to be undertaken during the presurvey visit to the selected clusters:
  - processes for explaining the purpose and procedures of the survey to community members, and for obtaining community consent if applicable;
  - situation assessment:
    - accessibility of the cluster during different seasons;
    - availability of electrical power;
    - identification of areas to set up the screening unit, CXR unit and field laboratory;
    - availability of accommodation and cooking facilities for the field team;
  - identification of the survey population within the selected cluster and the need for subsampling, if required; and
  - linkages with the local health centre, hospital or antiretroviral therapy centre for participants' referral.

5.4 Survey census

- Definition of when, how and by whom the survey census will be performed.
- Reference to examples of registries in the annex of the protocol that will be used to record the information for all eligible people (≥15 years and resident) and children (<15 years).
- Use of existing population lists or development of population lists as part of the survey.
- Procedures for collection of household data such as sociodemographic and socioeconomic status (i.e. using assets), if required.
- Distribution of invitation cards at the household level.
- Quality assurance (QA) procedures (e.g. population coverage and household interviews).

5.5 Reception and informed consent

- Individual or group information.
- Informed consent process for eligible participants.
- Family member or guardian provides assent for minors (15–17 years).
  QA procedures.

5.6 Symptom screening interview

- Who will undergo symptom screening.
- Where symptom screening will take place.
- Description of field team members who will conduct the symptom screening.
- Symptom screening criteria.
- Procedures for those unable to understand or to answer the symptom screening interview.
- QA procedures.
- Health seeking behaviour – questions are asked only of those who have symptoms, and those who are screen-positive.
- Ask all participants if they have a current and/or past history of TB.

5.7 CXR screening

- Who will be invited for CXR screening.
- Protective measures that will be taken (e.g. lead shielding) and full details of all safety procedures in SOPs.
- Who will perform and read the CXR.
- Criteria that will be used to define an abnormal CXR result.
- Criteria that will be used to define final CXR results.
- Use of computer-aided detection, if applicable.
- Procedures for those unwilling or unable to undergo CXR.
- Referral of individuals who are sick or have CXR abnormalities that require an immediate medical investigation or intervention to an appropriate medical facility.
- Purpose and methods of central reading of the CXRs.
- Archiving of CXRs.
- Transportation and transmission of CXRs to the central level.
- QA procedures at field and central level.
- Radiation board approval.

5.8 Sputum eligibility

- Which individuals are sputum eligible (or screen positive).
- Where and how individuals eligible for sputum examinations will be registered.
- How individuals eligible for sputum examination will be identified (by an automated process or manually).
- Diagnostic tests that will be used for individuals who are sputum eligible.
- QA for sputum eligibility.

5.9 Additional questions – description of the information collected during this interview

- Who is eligible for the interview and which individuals will be asked the additional questions – all or a subgroup (e.g. all those who are symptomatic or a random subset of participants or households).
- Where the in-depth interview, if required, fits in the field flow.
- QA procedures.

Examples of topics on which additional questions could be asked are:

- *Health seeking behaviour* – recent surveys have integrated questions about such behaviour into the symptom screening interview, with these questions asked only of participants reporting symptoms.
- *Risk factors* – recent surveys have embedded a separate risk factor study into their survey, asking all identified survey TB cases and a random subset of all participants questions about, for example, smoking, substance abuse and occupational hazards. Risk factors have been embedded by asking all sputum-eligible individuals this set of questions (because all cases come from this group) as well as a randomly selected subset of all participants.
- *TB case study* – in-depth and follow-up questions are asked of all cases identified in the survey.
- *Routine-survey case–control study* – in Rwanda, questions were asked of all people diagnosed with TB as part of the survey (i.e. survey TB cases); in the same period, a subset of people with TB identified in the TB clinics (i.e. routine cases) around the survey were interviewed. The same set of questions were asked of both groups; examples of included topics were demographics, socioeconomic status, risk factors and reported symptoms. A comparison was then made between cases routinely identified and those identified as part of the survey, to help identify which type of cases were being missed in the routine process.

5.10 Sputum examination

- What diagnostic algorithm will be used and where the different steps will be carried out (e.g. at field, regional or central level).
- Whether there is a need for sputum transportation of samples (if yes, refer to the appropriate section where this is described).

5.10.1 Sputum collection

- Number and type (spot, morning) of sputum samples to be collected, with respective procedures.
- Sensitization procedures for sputum collection; that is, instructions to explain how to produce quality sputum (e.g. with leaflets, images and full details in SOPs).
- Who will perform the sputum collection.
- Collection of sputum samples from special groups (e.g. those not undergoing CXR, and individuals who are sick and cannot come to the field site to be screened).
- Procedures for those who are unwilling or unable to submit a sputum sample.
- Sputum sample labelling, packaging and storage in the field.
- Cold chain maintenance in the field.
- QA procedures.
- Description of infection control procedures (full details in SOPs).

5.10.2 Sputum transportation and reception of samples

- Transportation of sputum samples to central or regional laboratories.
- Cold chain maintenance.
- Storage procedures for sputum samples in the laboratory.
- Sputum sample collection at reception of the laboratory.
- QA procedures.

5.10.3 Sputum microscopy (only for repeat surveys, where applicable)

- For which samples sputum smear will be done.
- Where microscopy will be done and who will do it.
- Outline of procedures for preparing sputum smears (details in SOPs).
- Type of staining and microscopy to be used for sputum smears.
- QA procedures.
- Reporting of smear results (i.e. who will receive information about sputum smear-positive cases and over what timeframe).

5.10.4 Sputum Xpert testing (or equivalent test)

- Which samples will undergo Xpert testing.
- Where Xpert testing will be done and who will do the testing.
- Outline of procedures for preparing samples for Xpert testing (details in SOPs).
- QA procedures in the field.
- Reporting of Xpert results (including for rifampicin-resistant TB), including timeframe, follow-up actions and linkage to care.

5.10.5 Sputum culture

- Where culture will be done and who will do the culturing.
- Which sputum sample or samples will be cultured.
- Type of culture that will be used.
- Procedures for sputum decontamination, inoculation and incubation (note: a short outline of the procedures should be given in the main text, with reference to detailed SOPs in an annex).
- Outline of procedures for identification of *Mycobacterium tuberculosis* and nontuberculous mycobacteria (details in SOPs).
- QA procedures.
- Reporting of results (i.e. who will receive information about positive Xpert or cultures [or both]) and over what timeframe.

5.11 Follow-up procedures

- Procedure for follow-up of participants who have not undergone all required procedures (including follow-up of those who were invited but did not attend, or where additional samples are required), and description of how those participants will be identified (e.g. crosschecking of registers and data summaries) and what follow-up will be done.

5.12 Clinical management

- Procedure for follow-up (and linkage to care) of participants with TB or non-TB diagnoses that were identified during the survey (in the field and centrally).
- Procedure for the management of participants identified as having any severe illness.
- Plans for referral and treatment for individuals with positive laboratory results.
- Plans for the communication of laboratory results (whether positive or negative) to the participants.
- Composition of medical panel, and types of cases that will be discussed.
- How often the medical panel will convene.
- Medical panel feedback mechanism: who will receive the feedback, and how and when they will receive it.
- Follow-up mechanism.
- How patient confidentiality will be ensured.
- QA procedures.

5.13 HIV testing and comorbidities

- Who is eligible to undergo HIV testing and how those individuals will be identified.
- Description of the national HIV testing algorithm.
- Description of the testing procedures.
- How patient confidentiality will be ensured.
- How results will be communicated, when and to whom.
- Follow-up procedures for eligible participants.
- Plans for referral or treatment for individuals with an HIV-positive result.
- Which other comorbidities will be tested in the survey (address similar questions as for HIV).
- QA procedures.

5.14 Optional sections

The protocol can include additional sections for optional components, to describe any add-on or embedded studies in more detail. The following is the minimum that should be described for each additional sample collected, test undertaken or questionnaire administered:

- Specific objective that the collection of such data will contribute to:
  - Is this study really needed?
  - How will these data improve the NTP?
  - How will the data inform policy?
- Design and data collection procedures in place.
- Who will conduct the study.
- Whether the study might obstruct the prevalence survey.
- Who is eligible to undergo the additional procedures and how such individuals will be identified.
- Testing procedures.
- How patient confidentiality will be ensured.
- How results will be communicated and to whom.
- Procedures for identifying all eligible participants who have been approached.
- Follow-up procedures for eligible participants.
- How samples will be stored and transported (where applicable).
- QA procedures.
- Whether ethical approval has been obtained, with details of the study and informed consent procedures outlined in the information sheet.

Topic 6. Piloting of survey procedures

Piloting of survey procedures is important to test how they work in practice and to make any necessary corrections before starting the main survey. The protocol should describe:

- Procedures for and timing of a pre-test (e.g. desk simulation) of the survey procedures.
- Procedures for and timing of a pilot of the survey procedures.
- Process for incorporation of lessons learned from the pilot, including procedures for updating SOPs.

Detailed guidance is provided in **Chapter 13**.

Topic 7. Monitoring and quality assurance

How the survey will be monitored, including quality assurance, should be described. The protocol should describe:

- Procedures and systems that will be put in place to ensure quality data are collected at the field and central levels.
- Monitoring procedures for the survey at different levels, including team leader to field teams, survey coordinator to field teams and central level, central level to field level (laboratory and CXR), field supervision by the steering committee and monitoring missions by external partners.
- External QA by a supranational reference laboratory.

Detailed guidance on these topics is provided in **Chapters 6**, **7**, **8** and **14**.

Topic 8. Training

The following items should be described:

- Organization and process of the training for the survey and the development of the training manual.
- A description of who will be trained, for how long and when.

- The protocol (which outlines the key aspects of the training) and the SOPs (which provide details of all procedures that form the basis for the training).

Detailed guidance is provided in **Chapter 12**.

Topic 9. Data collection and management

The protocol should describe data collection tools and data management. Detailed guidance is provided in **Chapters 6** and **16**.

- **Data collection tools**
  - Detailed overview of registries and forms (which will be converted into digital format), including reference to annexes as appropriate.
  - Minimum suggested list of registers and forms:
    - census register;
    - symptom screening questionnaire;
    - CXR screening and results register (field and central level);
    - individuals eligible for sputum examination register;
    - specimen dispatch register;
    - laboratory results register;
    - case management register; and
    - survey TB case register.
- **Data management**
  - Roles of the data management team in the field and centrally.
  - System or systems that will be used for managing the data.
  - Procedures that will be used for capturing and storing survey data, files and forms (if used).
  - Procedures that will be used for data entry, data cleaning and validation, and data management (with details in SOPs and a data management manual).
  - Where data entry will take place and who will enter the data.
  - Who will be responsible for ensuring data quality and how this will be monitored.
  - QA procedures.

Topic 10. Data analysis and reporting

The main items to be covered are:

- Who will develop the data analysis plan.
- Basic description and summary of data, and outline of table shells.
- Procedures for accounting for clustering or stratification, accounting for missing data, undertaking multivariate analysis and adjusting for demographic change.
- How comparisons will be made with previous surveys, if applicable.
- Description of procedure for analysing supplementary data.
- Who will be responsible for writing the final report of the survey and within what timeframe.
- How results will be disseminated nationally and globally.
- Publication of report and submission of an article to a peer-reviewed journal.
- Storage of data in publicly available data repositories.

Detailed guidance is provided in **Chapters 17** and **18**.

Topic 11. Survey management

The main items to be covered are:

- Description of survey management:
  - organigram;
  - reporting lines;
  - roles and responsibilities of the steering committee, technical working group, survey coordinator and survey teams (central and field); and
  - methods of communication between reporting lines, and frequency of meetings.

Detailed guidance is provided in **Chapter 12**.

Topic 12. Ethical considerations

The main items to be covered are:

- All known and potential ethical issues in the survey:
  - informed consent and participant information sheet (see **Chapter 6**);
  - involvement of human subjects (sensitization procedures, including a description of risks and benefits, how risks are minimized and a guarantee of the right of every participant to refuse the procedure);
  - participants' safety during the CXR process;
  - case management of TB and non-TB diagnoses: referral and linkage to care;
  - storage of biological samples (for how long and for what purpose);
  - HIV testing and notification of results;
  - submission of the protocol to a research ethics committee(s);
  - confidentiality and anonymization of data;
  - reuse of data for other objectives;
  - reimbursement of costs for participants or provision of token for participation (e.g. mobile phone credit, food, soap);
  - training in the principles of good clinical practice and good data management practice;
  - misconduct by the survey staff;
  - ethical approval.

Detailed guidance is provided in **Chapter 11**.

Topic 13. Timeline of the survey

A realistic timeline for the survey should be defined, considering the time needed for preparations, securing funding, procuring supplies and hiring staff. All components of the survey, from preparation through to dissemination and publication, should be included in the timeline.

Topic 14. Technical assistance

The main items to cover are:

- Plan for the provision of technical assistance.
- Description of the kind of technical assistance needed and for which elements of the survey.
- Who will financially support technical assistance.

More detailed guidance is provided in **Chapter 12**.

Topic 15. Reporting and dissemination

The main items to cover are:

- Plans for dissemination and publication of the survey findings.
- Who will write the survey report and peer-reviewed publication.
- Who the survey results will be disseminated to and in what timeframe.

More detailed guidance is provided in **Chapter 19**.

Topic 16. Budget and financing

The main items to cover are:

- The overall budget with a breakdown by major line item.
- A detailed budget line in an annex.
- Sources of funding, if known.

More detailed guidance is provided in **Chapter 15**.

Topic 17. References

A full reference list of sources quoted in the text should be provided.

2.3 Standard operating procedures

SOPs document specific instructions for implementing the protocol. Although the protocol provides a general overview of the survey procedures, the SOPs give full details of all procedures. SOPs should be developed through a consultative process similar to that used for the protocol.

In a national TB prevalence survey, SOPs are important to establish the roles and responsibilities of all team members and ensure that they perform the tasks in a standardized way. The magnitude and complexity of a national TB prevalence survey, where multiple survey teams are operating simultaneously, necessitates such standardization. All aspects of the survey should be standardized. The SOPs can be seen as a general script for conducting the survey – they serve as the basis for the training and will need to be followed closely. An outline of the key elements of an SOP is given below:

1. Background:
   - Synopsis of survey
   - Role of SOPs in a TB prevalence survey
   - General instructions for the SOPs
2. SOP general overview
3. SOP presurvey visit or visits
4. SOP field data collection:
   - SOP survey census
   - SOP enrolling participants and informed consent
   - SOP symptom screening interview
   - SOP in-depth interview, if applicable
   - SOP follow-up activities
5. SOP CXR:
   - SOP CXR at field level
   - SOP CXR at central level
6. SOP sputum processing:
   - SOP sputum collection, packing, storage and shipment
7. SOP laboratory procedures:
   - SOP laboratory field procedures
   - SOP laboratory procedures for district or central level
8. SOP HIV testing and referral
9. SOP comorbidity testing (e.g. diabetes), if applicable
10. SOP clinical management
11. SOP supervisory monitoring in the field and centrally
12. SOP data management plan:
    - Data monitoring
    - Data validation
13. SOP case classification ascertainment
14. SOP data analysis plan
15. Optional SOP:
    - SOP TB patient interview
    - Add-on studies

Reference

1 Global Task Force on TB Impact Measurement [website]. Geneva: World Health Organization; 2025 (https://www.who.int/groups/global-task-force-on-tb-impact-measurement).

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
SURVEY GOAL AND OBJECTIVES (Chapter 1)		
1. Goal	To obtain a robust and reliable direct measurement of the burden of TB disease in the population (countries implementing a first-ever survey) To obtain a robust and reliable direct measurement of the burden of TB disease in the population and assess the trend since the last survey (countries implementing a repeat survey)	
2. Objectives	Major objectives are: 1. To measure the prevalence of bacteriologically confirmed TB disease among the population aged ≥15 years, and its distribution by age and sex; 2. To assess whether the prevalence of bacteriologically confirmed TB disease among the population aged ≥15 years has fallen since the last survey (for repeat surveys). Examples of additional objectives that could be included are: 1. To identify the extent to which people with TB disease or those with symptoms suggestive of pulmonary TB disease have already sought care from healthcare providers and, if so, with which types of care provider; 2. To assess the level of underreporting of people diagnosed with TB disease; 3. To update estimates of TB incidence, using results from the prevalence survey combined with an in-depth assessment of surveillance and programmatic data and other survey data.	
SCREENING STRATEGY AND CASE DEFINITIONS (Chapter 3, Chapter 4)		
3. Screening strategy and diagnostic algorithm	Two options: Option 1: Chest X-ray (CXR) and an interview about symptoms for all of the survey-eligible population (those aged ≥15 years who meet residency criteria), followed by two Xpert® Ultra tests for all participants who screen positive, and then two tests using liquid culture (MGIT) for all those with at least one Xpert Ultra positive result. Option 2: CXR and an interview about symptoms for all of the survey eligible population (those aged ≥15 years who meet residency criteria), followed by two tests using liquid culture (MGIT) for all those who screen positive, in addition a rapid molecular test for all those who screen positive, to ensure provision of a rapid result. Of these two options, Option 1 is expected to be the most feasible and widely used.	
4. Case definitions	Definitions that will be used to categorize survey participants as a case of bacteriologically confirmed TB disease, not a case of bacteriologically confirmed TB disease or someone for whom survey TB case status cannot be determined based on laboratory test results should be clearly defined in the protocol.	

CXR, Chest X-ray; MGIT, mycobacteria growth indicator tube.

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey (continued)

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
SAMPLING DESIGN (Chapter 5)		
5. Exclusion criteria	1. Reasons why parts of the population will be excluded should be explicitly commented on in the protocol. 2. The excluded population should not be more than 5% of the total population. 3. Exclusion criteria must be clearly identified for the different stages of the survey. i. Sampling frame: need to have a good estimate of the population living in excluded areas. ii. Within selected areas: description of mobile and institutionalized populations. iii. Household and individual level: description of enrolment procedures for inclusion of seriously sick people, or others who are unable or unwilling to attend the field site or the X-ray examination. It is imperative to enumerate all eligible individuals, and classify them as a survey participant, absent or no consent provided.	
6. Participation rate in survey in sampled areas	At least 85% (or as defined in the protocol) of the eligible population must be sampled, and the expected percentage should be identified in the protocol.	
7. Missing laboratory diagnostic test results	Assume 10–15% of sputum-eligible individuals will having missing Xpert Ultra or culture test results.	
8. Sample size calculation	Use standard formula, justifying choices of values for the cluster size, a prior guess of the true population prevalence, the coefficient of between-cluster variation (k) and the relative precision (d).	
9. Relative precision	Should be 20% or a maximum of 25% for the national estimate of prevalence.	
10. Subnational estimation	If proposed, a justification for doing a survey with subnational estimation should be provided, along with a description of the assumptions used to calculate the sample size.	
11. Stratification in sampling	Stratification should be used to increase the national representativeness of the sampled population and the precision of the final results (e.g. urban/rural, north/central/south).	
12. Sampling strategy for cluster selection	Probability proportional to size (PPS) sampling should be used. In advance, it is necessary to identify reasons why clusters could be excluded after initial selection (e.g. inaccessibility as verified during assessment visit) and how they would be replaced.	
13. Number of clusters	At least 50.	
14. Cluster size	Preferably at least 400 people, with a maximum of 800 people.	
15. Age groups to be included in survey	People aged ≥15 years old only.	
16. Information on children *and* those who do not comply with residency definition	The protocol should include identification of the percentage of children and individuals in the population of each cluster who do not comply with residency criteria.	

PPS, Probability proportional to size.

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey (continued)

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
SCREENING: QUESTIONNAIRE ABOUT TB-RELATED SYMPTOMS AND COMORBIDITIES, AND CHEST RADIOGRAPHY (Chapter 6, Chapter 7, Chapter 10)		
17. Symptoms	Ensure screening questions about symptoms are accurately detailed in the protocol. They should align with the national screening strategy to facilitate comparisons with the screening strategy used in routine health services.	
18. Health care-seeking behaviour	Must be included in the interview for participants who report screening symptoms.	
19. HIV testing	Must be offered according to national policy and the HIV testing strategy used by the survey (e.g. HIV testing offered to all survey participants). The survey team must be able to provide clinically-relevant results to participants and facilitate referral for appropriate care.	
20. Comorbidities	Undernutrition, diabetes mellitus, alcohol use disorders and tobacco use can be asked about during the interview and tested for as required. The survey team must be able to provide clinically-relevant results to participants and facilitate referral for appropriate care.	
21. X-ray equipment and safety	X-ray equipment for chest radiography must comply with the regulations of the national radiation authority and approval from this authority must be obtained. A safety protocol must be developed that sets out how a restricted zone in every cluster will be provided, to ensure that radiation exposure is limited to those being X-rayed.	
22. Digital X-ray technologies	The choice of digital X-ray technology should be justified in terms of cost, opportunities to use the equipment and software after the survey is completed (e.g. routine programmatic use or active case finding), workload during the survey, field conditions and the availability of staff.	
DIAGNOSTIC TESTING (Chapter 8)		
23. Laboratory capacity	Laboratory capacity of sufficient quality (especially for culture) should be available, and laboratories used in the survey should have at least 6 months experience of using the methods to be used in the survey. Laboratory workload should be estimated in advance of the survey: when Option 1 is used, about 10–20% of survey participants will need to have Xpert Ultra (or equivalent) done in the field, and 5% of these will require tests using liquid culture at an approved quality laboratory.	
24. Number of samples to be collected	Option 1: At least two sputum samples should be collected from every screen positive participant for Xpert Ultra: spot and early morning, or two specimens one hour apart on the same day, according to operational considerations. For those who are Xpert Ultra positive, a further two samples should be collected (on the spot) for liquid culture (MGIT); ideally, two MGITs per sample. Option 2: At least two sputum samples should be collected from every screen positive participant for liquid culture (MGIT), and an additional sample for Xpert Ultra testing in the field for clinical case management purposes.	

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey (continued)

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
25. Sample transportation system	It is often necessary to establish a survey-specific system for transportation of sputum specimens, since most countries do not have a reliable and regular courier system with reverse cold chain (from periphery to central level). The sample transportation system should ideally be piloted from all distant and hard-to-reach areas.	
26. Time from collection of sputum to reaching laboratory for culture	Preferably within 3 days and not more than 5 days. It is essential to record the time and day of sputum collection and the start of laboratory processing for all samples.	
27. Methods for culture examinations	Concentrated culture using liquid media (i.e. MGIT). Solid culture may be relevant for those with at least one Xpert Ultra positive result, to facilitate comparisons with a previous survey that relied upon solid culture.	
ETHICS, CLINICAL MANAGEMENT AND BUDGETING (Chapter 9, Chapter 11, Chapter 15)		
28. Ethical issues	Must be addressed in the protocol, with ethical approval then obtained from national bodies and any international agencies providing technical assistance. Informed consent must be obtained from all participants prior to them taking part in the prevalence survey and answering any questions.	
29. Training in Good Clinical Practices and Good Data Management Practices	Core survey staff should undergo training in good clinical practice and good data management practice, and all staff should be familiar with these principles.	
30. Clinical management	For people diagnosed with TB or other serious non-TB health conditions during the survey, the survey team must be able to provide clinically-relevant results to participants and facilitate referral for appropriate care. How this will be done should be defined in the survey SOPs.	
31. Budget	Must be as detailed as possible and all sources of funding documented. Must allow for contingency situations. Must allow for variations in currency exchange rates.	
SURVEY MANAGEMENT, ORGANIZATION AND FIELD OPERATIONS (Chapter 12, Chapter 13)		
32. Pre-testing and piloting of survey	Pre-testing of survey tools followed by a pilot survey conducted in different environments (e.g. rural and urban areas). Time must be provided to amend any SOPs following the testing.	
33. Accuracy of sampling frame	Must be checked during the census.	
34. Survey organization	A complete organigram including the core survey team as well as groups providing oversight and advice (e.g. steering committee, technical advisory group). Job descriptions for members of the core survey team and terms of reference for committees or advisory groups.	

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey (continued)

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
35. Number of field teams	The number of field teams is often defined according to the capacity of culture laboratories. A smaller number of field teams increases survey duration and costs, but allows closer supervision and standardization.	
36. Involvement of local government and community	This is essential. Support is needed from the ministry of health (or equivalent), and this support should be communicated to all relevant authorities at the administrative levels that are involved in the implementation of the survey, such as states, provinces, districts and local communities. Three occasions should usually be used to facilitate community involvement at the cluster level: the initial assessment visit, the previsit and cluster operations.	
37. Follow-up procedures	To increase the participation rate, particularly in urban areas where participation is expected to be comparatively low, households should be re-visited and invitees re-contacted. Follow up of people from whom additional samples are required is also necessary. It is essential to allocate enough time to these activities, as well as human and financial resources.	
38. Other studies	Other studies (e.g. case-control studies) need to have well-defined objectives. Ensure adequate human and financial resources are available so that the main goal and objective(s) of the survey are not compromised.	
MONITORING AND QUALITY ASSURANCE (Chapter 14)		
39. Monitoring and quality assurance	Data monitoring and the completion of monitoring checklists should take place as quickly as possible after data collection and processing in the field. This is essential for key indicators (e.g. the participation rate, the completion rate for data collection forms, the percentage of individuals eligible for sputum collection, X-ray quality, the average time from sputum collection to processing, the culture contamination rate, the percentage of samples that were missing).	
40. Indicators and benchmarks	Indicators and benchmarks should be clearly defined in the survey SOPs and team leaders and supervisors should be trained to take action whenever benchmarks are not being met. Examples include: i. Data clerks should check the individual form to confirm all necessary areas are completed. If not, the form should be immediately sent to the appropriate section to be completed; ii. The survey registry should be reviewed every day by the team leader to monitor the participation of people eligible to participate in the survey. If this is below 85–90%, follow-up actions are needed.	
41. Supervision	Strong lines of supervision are needed throughout the study to ensure proper implementation of survey activities. Supervision activities must be well planned and budgeted. A designated M&E (quality assurance) officer can lead the monitoring activities and devise a monitoring plan.	

Annex 2.1 Checklist that can be used to review a protocol for a national TB prevalence survey (continued)

TOPIC/ISSUE	RECOMMENDATIONS	IS THE PROTOCOL CONSISTENT?
DATA MANAGEMENT, ANALYSIS AND REPORTING (Chapter 16, Chapter 17, Chapter 18, Chapter 19)		
42. Staff for data management and analysis	A data manager and statistician should be involved in the survey from the beginning, and a thorough data management and analysis plan described in the protocol.	
43. IT capacity	Each field team should have the necessary equipment and a dedicated field data manager with IT skills. It is essential to allocate adequate human and financial resources.	
44. Data entry	Data entry should be a continuous process with consistent validation via digital and manual cross-checks.	
45. Confidentiality	All survey staff handling data (both on paper and digitally) should respect the confidentiality of the information collected.	
46. Analysis strategy	1. In analysis, missing value imputation should be used to address bias introduced by non-participation; 2. Sensitivity analysis should be done to assess the possible impact of non-participation on the estimate of TB prevalence; 3. A cluster-level analysis (simple, and valid) should be done first, followed by an individual-level analysis; 4. Individual-level analysis should use robust standard errors to allow for clustering in the study design; 5. Individual-level analysis should be conducted with and without multiple imputation of missing data, and both results presented and compared; 6. How results will be used to produce estimates for all forms of TB, and all ages, should be explained.	
47. Feedback of results to local authorities	Survey results should be reported to local authorities (and communities) as soon as they become available.	
48. Dissemination	All survey results should be publicly disseminated at an open forum and via an official report.	
49. Writing of the report and publication	Ensure a dedicated team is available to write a report and publication for a peer-reviewed journal in a timely fashion. It is essential to allocate adequate human and financial resources for this task.	
50. Data sharing	After publication of the report and publication, data should be deposited in a public repository in accordance with Open Data practices, to ensure reproducibility of results, transparency and credibility, and to contribute to the global knowledge base and preservation of the scientific record.	

CHAPTER 3

Screening and diagnostic algorithms

In a national tuberculosis (TB) prevalence survey, systematic screening is necessary to rapidly identify people with possible signs or symptoms of TB disease. For people who meet the screening criteria ("screen-positive" individuals), diagnostic testing for TB disease is required.

This chapter starts by describing the recommended approach to screening, using a combination of chest X-ray (CXR) and an interview about symptoms. It then provides the rationale for updated recommendations (compared with those in the previous edition of this guidance, the "*lime book*") for the diagnostic algorithms to use in national TB prevalence surveys *(1)*. The third section defines and explains the two diagnostic algorithms now recommended for use in surveys, referred to as "Option 1" and "Option 2". The final section comments on how results from surveys that use Option 1 or Option 2 can be compared with those from previous surveys.[1]

3.1 Screening for TB disease

3.1.1 Definition and rationale

Screening is the examination of people to assess whether they are at high risk of having a certain condition or disease. In a national TB prevalence survey, systematic screening is necessary to rapidly identify people with possible signs or symptoms of TB disease.

National TB prevalence surveys include large population numbers: sample sizes are typically in the range of 30 000–70 000 (see **Chapter 5**), but some recent surveys (e.g. the 2019–2021 survey in India) included hundreds of thousands of people. Screening is necessary to identify people at high risk of TB disease (referred to as "screen-positive" individuals), so that sputum samples for diagnostic testing only need to be collected from a relatively small fraction of the surveyed population. It is necessary to restrict the number of people for whom diagnostic testing for TB disease is done because of logistics, cost and workload; it is particularly important to ensure that laboratories are not overloaded.

3.1.2 Screening methods

Two screening tools are recommended in a national TB prevalence survey: an interview about symptoms (using a standardized and structured questionnaire, see **Chapter 6**) and a CXR. A person is considered screen positive, and thus is eligible for diagnostic testing for TB disease, in any of the following situations:

- the questionnaire indicates that the person has symptoms suggestive of TB; or
- the CXR shows any lung abnormalities; or
- the CXR is above a predefined threshold if computer-aided detection (CAD) is used (see **Chapter 7**).

Symptom screening is especially useful if a CXR cannot be taken (e.g. if a person is exempt from or refuses a CXR, or the machine has broken down),[2] or when a CXR abnormality is missed by the person responsible for reading the CXRs.

Interview about symptoms, using a standardized and structured questionnaire

There is a "core" set of symptoms that should be used for screening in all surveys. These are:

- cough (either a cough of any duration,[3] or a cough that has lasted for at least 2 weeks);
- productive cough with sputum production;
- haemoptysis over the past month;
- fever over the past month;
- chest pain over the past month; or
- weight loss over the past month.

If a person answers "yes" to any one of these symptoms, they are considered to be screen positive.[4]

This core list of symptoms corresponds to the symptoms that were typically used for screening in surveys implemented between 2007 and 2021 (for details, see **Annex 3.1**). In most surveys implemented between those years, the symptoms used for screening were based on those used by the national TB programme (NTP) in routine clinical care.[5]

In a few surveys, people with a previous history of TB

[1] Comparisons with previous surveys are discussed in more detail in **Chapter 18**.

[2] Pregnant women are especially vulnerable to ionizing radiation from radiography. However, CXR screening has been assessed as not posing a significant risk, provided that good practices are observed, because the primary beam is targeted away from the pelvis.

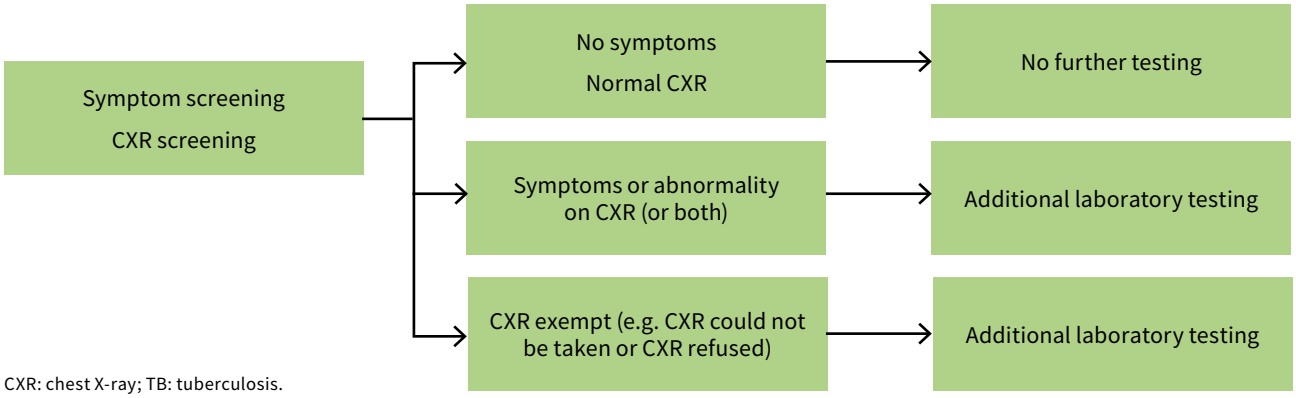
[3] A cough of any duration is particularly useful in settings with a high prevalence of HIV infection in the general population.

[4] The use of additional symptoms risks defining too many people in the surveyed population as being screen positive, which could overload the survey team and in turn the laboratories. Unnecessary widening of symptom screening criteria should be avoided.

[5] This is also helpful for later assessment of the effectiveness or limitations of NTP screening criteria and routine case detection practices.

Fig. 3.1

Screening strategy recommended for use in national TB prevalence surveys



CXR: chest X-ray; TB: tuberculosis.

(e.g. within the past 5 years) have been defined as eligible for sputum examination, irrespective of symptoms or CXR results. The collection of data about whether someone has a current and/or previous history of TB (and, if so, the dates of the last episode) is necessary for survey case definitions and data analysis (**Chapter 4** and **17**). Collection of these data is discussed further in **Chapter 6**.

In surveys implemented from 2007 to 2016, the proportion of survey participants who screened positive varied from 3% to 21% in African countries and from 2% to 13% in Asian countries *(2–4)*.

CXR

If the only test used is symptom screening, then the prevalence of TB disease will be seriously underestimated in a national TB prevalence survey. In surveys implemented since 1990, a large proportion of people with bacteriologically confirmed TB were only screen positive based on CXR screening: on average, this proportion was 44% in African countries *(4)* and 62% in Asian countries *(3)*. Although a CXR abnormality is not sufficiently specific to make a definite diagnosis of TB, it is highly sensitive as a screening method.

In a prevalence survey, all adults who are included in the survey and consent to the process should have a CXR. Recent surveys have used digital CXR technology (**Annex 3.1**) and some have used CAD software (**Chapter 7**).

An individual is screen positive, and therefore considered eligible for sputum examination and diagnostic testing, if the CXR shows an abnormality suspected of being TB or any abnormality in the lung,[1] or if the CAD score is above a predefined threshold.[2] Based on evidence from surveys implemented from 2007 to 2016 *(2)*, it is estimated that 5–25% of survey participants will meet this definition.[3]

3.1.3 Screening strategy

The screening strategy recommended in a national TB prevalence survey is illustrated in **Fig. 3.1**.

People who are screen positive based on results from CXR screening and an interview about symptoms are defined as "eligible for sputum examination". People without either CXR abnormalities or reported symptoms suggestive of TB are not eligible for sputum examination and do not have to submit sputum samples. The number of potential TB cases among people without symptoms and with a normal CXR is assumed to be extremely low.[4]

The survey protocol should specify what to do for individuals for whom a CXR is not done (e.g. pregnant women who opt out, those who are unable to visit the study site, or those who could not have a CXR due to breakdown of equipment). It is recommended that sputum samples for diagnostic testing are collected from all individuals exempted from CXR.

3.2 Algorithms for diagnosis of TB disease: rationale for updated recommendations

People who meet the screening criteria require diagnostic testing for TB disease. The main diagnostic testing strategy recommended for all screen-positive individuals in the lime book *(1)* was the collection of two sputum samples for diagnostic testing using smear microscopy and culture (either solid or liquid).

[1] People who are immunocompromised, such as those living with HIV or diabetes, may have atypical signs of TB in a CXR. This is the reason for using "any CXR abnormality in the lung" to define an individual as being screen positive.

[2] Depending on the use case of CAD.

[3] When CXRs are read by experienced readers, the figure might fall to about 1–6%; however, in surveys, readers are advised to "over-read", to increase the sensitivity of CXR screening.

[4] A Cochrane review, published in 2022, to assess systematic screening for TB among adults without HIV (or unknown status), based on symptoms and CXR, included data from many prevalence surveys *(5)*. The sensitivity of CXR was high (94.7% for any CXR abnormality), irrespective of symptom screening. With the combination of CXR and symptom screening, sensitivity increased to 99.2%.

From 2015 onwards, there was a considerable increase in the use of Xpert® assays[1] in national TB prevalence surveys. Initially, these assays were used for additional testing of samples that were positive on smear microscopy; subsequently (from 2017), they were used for all screen-positive individuals (or 50% of them), alongside culture testing. This use of Xpert assays was in line with their growing use in routine clinical care, but it also led to increasing variation in the diagnostic testing strategies used in national surveys (making survey results harder to compare), and difficulties in interpreting discordant Xpert and culture results. From comprehensive documentation about the methods, results and lessons learned from national TB prevalence surveys implemented in 2007–2016, it was also clear that the main challenge identified by survey teams was culture testing for all screen-positive individuals *(2, 6)*.

In 2018, the World Health Organization (WHO) initiated discussions on how to address these problems. Meetings and workshops were convened, with participants including: lead investigators from the national TB prevalence surveys that were underway or nearing completion at that time; people from international agencies and WHO consultants who were providing technical assistance to these surveys; global experts from the TREATS (TB Reduction through Expanded Antiretroviral Treatment and Screening) study, which included assessment of diagnostic algorithms to be used in the context of a subnational TB prevalence survey; staff from the Foundation for Innovative New Diagnostics (FIND) who had led the analysis of data used to evaluate the Xpert Ultra assay; and staff from the WHO Global Programme for Tuberculosis & Lung Health (WHO/GTB).

Alongside these meetings and discussions, a background document on the diagnostic algorithms to recommend for use in future national TB prevalence surveys was prepared. That document went through four major cycles of drafting and review before being finalized and published by WHO in May 2023 *(6)*. The final version was based on the outcomes of the first meeting of the author group of this third edition of WHO guidance on national TB prevalence surveys, held in September 2022.

The full range of evidence that provides the rationale for the two diagnostic algorithms recommended in this chapter is available in the May 2023 WHO publication *(6)*. The key points, and associated conclusions, are summarized here.

The key points were as follows:

- The recognized microbiological reference standard test for diagnosis of pulmonary TB disease is *liquid culture*. Hence, liquid culture is also the reference standard test in the context of a national TB prevalence survey, in which the objectives are to obtain a reliable direct measurement of the number of people with pulmonary TB disease in the community and, if the survey is a repeat survey, to reliably assess trends in this number.
- It is challenging to ensure high-quality culture testing in the context of a national TB prevalence survey, and culture testing was the main challenge (identified by 16/25 countries) in national surveys implemented between 2007 and 2016.
- Most national TB prevalence surveys implemented in 2007–2019 relied on *solid*-culture methods. Only a few countries managed to implement a survey that included liquid-culture testing of two samples from all screen-positive individuals.
- There are major advantages of using Xpert assays in national TB prevalence surveys; in particular, these assays are much easier to use in a reproducible way at large scale in countries with limited diagnostic culture capacity, compared with culture.
- The Xpert Ultra assay has a sensitivity of about 80–90% compared with liquid culture, but it is *more sensitive* than solid culture *(6)*. Sensitivity can be improved if two Xpert Ultra tests are done.
- In the context of a national TB prevalence survey, the main limitation of the Xpert Ultra assay is that it will result in large numbers of people with a false positive test result (i.e. a person has a positive Xpert Ultra result but does not have TB disease at the time of the test).[2] It is possible that more than half of positive Xpert Ultra results in a prevalence survey will be false positives.[3] This means that confirmatory testing with liquid culture is required.

The key conclusions were as follows:

- The best diagnostic algorithm (in terms of sensitivity) is to test two samples from all screen-positive individuals with liquid culture, but this is only the case if a high quality of liquid-culture testing can be achieved.
- If high-quality testing of **all** individuals who screen positive using liquid culture is not feasible (or is unlikely to be feasible), then initial testing of all individuals who screen positive using Xpert Ultra is a better approach than testing with solid culture.
- The sensitivity of a diagnostic algorithm in which all screen-positive individuals are initially tested using

[1] These are based on polymerase chain reaction (PCR).

[2] This differs from, and should not be confused with, a person with TB disease who has a positive Xpert Ultra result and a negative culture result. In this case, the problem is a "false negative" culture result.

[3] This is because the specificity of Xpert Ultra, compared with the reference standard of liquid culture, is about 95%, whereas only about 1–5% of individuals who screen positive for TB in a survey are expected to have bacteriologically confirmed pulmonary TB disease. In other words, for every 100 people who screen positive in a survey, about five would have a false positive Xpert Ultra result, and between one and five would have a true positive Xpert Ultra result.

Xpert Ultra will be closer to that of liquid-culture testing if two Xpert tests are done.

- If a strategy of initial testing of all screen-positive individuals with Xpert Ultra is used, then confirmatory testing with liquid culture is necessary for any individuals with an Xpert-positive test result, to avoid the problem of false positive results.

A further important consideration for any survey that includes testing of all screen-positive individuals using liquid culture is that results from such testing take time to obtain. From an ethical perspective, it is not acceptable for people tested for TB to wait weeks for a result, given that WHO-recommended rapid diagnostic tests (mWRDs) are available. Therefore, in a survey in which samples for liquid-culture testing are taken from all screen-positive individuals, a rapid test should also be done for all individuals who screen positive, to ensure that they receive a timely result.

Based on these findings and conclusions, two major options for diagnostic algorithms to use in future national TB prevalence surveys were defined; they are referred to as "Option 1" and "Option 2", and are explained in the next section.

3.3 Algorithms for diagnosis of TB disease: two recommended options

Based on the accumulation of experience and evidence related to diagnostic algorithms to use in national TB prevalence surveys (summarized above in **Section 3.2**), two options are recommended for surveys implemented from 2023 onwards, defined here as Option 1 and Option 2.

Option 1 is an Xpert Ultra-based survey: Xpert Ultra testing followed by confirmatory testing using liquid mycobacterial growth indicator tube (MGIT™)[1] culture. This is presented first, because it is considered the most widely applicable option and thus the most likely to be used. Option 2 is a survey based on liquid culture, which also includes one rapid Xpert Ultra test for all screen-positive individuals.

Although both options refer to Xpert Ultra, any other mWRDs with equivalent or better performance in terms of sensitivity could be used as an alternative.[2]

Given that an important consideration and concern is how to compare results from future surveys with those of previous surveys that relied primarily on testing using solid culture or the Xpert MTB/RIF assay, suggestions are provided for both options in **Section 3.4**; comparisons with previous surveys are discussed further in **Chapter 18**.

3.3.1 Option 1: Xpert Ultra testing followed by confirmatory testing using liquid (MGIT) culture

Option 1 can be summarized as follows: two Xpert Ultra tests on two separate samples from all screen-positive individuals, followed by confirmatory culture testing using liquid culture (MGIT) for all individuals with at least one Xpert-positive result.

In this option, only a small percentage (not more than 10% and probably less than 10%) of screen-positive individuals are expected to require confirmatory testing using MGIT culture.[3]

Option 1 is illustrated in **Fig. 3.2**. It is recommended for all countries that do not have the capacity to ensure high-quality testing of all screen-positive individuals using liquid culture.[4]

Option 1 massively reduces the need for culture testing (compared with Option 2), to typically less than 1000 tests in total.[5] Also, it simultaneously addresses the problem of the suboptimal specificity of Xpert Ultra (and associated large number of false positive results in the context of a national TB prevalence survey) by using liquid culture for confirmatory testing. Those with an Xpert Ultra-positive *and* a MGIT culture-positive result would be classified as having pulmonary TB disease.[6]

At the same time, **a high quality of testing using liquid culture is essential to avoid false negative culture results**. False negative culture results would result in misclassifying some individuals who are Xpert-positive but MGIT culture-negative as having a false positive Xpert result when in fact the Xpert test result was correct. **The small number of culture tests required in Option 1 should allow the laboratory (or laboratories) used in the survey to ensure liquid-culture testing of high quality**.[7] During the pilot phase of a survey and the early phases of the main survey, culture and Xpert Ultra results should be compared, and laboratory performance monitored, to assess the performance of culture testing. Prompt action should be taken to correct any identified problems.

There are **logistical issues to consider in terms of the organization of Xpert Ultra testing**. This testing needs to be organized such that results are available

[1] MGIT is a liquid media for the cultivation of mycobacteria. MGIT is the current reference standard for the diagnosis of *Mycobacterium tuberculosis*.

[2] At the time of writing, such tests do not exist, but they may become available in future.

[3] Based on surveys implemented from 2007 to 2016, about 1–5% of screen-positive individuals are expected to have TB disease; almost all of these individuals are expected to have at least one positive Xpert Ultra result. Given that the Xpert Ultra assay has a specificity of about 95%, it is also expected that about 5% of people who do not have TB disease will have a positive Xpert Ultra result.

[4] Culture can be undertaken in a qualified culture laboratory (e.g. regional or national TB reference laboratory).

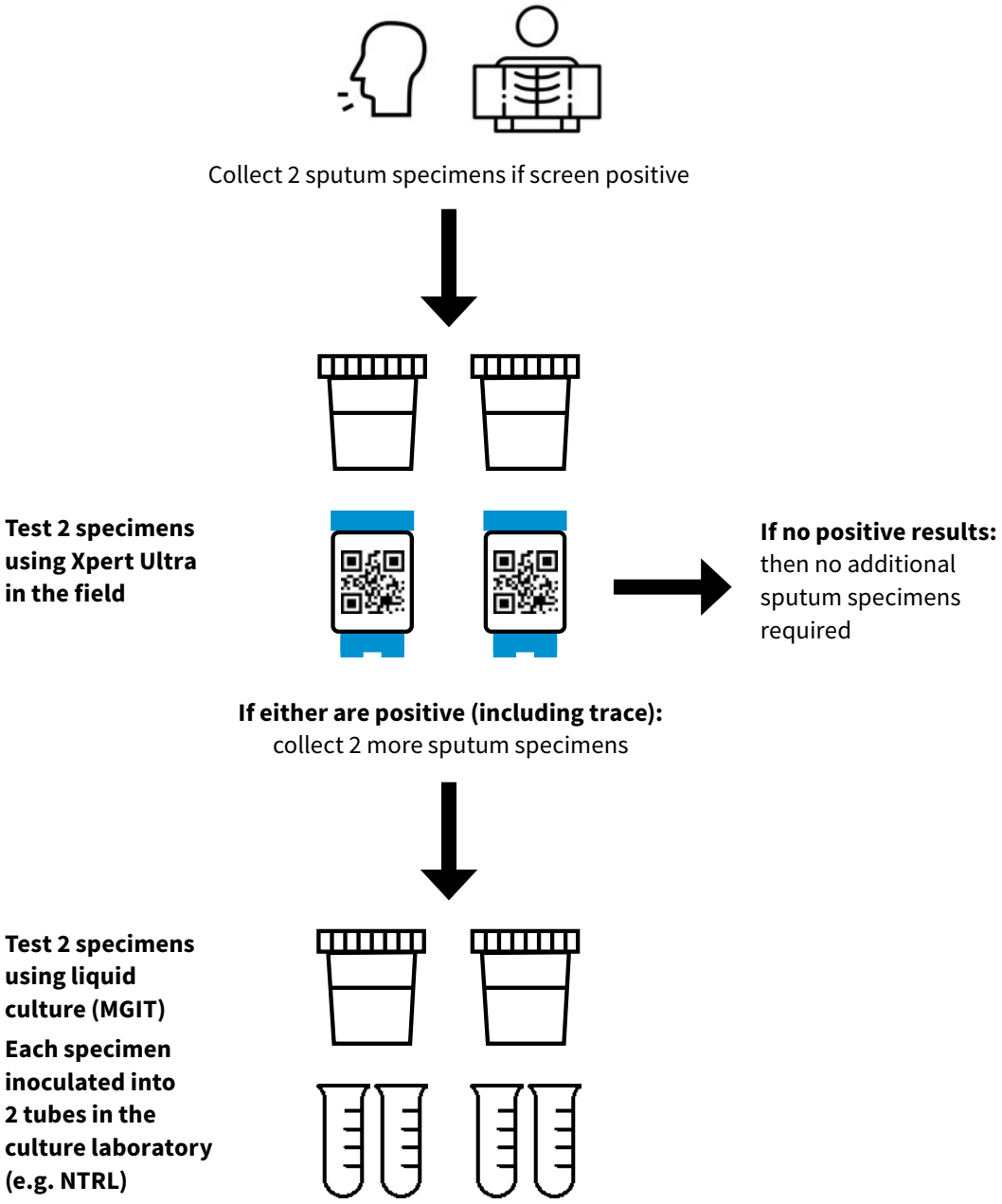
[5] **Chapter 8** provides worked examples to illustrate laboratory capacity requirements for the two diagnostic algorithms (**Table 8.1** and **Table 8.2**).

[6] Detailed recommendations on case definitions for both Option 1 and Option 2 are provided in **Chapter 4**.

[7] It may be possible to conduct all culture testing in a single laboratory, avoiding variability among laboratories.

Fig. 3.2

Illustration of the diagnostic algorithm "Option 1"[a]



MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for Xpert Ultra testing and, if either specimen is positive, two additional sputum samples are collected for confirmatory testing using liquid culture (MGIT).

within a few hours of taking the sample, so that subsequent specimens required for culture testing can be collected in a timely manner for those with an Xpert Ultra-positive result. To ensure prompt results, Xpert testing will need to be done either onsite or at a nearby health facility. The survey team may need to bring Xpert machines and cartridges with them to each field site, ensuring that machines are stored appropriately.

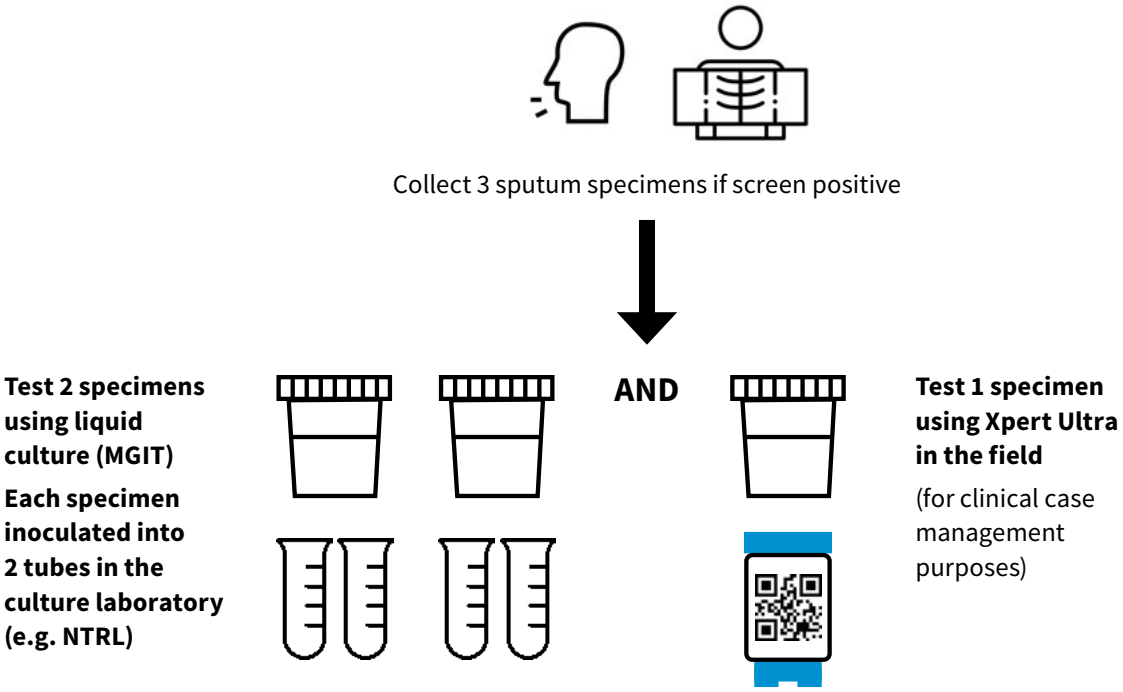
Laboratory quality assurance and the organization of Xpert Ultra testing are discussed in more detail in **Chapter 8**.

Option 1 is likely to cost much less than Option 2. The unit cost of an Xpert Ultra test (in Option 1) is much lower than the cost of a test using liquid culture (in Option 2); also, Option 2 requires two culture tests for all screen-positive individuals, plus a rapid test for clinical management.

Between 2018 and 2022, national surveys in Eswatini (2018–2019) and Nepal (2018–2019), and subnational surveys in South Africa and Zambia (implemented as part of the TREATS study), used a diagnostic algorithm

Fig. 3.3

Illustration of the diagnostic algorithm "Option 2"[a]



MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for liquid culture (MGIT) and one for Xpert Ultra testing. The Xpert Ultra test is used to ensure a rapid result is available to be used for clinical management purposes only (not the estimation of TB prevalence). The priority is to take two specimens for MGIT testing. Xpert Ultra testing can be done on the sediment of an MGIT sample; however, if this is not possible, a third sample should be collected for Xpert Ultra testing, to be done in the field. Further details are provided in **Chapter 8**. Clinical management of those with a positive Xpert Ultra result is discussed in **Chapter 9**.

similar to Option 1.[1] In late 2022, Timor-Leste started its first national survey and in mid-2023, Cambodia started its third national survey, both using Option 1.

The main disadvantage of Option 1 is that it will miss some of the people with TB disease (10–20%) who could have been detected using Option 2 (provided that Option 2 is implemented with high quality).

In some countries, implementation of Option 1 may require the establishment of liquid-culture testing capacity.

3.3.2 Option 2: a survey based on liquid culture

Option 2 can be summarized as liquid-culture testing (MGIT) of two separate sputum samples from all screen-positive individuals, plus an Xpert Ultra test to ensure that anyone who screens positive receives a rapid result (for clinical management).

Option 2 is illustrated in **Fig. 3.3**. This option should be considered by countries that have the capacity to ensure high-quality testing of all screen-positive individuals using liquid culture.[2]

If done well, liquid-culture testing using MGIT will detect the highest proportion of true positive cases of TB disease in the community, and will do so reliably.

The main disadvantage of Option 2 is that, as documented in many national TB prevalence surveys implemented since 2007, it is challenging to ensure high-quality culture testing in the context of a survey. From 2007 to 2019, only four countries did liquid-culture testing on two samples for all screen-positive individuals: the Gambia, Ghana, Zambia and Zimbabwe.[3] Only a small number of countries with a high burden of TB have a transport and laboratory network that is readily able to ensure that samples reach laboratories on time, or a laboratory network that can cope with the large additional volume of culture tests generated by a survey without compromising on quality. This is especially the case in countries where there are long distances to cov-

[1] In Eswatini, all screen-positive individuals were tested using Xpert MTB/RIF, followed by liquid culture (MGIT) testing if the Xpert result was positive. In Nepal, all screen-positive individuals were tested using Xpert MTB/RIF, but only every second screen-positive individual was tested, using one solid (Löwenstein–Jensen [LJ]) culture medium.

[2] Culture can be undertaken in a qualified culture laboratory (e.g. regional or national TB reference laboratory).

[3] An additional four countries did liquid-culture testing of one sample for all screen-positive individuals: India, Lesotho, Namibia and South Africa. In Namibia, there were major challenges with testing using liquid culture and the results could not be used.

er between survey sites and laboratories with culture capacity, and where the number of laboratories with culture testing capacity is small.

Given that a culture test is more expensive than an Xpert Ultra test, Option 2 has a much higher cost than Option 1 because 2 cultures are required from every person who screens positive. Other key factors beyond laboratory testing capacity that need to be considered when choosing between Option 1 and Option 2 are shown in **Table 8.3**.

3.4 Comparisons with previous surveys

Both Option 1 and Option 2 differ from the diagnostic algorithms used in most surveys implemented up to 2022. As explained above, two countries implemented a national survey using a diagnostic algorithm similar to (but not the same as) Option 1; and four countries implemented a survey that used liquid culture to test two samples from all screen-positive individuals (as required in Option 2). Of these four countries, one (the Gambia) no longer meets the epidemiological criteria for measuring TB disease burden using a national TB prevalence survey because the burden is too low *(6)*.[1]

Most of the countries that implemented a first or repeat survey between 2007 and 2021 continue to meet the epidemiological criteria for implementing another survey. As countries plan repeat surveys, careful consideration is needed about how to compare results from new surveys that use Option 1 or Option 2 with results from previous surveys, so that trends in TB disease burden can be assessed. A brief commentary is provided in this section; comparisons with previous surveys are discussed in more detail in **Chapter 18**.

3.4.1 Option 1

Most of the countries that implemented surveys from 2007 to 2021 used solid culture (24/33 surveys); of these 24 surveys, 14 used Löwenstein–Jensen (LJ) media and 10 used Ogawa media.[2] When any of these countries implement a future survey using Option 1, there are two main approaches that they could consider for the purposes of comparisons with previous surveys.

The first approach to consider is collecting additional samples from individuals with Xpert Ultra-positive test results, for testing using the solid-culture method of the previous survey. This would allow a direct comparison with results from the previous survey, on the basis that Xpert Ultra testing is more sensitive than solid culture and would therefore pick up any individuals who would (with the exact same test sample) have a positive solid-culture result. In other words, if all other things are equal, those with a positive solid-culture test result should be a subset of those with a positive Xpert Ultra test result. Estimates of prevalence based on individuals with an Xpert-positive result followed by a solid-culture-positive result could then be compared with those from the previous survey.

There are potential pitfalls with this approach; for example:

- laboratories need to be able to conduct solid-culture testing to a high standard – there is some evidence that laboratories that do not routinely use solid-culture methods may not do such testing well *(6)*;
- collection of additional specimens requires additional staff and time, which might risk compromising the collection and quality of samples for testing using liquid culture, and therefore the primary results of the survey;
- the quality of the testing using solid culture might differ between the two surveys (e.g. because the previous survey would have tested a much larger number of samples); and
- adding additional culture testing will increase survey costs.

If the previous survey conducted testing using smear microscopy, a lower cost alternative to additional culture testing would be the collection of additional samples for those with Xpert Ultra-positive results, to be tested with smear microscopy. This would allow the prevalence of smear-positive pulmonary TB in the most recent survey to be compared with that from the previous survey.

The second approach to consider is to make comparisons that account for differences between the sensitivity of Xpert Ultra and the solid-culture method of the previous survey, using evidence from the FIND studies *(6)*.

3.4.2 Option 2

It will be challenging to make fair comparisons with previous surveys if liquid culture was not used in the previous survey. However, smear microscopy could be used to make a direct comparison if the previous survey also used smear microscopy.

For comparisons with a previous survey that used an Xpert assay, samples of individuals with positive liquid-culture results could be tested using Xpert Ultra (the Xpert MTB/RIF assay is no longer produced), given that, if all other things are equal, individuals with a positive Xpert Ultra result should be a subset of those with a positive liquid-culture result.

Comparisons with a previous survey based on solid culture could be made using existing evidence about the relative sensitivity of solid and liquid culture *(6)*.

[1] **Chapter 1** defines the countries that met epidemiological criteria for implementing a survey from the end of 2023.

[2] LJ and Ogawa are two types of solid-culture media that can be used to cultivate mycobacteria.

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Annex 3.1 Screening and diagnostic tools used in national TB prevalence surveys, 2007–2021

This annex summarizes screening and diagnostic tools used in national tuberculosis (TB) prevalence surveys between 2007 and 2021 *(1–3)*.

COUNTRY	SYMPTOM SCREENING	CXR SCREENING	OTHER SCREENING CRITERIA	PROPORTION OF PARTICIPANTS SCREEN POSITIVE (%)		
				SYMPTOMS ONLY	CXR ONLY	BOTH
Bangladesh 2015–2016	Scoring system: eligible if the total score was ≥3[a]	Direct digital	CXR exempted[a]	4.3	13	3.1
Cambodia 2010–2011	Cough for ≥2 weeks or haemoptysis (or both)	Conventional	CXR exempted	3.2	7.2	1.9
China 2010	Cough for ≥2 weeks or haemoptysis of any duration (or both)	Conventional	Participants with known active pulmonary TB with normal CXR, and those who were CXR exempted	1.8	0.87	0.32
Democratic People's Republic of Korea 2015–2016	Cough for ≥15 days or haemoptysis (or both)	Conventional	None	3.2	3.1	1.7
Eswatini 2018–2019	Cough of any duration, or fever for ≥2 weeks, or unexplained weight loss for ≥2 weeks, or night sweats for ≥2 weeks	Direct digital (with CAD)	CXR exempted	6.2	14	2.4
Ethiopia 2010–2011	Cough for ≥2 weeks	Conventional	Participants who were exempt from or declined CXR but met one of the following criteria: weight loss ≥3 kg in the past month, night sweats for ≥2 weeks, fever for ≥2 weeks or contact with a TB patient in the past year	4.8	6.5	1.7
Gambia 2011–2013	Cough for ≥2 weeks, or cough for <2 weeks with two or more other symptoms, or no cough with three or more other symptoms: chest pain, night sweats, shortness of breath, loss of appetite, weight loss, fever or haemoptysis	Direct digital	CXR exempted	5.7	5.5	2.4
Ghana 2013	Cough for ≥2 weeks	Direct digital	CXR exempted	1.9	7.1	1.2
India 2019–2021	Any one of the following: cough for ≥2 weeks, fever for ≥2 weeks, significant weight loss, presence of blood in sputum any time during the past 6 months, chest pain in the past 1 month, or history of anti-TB treatment (previous or current) at the time of interview	Direct digital	None	3.3	7.0	2.8
Indonesia 2013–2014	Cough for ≥2 weeks or haemoptysis (or both)	Direct digital	CXR exempted but had at least one of the following symptoms: cough, haemoptysis, fever, chest pain, night sweats, loss of appetite or shortness of breath	6.0	10	6.6
Kenya 2015–2016	Cough for ≥2 weeks	Direct digital	CXR exempted	4.6	8.2	2.0
Lao People's Democratic Republic 2010–2012	Cough for ≥2 weeks within the past month or haemoptysis within the past month (or both)	Conventional	None	4.9	7.9	3.3

Annex 3.1 Screening and diagnostic tools used in national TB prevalence surveys, 2007–2021 (continued)

COUNTRY	SYMPTOM SCREENING	CXR SCREENING	OTHER SCREENING CRITERIA	PROPORTION OF PARTICIPANTS SCREEN POSITIVE (%)		
				SYMPTOMS ONLY	CXR ONLY	BOTH
Lesotho 2019	Any one of the following: cough of any duration, fever, unexplained weight loss in the past month or night sweats	Direct digital (with CAD)	CXR exempted	6.7	19	7.5
Malawi 2013–2014	Any of the following symptoms for ≥1 week: cough, sputum production, haemoptysis, chest pain, weight loss, night sweats, fatigue, fever or shortness of breath	Conventional	None	7.4	2.3	1.2
Mongolia 2014–2015	Cough for ≥2 weeks	Direct digital	CXR exempted	3.4	14	1.6
Mozambique 2017–2020	Cough for >2 weeks, or blood in sputum, or any cough with one or more of the following symptoms: chest pain (≥2 weeks), unexplained fever (≥2 weeks), night sweats (≥2 weeks), unexplained body weight loss within the past 12 months, or low MUAC (<22 cm for women or adolescents and <23 cm for men); or two or more of the five listed symptoms	Direct digital (with CAD)	CXR exempted	10	16	2.3
Myanmar 2009–2010	Cough for ≥3 weeks or haemoptysis (or both)	Conventional	CXR exempted	0.84	18	2.4
Myanmar 2018	Cough for ≥14 days	Direct digital	CXR exempted	1.2	13	0.86
Namibia 2019	Any one of the following: cough, drenching night sweats, fever, unintentional weight loss over ≥2 weeks	Direct digital (with CAD)	CXR exempted	14	11	5.8
Nepal 2018–2019	Cough for ≥2 weeks, or cough for <2 weeks with at least one additional TB symptom (body weight loss, fever, chest pain, loss of appetite, haemoptysis, breathing difficulty, night sweating or tiredness)	Direct digital	CXR exempted	2.3	20	3.0
Nigeria 2012	Cough for ≥2 weeks	Computed radiography	None	3.9	5.0	1.7
Pakistan 2010–2011	Cough for ≥2 weeks, or cough of any duration if there was no available CXR result	Direct digital	On TB treatment at the time of the survey	2.5	4.8	2.7
Philippines 2007	N/A[b]	Conventional	None	N/A	22	N/A
Philippines 2016	Cough for ≥2 weeks or haemoptysis (or both)	Direct digital	CXR exempted	2.9	23	3.1
Rwanda 2012	Cough of any duration	Direct digital	CXR exempted	4.9	4.9	1.3
South Africa 2017–2019	Any one of the following: cough (persistent of any duration), drenching night sweats, unexplained weight loss and unexplained fever for ≥2 weeks	Direct digital	CXR exempted	9.8	10	4.9
Sudan 2013–2014	Cough for ≥2 weeks	Direct digital	CXR exempted or on TB treatment at the time of the survey	1.0	12	2.2
Thailand 2012	Scoring system: eligible if the total score was ≥3[c]	Direct digital	CXR exempted[c]	2.8	6.0	0.84
Uganda 2014–2015	Cough for ≥2 weeks	Conventional	CXR exempted	5.3	5.6	1.3

Annex 3.1 Screening and diagnostic tools used in national TB prevalence surveys, 2007–2021 (continued)

COUNTRY	SYMPTOM SCREENING	CXR SCREENING	OTHER SCREENING CRITERIA	PROPORTION OF PARTICIPANTS SCREEN POSITIVE (%)		
				SYMPTOMS ONLY	CXR ONLY	BOTH
United Republic of Tanzania 2011–2012	Any of the following symptoms: cough for ≥2 weeks, haemoptysis, fever for ≥2 weeks, weight loss or excessive night sweats	Computed radiography	None	6.9	4.0	1.6
Viet Nam 2006–2007	Productive cough for ≥2 weeks	Digital scan onsite and mass miniature radiography (70 × 70 mm)	CXR exempted, on TB treatment at the time of the survey or history of TB in preceding 2 years	3.7	3.2	0.55
Viet Nam 2017–2018	Cough for ≥2 weeks (or cough of any duration for pregnant women)	Direct digital	Self-reported TB treatment in the preceding 2 years	3.6	3.0	1.1
Zambia 2013–2014	Any one of the following symptoms for ≥2 weeks: cough, fever or chest pain	Direct digital	None	6.4	4.9	3.3
Zimbabwe 2014	Any one of the following symptoms: cough of any duration, haemoptysis in the past 12 months or drenching night sweats	Direct digital	CXR exempted	3.6	8.3	1.9

CAD: computer-aided detection; CXR: chest X-ray; MUAC: mid-upper arm circumference; N/A: not applicable; TB: tuberculosis.

[a] In Bangladesh, a participant was eligible if their total score was 3 points or more: cough ≥2 weeks (3 points), cough <2 weeks (1 point), haemoptysis in the past month (3 points), weight loss in the past month (1 point), fever ≥1 week in the past month (1 point) and night sweats in the past month (1 point). If the CXR was exempted, then a clinical score of 1 or 2 classified a participant as symptom-screen positive.

[b] In the Philippines (2007), symptom screening was not used as a selection criterion for sputum submission, but an interview about TB symptoms and TB history was undertaken for participants aged 20 years or older.

[c] In Thailand, a participant was eligible if their total score was 3 or more (or ≥1 with CXR exempted): cough for ≥2 weeks (3 points), haemoptysis over the past month (3 points), cough <2 weeks (2 points), weight loss in the past month (1 point), fever ≥1 week within the past 2 weeks (1 point) and night sweats in the past month (1 point).

References for Annex 3.1

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CHAPTER 4

Survey case definitions: classifying who is, and who is not, a survey TB case

4.1 Introduction

Surveys of the prevalence of tuberculosis (TB) disease measure the number of people aged 15 years and older in the population who have bacteriologically confirmed pulmonary TB disease at the time of the survey. Accurate measurement requires **strict** counting of numbers of such people, who are classified as a **"survey TB case"**.

To ensure strict counting of survey TB cases, clear and standardized criteria are needed to classify survey participants as one of the following: a survey TB case; not a survey TB case; or someone for whom survey TB case status cannot be defined based on available diagnostic test results,[1] and for whom survey TB case status needs to be imputed as part of data analysis. These criteria should be included in the survey protocol (**Chapter 2**) and should not be modified subsequently (e.g. during the study or at the stage of data analysis). Use of standardized criteria is also essential to ensure that survey results can be reliably compared across countries and within countries over time.

This chapter explains how to classify survey participants as a survey TB case, not a survey TB case or someone for whom TB status cannot be determined based on diagnostic test results. This classification is done separately for the two algorithms for diagnosis of TB disease recommended in **Chapter 3**, referred to as "Option 1" and "Option 2". For ease of reference, these diagnostic algorithms are summarized in the first section of this chapter.

For surveys that use Option 1, **participants should be counted as a prevalent *survey* TB case ONLY if they meet the criteria provided in Section 4.3 of this chapter**. For surveys that use Option 2, **participants should be counted as a prevalent *survey* TB case ONLY if they meet the criteria provided in Section 4.4 of this chapter**.

For both Option 1 and Option 2, the final number of survey TB cases can then be used to estimate the prevalence of bacteriologically confirmed pulmonary TB disease in the national population (**Chapter 17**).[2]

Based on the strict counting of survey TB cases, the prevalence of bacteriologically confirmed pulmonary TB disease among people aged 15 years and older can also be usefully compared with routinely collected programmatic and surveillance data, to inform policy and programmatic action.[3] This is discussed further in **Chapter 20**.

It is important to highlight that the definition of a survey TB case is not the same as the case definition used in routine clinical care. For example:

- individuals already enrolled on TB treatment according to national guidelines are not counted as a prevalent TB case in the survey if they are bacteriologically negative at the time of the survey;
- in routine clinical care in which rapid test results can be interpreted by a medical doctor alongside a detailed assessment of reported TB symptoms, previous history of TB disease and other evidence such as a chest X-ray (CXR), an individual may be diagnosed with TB without the use of confirmatory culture testing; and
- people are only counted as survey TB cases if they have bacteriological confirmation, whereas in routine clinical care, people can be clinically diagnosed with TB (without bacteriological confirmation).

The clinical management of people who are classified as survey TB cases and of those who do not meet the crite-

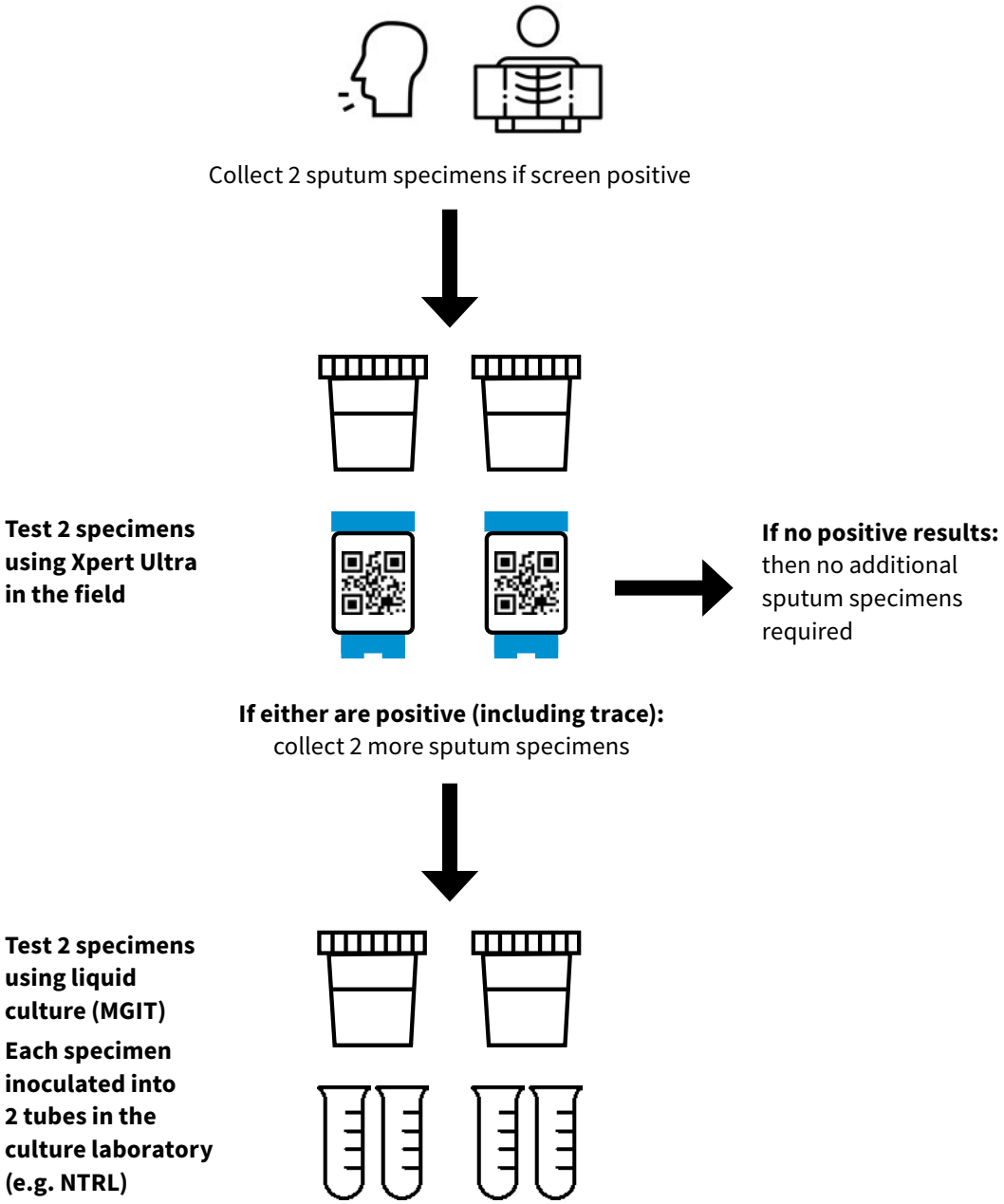
[1] This applies to individuals who were screen positive but had no valid Xpert® Ultra result (Option 1) and to individuals who were screen positive but had no valid culture result (both Option 1 and Option 2).

[2] For the purposes of estimating the overall burden of TB disease in the population, results from prevalence surveys can be used to estimate the overall prevalence of TB disease, for all forms of TB (i.e. pulmonary and extrapulmonary TB) and all ages (i.e. including people aged <15 years). The World Health Organization (WHO) uses estimates of the national prevalence of TB disease (for all forms and all ages) to inform national estimates of TB incidence, since these are required for monitoring of progress towards global TB targets set in the WHO End TB Strategy (2016–2035) and United Nations Sustainable Development Goals.

[3] For example, the prevalence of bacteriologically confirmed pulmonary TB disease per 100 000 population (P) can be compared with the notification rate (i.e. new TB cases per 100 000 population that were officially reported) of people newly diagnosed with bacteriologically confirmed pulmonary TB disease in the year of the survey (N) and expressed as a P:N ratio. The P:N ratio can also be estimated by sex and age group. Higher ratios in particular groups, or in one country compared with another country, indicate that a national TB control programme needs to address gaps in detection of cases or underreporting of people diagnosed with TB disease (or both). Examples of P:N ratios in recent surveys, both overall and by age and sex, are available elsewhere *(1)*.

Fig. 4.1

Illustration of diagnostic algorithm "Option 1"[a]



MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for Xpert Ultra testing and, if either specimen is positive, two additional sputum samples are collected for confirmatory testing using liquid culture (MGIT).

ria for being classified as a survey TB case but who have a positive diagnostic test result, or symptoms suggestive of TB or a CXR suggestive of TB disease, is discussed in detail in **Chapter 9**.

4.2 Algorithms for diagnosis of TB disease: Option 1 and Option 2

Chapter 3 explains the two algorithms for diagnosis of TB disease that are recommended for national TB prevalence surveys, which are referred to as Option 1 and Option 2.

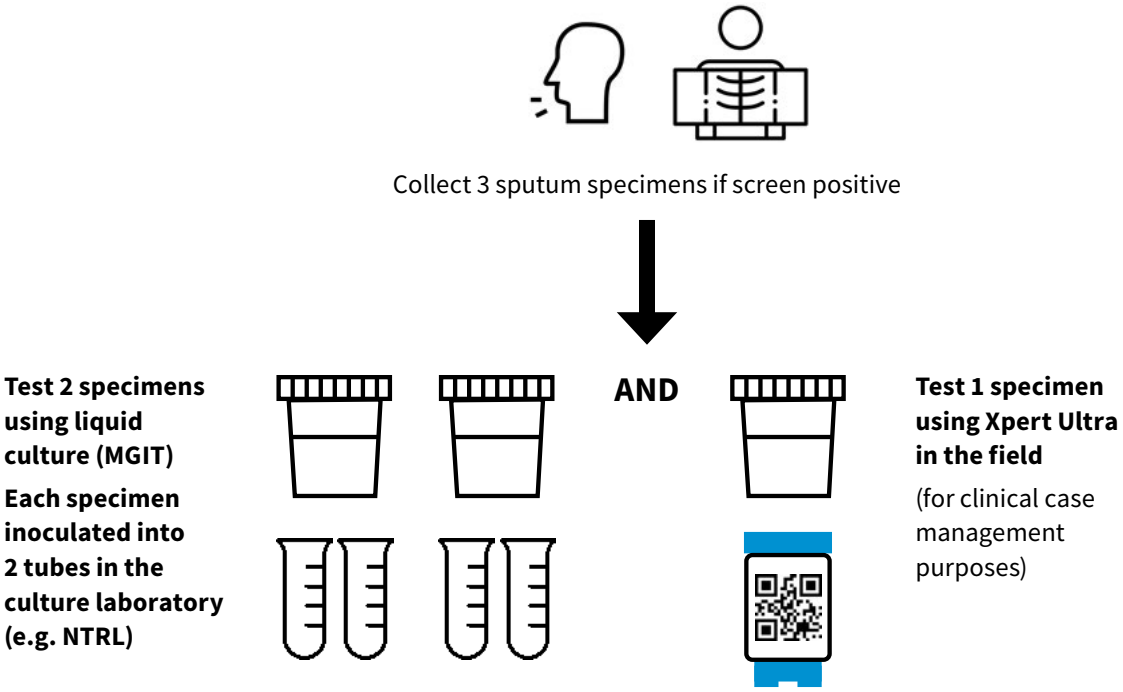
Option 1 is illustrated in **Fig. 4.1**. Two sputum samples are collected from all screen-positive participants and tested using Xpert® Ultra;[1] this is followed by confirmatory testing using liquid culture (mycobacterial growth indicator tube [MGIT™])[2] for all participants with at least one Xpert-positive result.

[1] Or an equivalent nucleic acid amplification (NAA) test with sensitivity equivalent to Xpert Ultra. Such a test does not currently exist but may become available in future.

[2] MGIT is a liquid media for the cultivation of mycobacteria. It is the current reference standard for the diagnosis of *Mycobacterium tuberculosis*.

Fig. 4.2

Illustration of diagnostic algorithm "Option 2"[a]



MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for liquid culture (MGIT) and one for Xpert Ultra testing. The Xpert Ultra test is used to ensure a rapid result is available to be used for clinical management purposes only (not the estimation of TB prevalence). The priority is to take two specimens for MGIT testing. Xpert Ultra testing can be done on the sediment of an MGIT sample; however, if this is not possible, a third sample should be collected for Xpert Ultra testing, to be done in the field. Further details are provided in **Chapter 8**. Clinical management of those with a positive Xpert Ultra result is discussed in **Chapter 9**.

Option 2 is illustrated in **Fig. 4.2**. Two samples are collected from all screen-positive participants and tested using liquid culture. In addition, ***for case management purposes only***, an Xpert Ultra test is also undertaken for everyone who screens positive, to ensure the availability of a rapid result for everyone who is tested during the survey.

As highlighted in **Chapter 3**, for the purposes of assessing trends since the last survey it may also be relevant to conduct additional tests: sputum smear microscopy for individuals who meet survey screening criteria (both Option 1 and Option 2), or solid culture testing for individuals with a positive Xpert Ultra result (Option 1 only). However, these tests are not part of the criteria used to classify survey participants as a TB case, not a survey TB case or someone for whom survey TB case status cannot be determined based on test results, in either Option 1 or Option 2. Hence, these additional tests are not discussed further in this chapter.[1]

4.3 Classification of survey TB case status based on diagnostic test results: Option 1

As highlighted in **Chapter 3** and discussed in detail elsewhere *(2)*, there are challenges with the interpretation of Xpert Ultra results in the context of a national TB prevalence survey. In a survey, it is plausible that more than half of the people with a positive Xpert Ultra result do not have TB disease.[2] This is different from the use of Xpert Ultra among people who have sought health care and for whom TB diagnostic testing is considered necessary based on signs or reported symptoms, among whom the pre-test probability of TB disease is much higher.

The explanation for a false positive Xpert Ultra result (i.e. a person has a positive Xpert Ultra result but does not have TB disease at the time of the test)[3] is that

[1] For further discussion of how to compare results with those from previous surveys, see **Chapter 3**, **17** and **18**.

[2] This is because the specificity of Xpert Ultra, compared with the reference standard of liquid culture, is about 95%, but only about 1–5% individuals who screen positive for TB in a survey are expected to have bacteriologically confirmed pulmonary TB disease. In other words, for every 100 people who screen positive in a survey, about five would have a "false positive" Xpert Ultra result and between about one and five would have a "true positive" Xpert Ultra result.

[3] This is different from, and should not be confused with, a person with TB disease who has a positive Xpert result and a negative culture result (i.e. has a "false negative" culture result).

although an Xpert Ultra test has correctly identified *Mycobacterium tuberculosis (Mtb)* complex, it may have detected dead rather than live TB bacilli, especially in a person with a recent history of TB treatment *(2)*. This is why Option 1 includes confirmatory testing for all individuals with a positive Xpert Ultra result, using the reference standard of liquid culture – such testing is essential to determine whether a surveyed individual with a positive Xpert Ultra result has active TB disease (live bacilli) at the time of the survey.

Before using diagnostic test results to classify screen-positive individuals as a survey TB case or not, careful checks are essential to ensure that positive laboratory results do not arise from cross-contamination (see **Chapter 8**), or from clerical or data management errors (see **Chapter 16**). Checks of the quality of laboratory testing should be systematically implemented throughout the survey, to ensure that results are accurate and reliable. This includes cross-checking of culture results with Xpert Ultra results (and their semiquantitative results) as well as CXR findings; for example, the percentage of people with a positive Xpert Ultra result (high) who have a culture-positive result should be very high.

4.3.1 Classification of survey TB case status: primary case definitions

Fig. 4.3 is a flow diagram that shows how to define screen-positive individuals as either a survey TB case, not a survey TB case or someone for whom survey TB status cannot be determined based on diagnostic test results. For individuals in the third category, survey TB case status (yes or no) needs to be imputed during data analysis (see **Chapter 17**). An alternative presentation of **Fig. 4.3** is provided in **Table 4.1**.

As shown in **Fig. 4.3** and **Table 4.1**, people with negative, invalid or missing culture results are sometimes classified as a survey TB case. However, stringent criteria need to be met: the individual must have two positive Xpert Ultra results that are both very low or higher[1] (see **Chapter 8**), and no history of TB treatment in the previous 5 years (after final treatment).[2] These criteria are based on evidence from the TREATS (Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for active TB) study *(4)*. It is expected that only a small number of people will be defined as survey cases based on a situation where the Xpert Ultra result is positive but the culture result is negative or missing.

All individuals categorized as survey TB cases should also be classified as either: new[3] or previously treated.[4] Within each of these categories, cases should be further classified as either: on anti-TB treatment or not on anti-TB treatment at the time of the survey.[5]

The use of a medical panel to classify the survey case status of people who are tested for TB disease, which was frequent in surveys implemented between 2007 and 2019, is no longer recommended (**Box 4.1**).

BOX 4.1
USE OF A MEDICAL PANEL IN THE CLASSIFICATION OF SURVEY TB CASE STATUS IS NO LONGER RECOMMENDED

In surveys implemented between 2007 and 2019, a group of experts (commonly referred to as a "medical panel") was often used to define whether a participant with missing or contradictory laboratory results should be defined as a survey case.

Use of such a panel is no longer recommended. The main reason is that many discordant Xpert and culture results can be expected when Option 1 is used, and it is important to avoid resorting to, and relying on, expert opinion about CXRs to decide which result is "correct" (given that expert opinion is subjective). The strict definitions in this chapter are designed to be objective and easy to apply in a consistent way, across countries and within countries over time.

When the survey TB case status (yes or no) of an individual cannot be defined because sputum specimens were not taken or diagnostic test results were invalid, survey TB case status should be imputed, using other survey data, at the stage of data analysis. Relevant data include the semiquantitative category of Xpert Ultra results, CXR results, reported symptoms, previous history of TB, HIV status, age and sex. This use of imputation is described in **Fig. 4.3**, **Fig. 4.4** and **Fig. 4.5**; imputation methods are explained in detail in **Chapter 17**.

[1] Xpert Ultra provides a semiquantitative categorization of the bacillary load. From highest to lowest, the categories are high, medium, low, very low and trace. These categories correlate with the sputum bacillary burden of *Mtb*. There is no semiquantitative category when the test result is negative.

[2] Further details about the justification for this cut-off are provided in WHO guidance on TB diagnostics *(3)*.

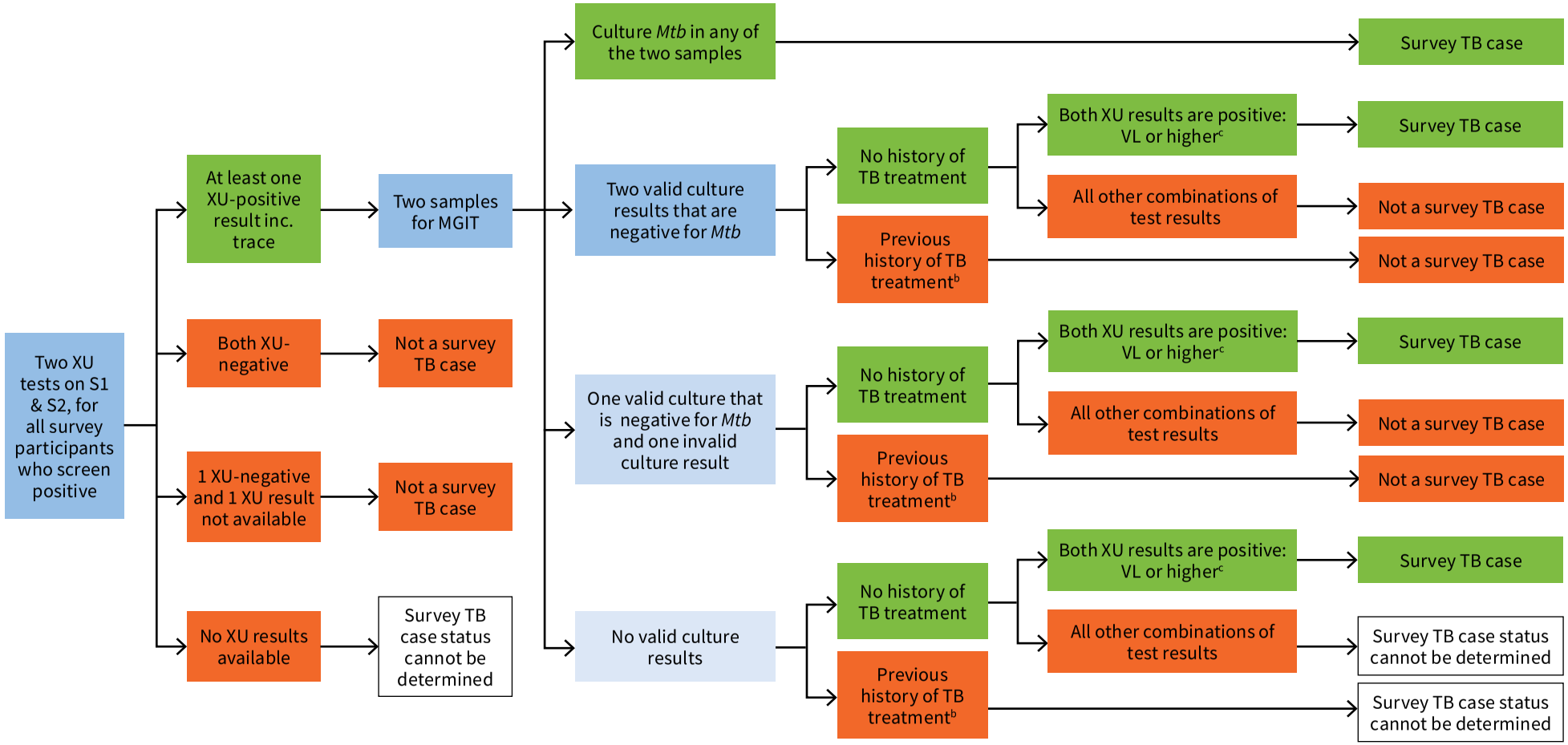
[3] A person who has never previously had treatment for TB for more than 1 month.

[4] A person previously treated for TB for more than 1 month. The time since the last treatment should also be determined.

[5] All survey participants should be asked at their screening interview whether they are currently on TB treatment, or whether they have ever been on treatment; if the answer is yes, participants should be asked for how long they were treated for TB in the past (see **Chapter 6**).

Fig. 4.3

Option 1 (primary case definitions, for primary analysis): classification of the survey TB case status of screen-positive individuals[a]



MGIT: mycobacteria growth indicator tube; *Mtb: Mycobacterium tuberculosis*; N: culture negative; NTM: non-tuberculous mycobacteria; S: sample; TB: tuberculosis; VL: very low; XU: Xpert Ultra.

[a] Two Xpert Ultra tests for all screen-positive individuals, followed by two confirmatory tests using liquid culture for all individuals with at least one Xpert-positive result.

[b] Previous history of TB within the past 5 years. If a person had TB more than 5 years before the survey, that person should be included in the box for "no history of TB treatment".

[c] Xpert Ultra provides a semiquantitative categorization of the bacillary load. From highest to lowest, the categories are high, medium, low, very low and trace. These categories correlate with the sputum bacillary load of *Mtb*. There is no semiquantitative category when the test result is negative.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results that are negative for *Mtb*:** N or NTM.
- **Invalid culture results:** the result is missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).
- **Valid Xpert Ultra results:** Xpert positive (including trace), Xpert negative.

Table 4.1

Option 1 (primary case definitions): classification of the survey TB case status of screen-positive individuals[a]

NO.	LABORATORY RESULTS	CATEGORY
1	≥1 XU positive *and* ≥1 culture *Mtb* positive	Survey TB case.
2	2 XU negative, no culture tests done	Not a survey TB case.
3	≥1 XU positive *and* 2 valid culture results that are negative for *Mtb*	**Not a survey TB case unless:** • no self-reported history of TB treatment (current or previous);[b] ***and*** • **both** (2) XU results positive at *very low* or higher.[c]
4	≥1 XU positive *and* 1 valid culture result that is negative for *Mtb* *and* 1 invalid culture result[d]	**Not a survey TB case unless:** • no self-reported history of TB treatment (current or previous);[b] ***and*** • **both** (2) XU results positive at *very low* or higher.[c]
5	≥1 XU positive *and* no valid culture results	**Survey TB case if:** • Criteria 1) no self-reported history of TB treatment (current or previous);[b] ***and*** • Criteria 2) **both** XU results positive at *very low* or higher. **If criteria 1 and 2 are *not* met, survey TB status is not known; therefore**, impute survey TB case status (yes or no) based on, for example, semiquantitative category of Xpert results and a prior history of TB treatment.
6	1 XU negative *and* 1 XU missing, *and* no culture tests done[d]	Not a survey TB case.
7	No valid XU results *and* no culture tests done	Survey TB case status cannot be determined based on diagnostic test results. Impute survey TB case status (yes or no) based on collected data (e.g. at least a prior history of TB, CXR, symptoms, age and sex).

CXR: chest X-ray; *Mtb: Mycobacterium tuberculosis*; N: culture negative; NTM: non-tuberculous mycobacteria; TB: tuberculosis; XU: Xpert Ultra.

[a] Option 1: two Xpert Ultra tests for all screen-positive individuals, followed by two confirmatory tests using liquid culture for all individuals with at least one Xpert-positive result.

[b] Previous history of TB within the past 5 years. If a person had TB more than 5 years ago then classify the person as no history of TB treatment.

[c] Xpert Ultra provides a semiquantitative categorization of the bacillary load. From highest to lowest, these categories are high, medium, low, very low and trace. These categories correlate with the sputum bacillary burden of *Mtb*. There is no semiquantitative category when the test result is negative.

[d] The participant has two opportunities to provide a specimen for Xpert Ultra testing, and so two opportunities to get an Xpert Ultra test result. A participant with ≥1 XU-positive result has two opportunities to provide a specimen for culture testing, and so two opportunities to get a culture result. If one culture (or Xpert) result is negative, and the other culture (or Xpert) result is invalid, then the negative result is the main source of evidence. Imputation is done when both results are invalid.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results that are negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).
- **Valid Xpert Ultra results:** Xpert positive (including trace), Xpert negative.

4.3.2 Classification of survey TB case status: secondary case definitions

Secondary case definitions can be used to produce results based on a slightly stricter set of criteria, in which people are defined as a survey TB case *only* if they have a culture-positive result. **Fig. 4.4** and **Table 4.2** show how these stricter criteria can be used to define whether someone is a survey TB case, not a survey TB case or someone for whom survey TB case status cannot be determined based on diagnostic test results. The number of people defined as being a survey TB case will be lower than the number defined as such using the criteria shown in **Fig. 4.3**; however, the two results should be close if the quality of culture testing is high. Ensuring a high quality of culture testing is essential to ensure that survey results are reliable (quality assurance of culture testing is discussed in **Chapter 8**).

4.4 Classification of survey TB case status based on diagnostic test results: Option 2

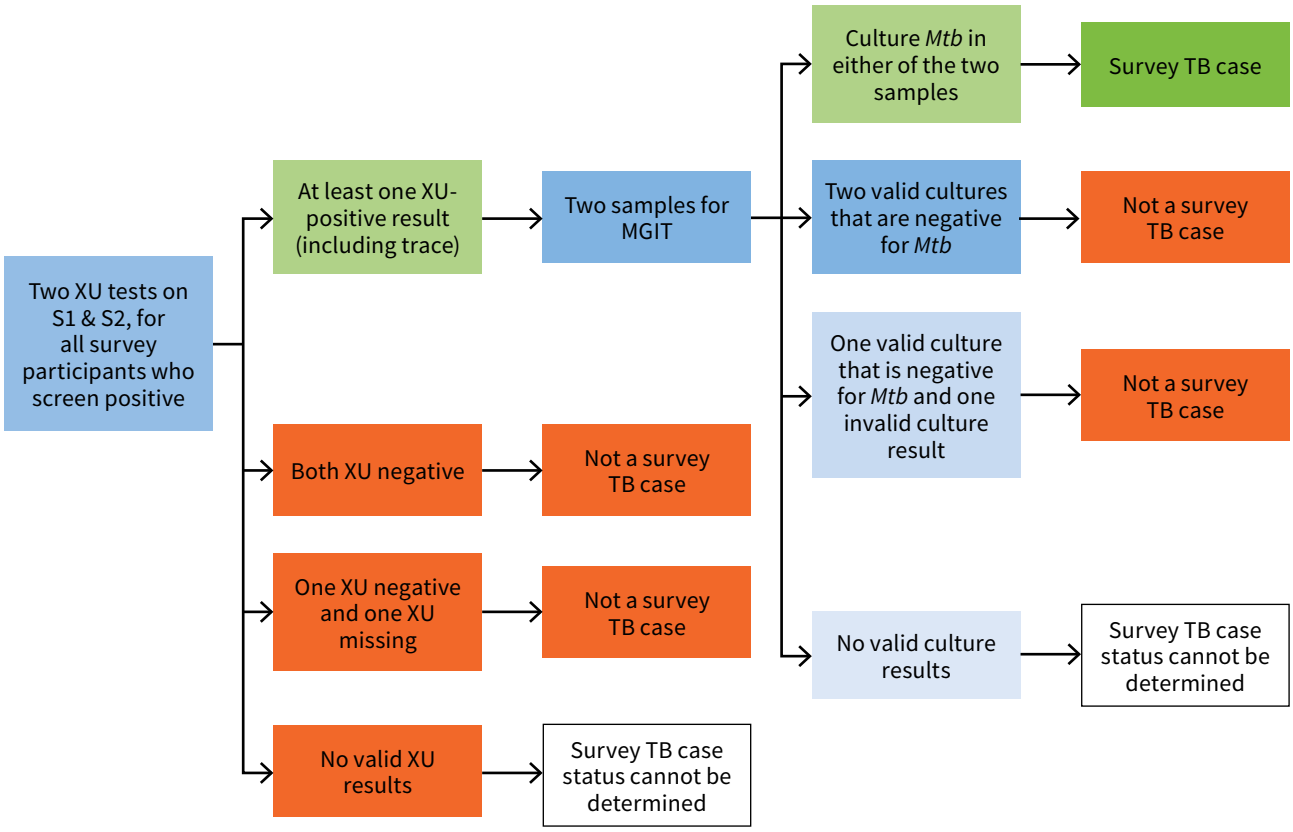
In Option 2, classification of the survey TB case status of screen-positive individuals is based on liquid culture test results alone.

Fig. 4.5 is a flow diagram that shows how to define screen-positive individuals as either a survey TB case, not a survey TB case or someone for whom survey TB case status cannot be determined based on diagnostic test results, and for whom survey TB case status (yes or no) needs to be imputed during data analysis.[1] An alter-

[1] When survey TB case status (yes or no) cannot be defined because sputum specimens were missed, or diagnostic test results were invalid, survey TB case status should be imputed using other collected data such as CXR results, symptoms, prior history of TB (current or past), HIV status, age and sex. Imputation methods are explained in detail in **Chapter 17**.

Fig. 4.4

Option 1 (secondary case definitions): classification of the survey TB case status of screen-positive individuals[a]



MGIT: mycobacteria growth indicator tube; *Mtb: Mycobacterium tuberculosis*; S: sample; TB: tuberculosis; XU: Xpert Ultra.

[a] Option 1: Two Xpert Ultra tests for all screen-positive individuals, followed by two confirmatory tests using liquid culture for all individuals with at least one Xpert-positive result.

This classification is stricter than that shown in **Fig. 4.3** and **Table 4.1**, because a culture-positive result is required to define an individual as a survey TB case.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results that are negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).
- **Valid Xpert Ultra results:** Xpert positive (including trace), Xpert negative.

native presentation of the same information is provided in **Table 4.3**.

As in Option 1, all individuals categorized as survey TB cases should also be classified as either new[1] or previously treated.[2] Within each of these categories, cases should also be classified as either on anti-TB treatment or not on anti-TB treatment at the time of the survey.[3]

[1] A person who has never previously had treatment for TB for more than 1 month.

[2] A person previously treated for TB for more than 1 month. The time since the last treatment should also be determined.

[3] All survey participants should be asked at their screening interview whether they are currently on TB treatment, or whether they have ever been on treatment; if the answer is yes, participants should be asked for how long they were treated for TB in the past (see **Chapter 6**).

4.5 Follow-up investigations and case management

In the previous edition of this guidance, published in 2011 *(5)*, the possibility of using evidence from follow-up investigations to define a survey case was left open. However, all experience from surveys implemented since 2011 shows that systematic follow-up investigations by the survey team were not feasible or part of the survey protocol. **Instead, what is essential is that appropriate clinical management is provided, according to local capacity** (see **Chapter 9**). Decisions related to case management are, however, not used in determining the number of survey TB cases, and in turn determining the burden of TB disease.

Careful attention needs to be given to any survey participant with a positive laboratory result, whether or not they meet the survey TB case definition. All such indi-

Table 4.2

Option 1 (secondary case definitions): classification of the survey TB case status of screen-positive individuals[a]

NO.	LABORATORY RESULTS	CATEGORY
1	≥1 XU-positive *and* ≥1 culture *Mtb* positive	Survey TB case.
2	2 XU-negative, no culture tests done	Not a survey TB case.
3	≥1 XU-positive *and* 2 valid culture results that are negative for *Mtb*	Not a survey TB case.
4	≥1 XU-positive *and* 1 valid culture result that is negative for *Mtb* *and* 1 invalid culture result	Not a survey TB case.
5	≥1 XU-positive *and* 2 invalid culture results	Survey TB case status is not known based on culture results. Impute survey case status (yes or no) based on, for example, semiquantitative category of Xpert results and a prior history of TB.
6	1 XU-negative *and* 1 XU missing *and* no culture tests done	Not a survey TB case.
7	No valid XU results *and* no culture tests done	Survey TB case status cannot be determined based on diagnostic test results. Impute survey TB case status (yes or no) based on collected data (e.g. at least a prior history of TB, CXR, symptoms, age and sex).

CXR: chest X-ray; *Mtb: Mycobacterium tuberculosis*; N: culture negative; NTM: non-tuberculous mycobacteria; TB: tuberculosis; XU: Xpert Ultra.

[a] Option 1: Two Xpert Ultra tests for all screen-positive individuals, followed by two confirmatory tests using liquid culture for all individuals with at least one Xpert-positive result. This classification is stricter than that shown in **Fig. 4.3** and **Table 4.1**, because a culture-positive result is required to define an individual as a survey TB case.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).
- **Valid Xpert Ultra results:** Xpert positive (including trace), Xpert negative.

Table 4.3

Option 2: classification of the survey TB case status of screen-positive individuals[a]

NO.	LABORATORY RESULTS	CATEGORY
1	2 culture *Mtb* positive	Survey TB case.
2	1 culture *Mtb* positive *and* 1 culture *Mtb* negative	Survey TB case.
3	1 culture *Mtb* positive *and* 1 with no valid culture result	Survey TB case.
4	2 valid culture results that are negative for *Mtb*	Not a survey TB case.
5	1 valid culture result that is negative for *Mtb* *and* 1 invalid culture result	Not a survey TB case.
6	No valid culture results	Survey TB case status cannot be determined based on culture results. Impute survey TB case status (yes or no) based on collected data (e.g. at least a prior history of TB, CXR, symptoms, age and sex).

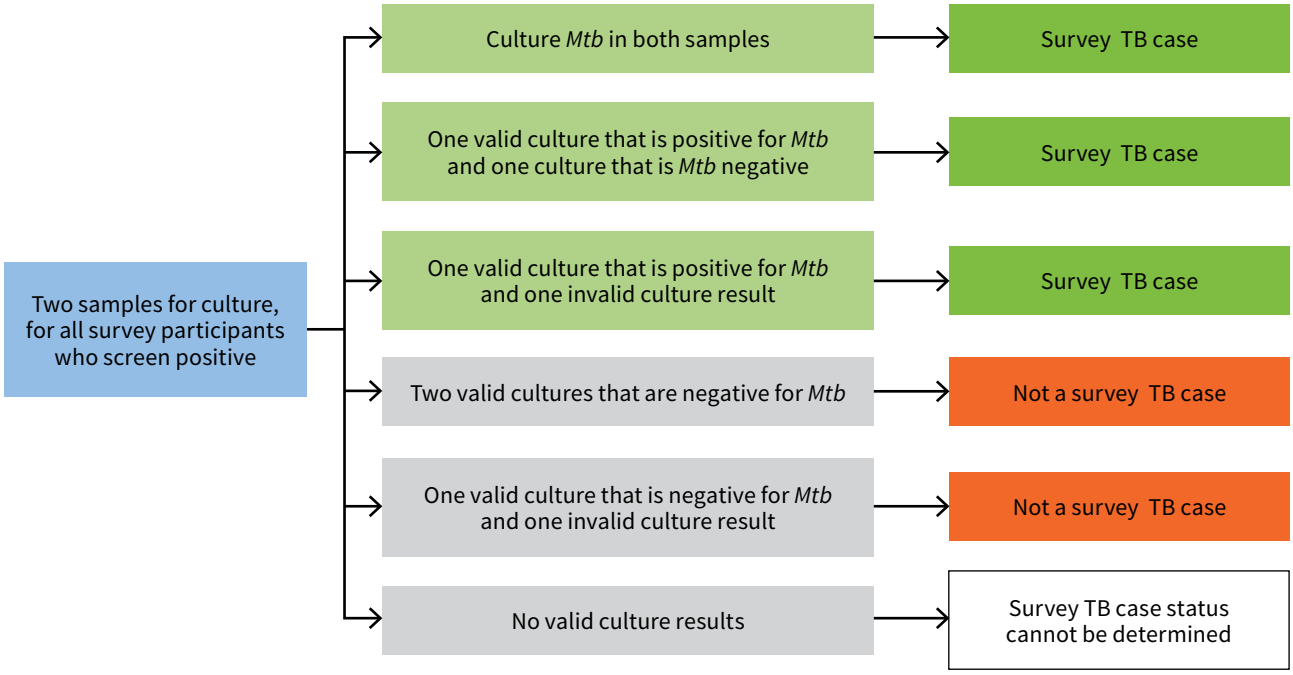
CXR: chest X-ray; *Mtb: Mycobacterium tuberculosis*; N: culture negative; NTM: non-tuberculous mycobacteria; TB: tuberculosis.

[a] Option 2: Two tests using liquid culture for all screen-positive individuals.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).

Fig. 4.5

Option 2: classification of the survey TB case status of screen-positive individuals[a]



Mtb: Mycobacterium tuberculosis; N: culture negative; NTM: non-tuberculous mycobacteria; TB: tuberculosis.

[a] Option 2: Two tests using liquid culture for all screen-positive individuals.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).

viduals should be appropriately reviewed by a group of experts (e.g. survey medical panel, see **Chapter 9**) and managed by the relevant health partner as per the survey standard operating procedures, and in accordance with national TB guidance.

References

1 National tuberculosis prevalence surveys, 2007–2016. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/341072).

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3 WHO consolidated guidelines on tuberculosis. Module 3: Diagnosis. Geneva: World Health Organization; 2025 (https://iris.who.int/handle/10665/381003).

4 Floyd S, Klinkenberg E, de Haas P, Kosloff B, Gachie T, Dodd PJ et al. Optimising Xpert-Ultra and culture testing to reliably measure tuberculosis prevalence in the community: findings from surveys in Zambia and South Africa. BMJ Open. 2022;12:e058195 (doi: https://doi.org/10.1136/bmjopen-2021-058195).

5 Tuberculosis prevalence surveys: a handbook. Geneva: World Health Organization; 2011 (https://iris.who.int/handle/10665/44481).

CHAPTER 5

Sampling design

Scientific rigour in the design of sample surveys is crucial to ensure that the final results of the national tuberculosis (TB) prevalence survey are accurate and representative. A poor-quality sampling design will undermine the value of the survey. This chapter outlines a step-by-step approach to the sampling design of a TB prevalence survey. It is followed by four major sections:

- **Section 5.2** covers the basic concepts of **sampling methodology**, explaining why cluster sampling is the optimal sampling design for prevalence surveys.
- **Section 5.3** covers **calculation of sample size**, describing the key components of a sample size calculation, and showing step by step how to calculate the sample size that is required. This section also defines and discusses important concepts such as relative precision and the design effect.
- **Section 5.4** discusses the **selection of clusters and of individuals within clusters**. It covers the definition of a cluster, the role of stratification, and the practical steps needed to select clusters and individuals from within a cluster.
- **Section 5.5** explains how to **define the eligible survey population**, and why this is critical to the estimation of the true countrywide prevalence of TB.

5.1 Introduction

This chapter has been written to ensure that all guidance required by the statistician advising on sampling design is provided. All survey teams should engage a statistician to advise on sampling design and should ensure that this material is highly accessible to statisticians and quantitative epidemiologists. This chapter should also be accessible to more general readers who are relatively numerate. **Sections 5.2**, **5.4** and **5.5** should also be accessible to all readers. **Section 5.3** is more challenging in terms of the mathematical concepts and methods that are covered; nevertheless, anyone leading or managing a survey is encouraged to read it to grasp the essential principles. The key principles and concepts covered in Section 5.3 are also summarized without mathematical equations in this introduction.

5.1.1 Eleven steps to sampling design of a TB prevalence survey for the mathematically faint at heart

This subsection outlines a step-by-step approach to the sampling design of a TB prevalence survey. Although understanding of statistics is required to set up the sampling design of a survey, even those with no statistical training should be able to understand this summary. The summary is not intended as a substitute for material covered in **Section 5.3**; rather, it is an introduction to the key concepts, necessary elements, and steps to sampling design.

Step 1: A prior guess of the true population prevalence of bacteriologically confirmed pulmonary TB

The first step involves coming up with a prior guess for the true population prevalence of TB, the very thing we are trying to estimate with the survey. A good understanding of the epidemiology of TB in the country is required to produce this guess. Good starting points are previous national TB prevalence surveys and national surveillance data summarized in the annual World Health Organization (WHO) global TB report, in conjunction with other available research data. A close collaboration between the statistician and local TB experts is crucial in this first step.

Step 2: The relative precision

The precision of the estimate of TB prevalence drawn from a survey increases with the size of the survey, but so do the costs and logistical demands. The (relative) precision refers to “how far away” we will allow the survey’s estimate of prevalence to be from the true national prevalence; this is expressed as a percentage of the true prevalence itself. In statistical terms, the relative precision is translated into the required width of the 95% confidence interval around the TB prevalence estimate. Relative precision is recommended to be between 20% and 25%.

Step 3: A prior guess about the magnitude of the design effect

The nature of TB prevalence surveys is such that groups of people, typically several hundred people, as opposed to individuals, are sampled from each selected area. Each group of people is termed a cluster, and the approach whereby sampling units are groups rather than individuals is called clustered sampling.

Cluster-sample surveys result in more uncertainty about the true prevalence of TB than would be the case with an individual-sample survey of the same size. Thus, sample size in a cluster-sample survey must be larger than in a simple random-sample survey. The increased uncertainty arises because individuals sampled as part of the same cluster are not independent of each other, and so they provide less information than would be the case if they were sampled individually. Indeed, individuals in the same cluster are likely to be more similar to each other, in terms of TB prevalence and associated risk factors, than they are to individuals in other clusters. This loss of efficiency (from a statistical perspective) caused by using a cluster sampling design, rather than a simple random-sampling design, is referred to as the "design effect".

In statistical terms, the design effect represents the magnitude of variance inflation attributed to cluster sampling compared with simple random sampling. In practice, the design effect is used as the multiple by which the sample size must be increased when using cluster sampling, compared with the sample size that would be required if simple random sampling was used. The value of the design effect depends on three key elements: the number of eligible individuals in each surveyed cluster (i.e. the cluster size); the true national prevalence, so that a prior guess is needed (Step 1 above); and the difference in the TB prevalence among clusters compared with the overall national prevalence (this is referred to as the between-cluster variability, and it is difficult to measure). Two methods used to measure the between-cluster variability are illustrated in **Section 5.3**. Between these methods, preference is given to the coefficient of between-cluster variation because of its (relative) simplicity. **Based on the results of completed TB prevalence surveys, it is reasonable to assume that the coefficient of between-cluster variation will be at least 0.3 and possibly as high as 0.8, but typically between 0.4 and 0.6.**

The design effect will be large if any one or a combination of the following apply:

- the prevalence of TB varies considerably among clusters, such that the measure of between-cluster variation is large; the number of survey clusters should be at least 50;
- the number of eligible individuals selected for (i.e. invited to participate in) the survey in each cluster is large; the cluster size should be 400–800 people; or
- the prevalence of TB is expected to be relatively high, so that the prior guess of the true national prevalence is relatively large.

The design effect can be estimated in one or both of two ways:

- from the results of previous surveys; or
- from an assessment of likely between-cluster variation and different choices of cluster size.

Step 4: Final equation for the sample size calculation

The equation for calculating the sample size for a TB prevalence survey, corrected for the design effect, is shown in **Section 5.3.7**; examples are provided in **Box 5.2** and **Box 5.3**.

Step 5: A prior guess of the participation rate

In a field survey, some people will either not attend the initial screening, or will drop out during the survey. Therefore, the sample size should be adjusted to allow for non-participation in the survey. This is addressed in a straightforward way by dividing the sample size computed after Step 4 by the expected proportion of eligible individuals who will participate in chest X-ray (CXR) screening and symptom screening in each of the sampled clusters. For TB prevalence surveys, this proportion is typically assumed to be 85–90% (i.e. 0.85–0.90 if expressed as a proportion).

Step 6: A prior guess of the proportion of individuals with complete TB diagnosis data

It is anticipated that a proportion of laboratory results will be missing among individuals who participate in the survey, screen positive and are eligible for diagnostic testing for TB. This could be for different reasons; for example, sputum samples not being collected (for Xpert® or for culture testing), samples being lost during transportation, or the culture test result being contaminated. Missing results can be addressed by dividing the sample size computed after Step 5 by the expected proportion of sputum-eligible individuals with sufficient laboratory diagnostic test results for them to be classified as survey case (prevalent TB=Yes) or not a survey case (prevalent TB=No). This proportion is typically assumed to be 85–90% (i.e. 0.85–0.90 if expressed as a proportion).

Step 7: Final sample size

The final sample size, defined as the total number of individuals invited to participate in the survey, is the sample size obtained after Step 6.

Step 8: Stratification to ensure a representative and precise overall estimate of prevalence

TB prevalence will typically vary across different geographical regions of a country, generically referred to as strata. For example, the prevalence of TB could be different in urban and rural settings or between northern and southern geographical areas of the country. In this case, a stratified design should be used to increase the precision and representativeness of the overall estimate of TB prevalence for the whole country. In fact, the use of a stratified design is encouraged even for countries with

small differences among geographical regions, or when little is known about region-specific prevalences. Using stratification can increase the accuracy of the final prevalence estimate without requiring a larger sample size.

Prevalence estimates for each stratum can be calculated, but they will not be as accurate as the overall estimate and should be interpreted with caution. Increasing the precision of prevalence estimates within each stratum is not directly linked with the primary objective of a nationwide prevalence survey – to estimate the overall national prevalence of TB – and will increase total sample size and cost substantially. **The only objective of the sample size calculation for the overall survey should be to achieve a reliable (precise and representative) estimate of the overall (national) true population prevalence of TB, and not to also obtain reliable estimates of prevalence within each stratum.**

Step 9: Cluster selection

Once the cluster size has been chosen (which is generally between 400 and 800, for mostly logistical, but also statistical, reasons) and the total sample size has been calculated (as explained in Steps 1–7 above and in detail in **Sections 5.3.3–5.3.7**), the total number of clusters to be sampled is calculated by dividing the sample size by the assumed cluster size. The recommended number of clusters for a survey is at least 50 (see **Fig. 5.1**). Then the clusters themselves need to be selected.

The definition of a cluster as a sampling unit needs to be adapted for each country. A cluster could be any well-defined geographical area of similar population size. Clusters typically use as their building blocks census enumeration areas (EAs), villages or towns.

Cluster selection will most probably be a multistage process, selecting first from the larger primary sampling units, then smaller secondary sampling units, and so on, until the last level of geographical areas, which comprise only clusters. At each of these stages, the selection of sampling units should ensure that the probability of selecting a unit is proportional to its population size, dubbed probability-proportional-to-size (PPS) sampling. The use of PPS sampling in conjunction with a fixed target cluster size simplifies the analysis because it avoids the need to apply population weights.

During the final stage, where a single cluster must be selected from a selected geographical area, all possible clusters are listed, and one is randomly selected. If the clusters vary considerably in their population size, which might be the case with towns and villages, then the cluster is selected with PPS sampling. If the clusters have similar population sizes, which is expected if EAs are used as the clusters and may also be the case with villages, then the cluster is selected with simple random sampling – that is, each cluster has the same probability of being selected.

Step 10: Selection of individuals within a cluster

Once a cluster has been selected, a target number of eligible individuals needs to be identified and invited to participate in the survey. The target number should be as similar as possible across clusters. Even though the definition of a cluster in the survey protocol should take into consideration the target cluster size, it is possible for the total number of eligible individuals within a cluster to be either lower or higher than the target number. The following is advised:

a. If the cluster size is lower than the target size, then a neighbouring cluster must be randomly selected and combined with the one initially selected to reach the target size.

b. If the cluster size is only slightly higher than the target size, then the survey team might need to include the few extra individuals in the survey, to ensure buy-in from the local community.

c. If the cluster size is much higher than the target size, then a subset of cluster individuals equal to the target number must be randomly selected.

In scenarios a) and c), a subset of eligible individuals from a cluster should be selected, either from a neighbouring cluster (in addition to the cluster originally selected), or from within the original cluster. This can be done by dividing a cluster into household groups using existing divisions between households (e.g. paths, roads and natural boundaries); the groups to be included should be selected at random.

Step 11: Eligible survey population

Individuals eligible for the survey should be representative of the target population. Eligibility of an individual is based only on:

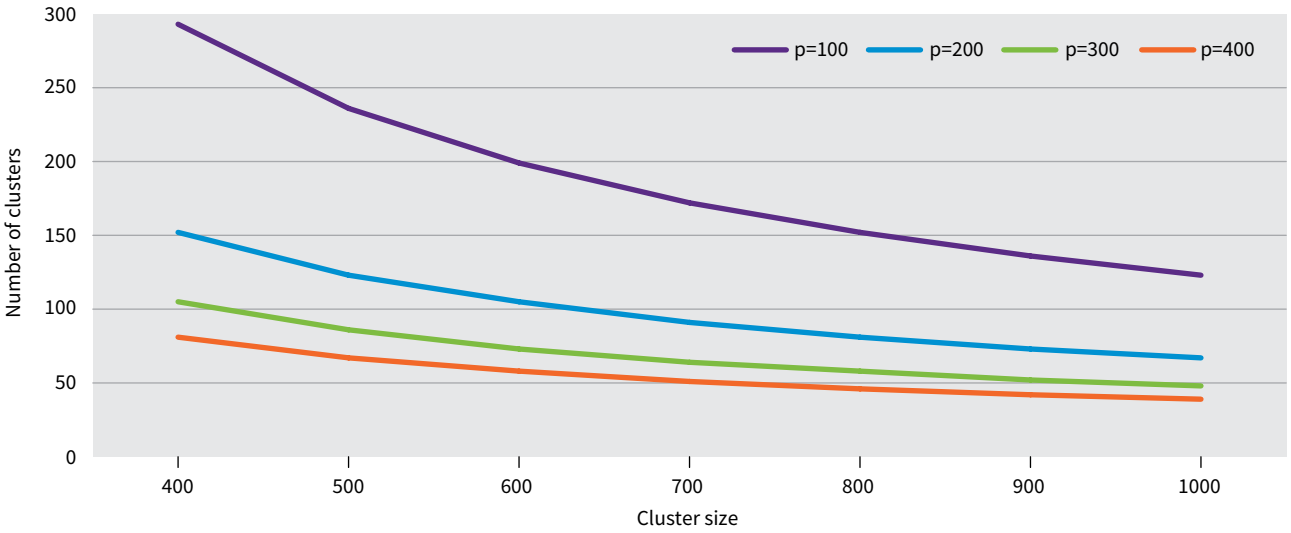
- age (aged ≥15 years); and
- residency status in the household (e.g. people living in the household for the past 4 weeks or a period equal to the time window between the pre-census and census visits; this therefore excludes individuals who move into the household in anticipation of receiving health care from the survey team).

All eligible individuals should be enumerated and later classified as “survey participant”, “absent” or “did not consent to participate”, in order to study potential biases introduced in the results. The closer the observed survey population (those who participated) is to the eligible survey population, the better the inference on TB disease prevalence that can be drawn from the survey.

It is equally important to enumerate and collect basic demographic information about children aged below 15 years and about individuals who do not satisfy the residency criteria. The former will allow the survey team to correct the TB prevalence estimate for demographic

Fig. 5.1

Cluster size and number of clusters for different estimates of TB prevalence (p) and other parameters[a]



TB: tuberculosis.

[a] Parameters used: coefficient of between-cluster variation k of 0.3; 20% relative precision; 85% participation rate.

changes in the population, while the latter provides an insight into the mobility of the population in the country.

5.2 Sampling methodology

The ultimate goal in sampling is to extract a sample that is as representative as possible of the general population of interest (e.g. it should be representative in terms of age and sex). One way to achieve this would be to choose the required number of people[1] at random from a complete list of everyone in the country, and then find out how many of them have TB. This approach, with individuals as the sampling unit, is called "simple random sampling". In practice, it is rare to have a complete list of the population; it is more common to have only estimates of the population and its distribution. A second major problem with simple random sampling is that collecting data from the selected population sample needs to be feasible in terms of cost and logistics. When data can be collected without direct contact with individuals (e.g. surveys conducted by telephone), simple random-sample surveys are feasible. However, where direct contact with a large number of individuals is required (such as a TB prevalence survey), the time and cost of collecting data individually from a completely random sample of the population is prohibitive.

When simple random sampling is not feasible, an alternative approach is to use "clustered sampling". In **clustered sampling**, the sampling unit, referred to as a "cluster", comprises groups of people (as opposed to individuals) in geographical proximity to each other. **This is the most appropriate sampling design for a TB prevalence survey**. The number and size of clusters to be sampled will vary among surveys, and both influence and are influenced by the calculation of sample size. Sample size calculations are explained in the next section.

5.3 Sample size determination and definition of terms

5.3.1 Sample size calculations: key components

To calculate the sample size for a prevalence survey with a cluster-sample survey design, the following six components are needed:

- a prior guess of the **true population prevalence of bacteriologically confirmed pulmonary TB** – for national TB prevalence surveys, the prevalence of bacteriologically confirmed pulmonary TB is defined using either Option 1 or Option 2 (**Chapter 4**) among individuals aged 15 years and older;
- the **relative precision** required for the estimate of the true population prevalence of TB that will come from the survey;
- the **sample size required for a simple random-sample survey**, calculated using the required relative precision and the prior guess of the true population prevalence of bacteriologically confirmed pulmonary TB;
- a prior guess about the **magnitude of the design effect** – the multiple by which a sample size must be increased, relative to the sample size required for a

[1] That is, the number needed to estimate the prevalence of TB with sufficient precision. The concept of "precision" is discussed further in **Section 5.3.2**.

simple random-sample survey, when using a cluster-sample survey design;

- a prior guess of the **participation rate** – that is, the percentage (proportion) of the eligible population that will participate in the survey; and
- a prior guess of the **proportion of individuals with complete TB diagnosis data** – that is, the percentage (proportion) of participants with sufficient laboratory diagnostic test results for them to be classified as a survey case (prevalent TB=Yes) or not a survey case (prevalent TB=No).

This section explains, step by step, how to calculate the sample size for a cluster-sample survey of TB prevalence, knowing that not all of the eligible population will agree to participate in the survey and not all survey participants will have complete screening and laboratory diagnostic test data. A total of eight equations (**Equation 5.1** to **Equation 5.8**) are used to calculate the total sample size.

5.3.2 Definitions of terms and notation

The true population prevalence of TB, the participation rate and the proportion of individuals with complete TB diagnosis data are relatively easy concepts to understand. The concepts of "relative precision" and the "design effect" are more challenging, and it is helpful to use mathematical notation to explain them. This subsection starts with a definition of the mathematical notation used throughout the chapter, and then explains the concepts of relative precision and the design effect.

Notation

Our notation is summarized in **Table 5.1**. The terms that are included in the sample size (**Equation 5.1** to **Equation 5.8**) are highlighted in grey or orange.

The between-cluster variation σ_B^2 and the intra-cluster correlation coefficient ρ are equivalent in what they measure but different in how they measure it: ρ is a relative measure constrained to be between 0 and 1, while σ_B^2 is an absolute measure *(1)*. The coefficient of between-cluster variation k is a relative measure that takes a value greater than 0 but is not constrained to be less than 1 *(2)*.

Prior guess of the true population prevalence of TB

The first step when calculating the sample size is to get a prior guess of the true population prevalence of bacteriologically confirmed pulmonary TB π_g. This is a critical step as π_g has a central role in the sample size calculation. A very good understanding of the TB epidemiology in the country is required to get a sense of π_g. The plausible values of π_g can be explored in multiple ways; for example:

- using the point estimate of the most recent national TB prevalence survey (if the survey was carried out within the preceding 10 years);
- using the point estimate of the most recent national TB prevalence survey (if the survey was carried out within the preceding 10 years) combined with a hypothesized proportion of the decrease in TB prevalence;
- using expert opinions;
- using any observational programmatic data or data from operational research studies.

In any case, it is important that the country study team works closely with a statistician to derive the prior guess of the true prevalence of TB.

Relative precision

Precision refers to the width of the 95% confidence interval for true TB prevalence, which is centered on the survey estimate p. Relative precision is the width of the confidence interval, expressed as a proportion (or percentage) of the true population prevalence π. For example, a relative precision of 0.2 (percentage of 20%) means that the 95% confidence interval for π is between and $p - 0.2\,\pi$ and $p + 0.2\,\pi$.

In sample size calculations for TB prevalence surveys, it is recommended that the value used for relative precision (d) should be between 20% and 25%. Expressed as a proportion, this means that d should be between 0.20 and 0.25. This requirement ensures that the 95% confidence interval for the value of true TB prevalence is narrow enough to be useful ($d \leq 0.25$) but also the required sample size is not impractically large ($d \geq 0.2$).

The design effect

As explained in **Section 5.2**, TB prevalence surveys are based on sampling all individuals in randomly selected geographical areas (clusters), rather than screening a completely random sample of the population from all parts of the country.

The design effect for a cluster-sample survey is used as the multiple by which the sample size must be increased, compared with the sample size that would be required if simple random sampling was used, to ensure that the estimate of the population prevalence of TB is as precise (i.e. the width of the confidence interval is as narrow) as that which would have been obtained from a simple random-sample survey.

In a cluster-sample survey, observations on individuals in the same cluster are not statistically independent. This is because individuals within a cluster are likely to be more similar to each other than to individuals outside the cluster, and thus each individual provides less information than would be the case with a simple random-sample survey. For this reason, **the design effect is always >1 for a TB prevalence survey**.

For those who would like to understand fundamental concepts about the design effect and its estimation, please see **Annex 5.1**.

Table 5.1

Notation used in equations for calculation of sample size and explanation of the concepts underlying calculation of sample size

Sample size for a simple random-sample survey (Equation 5.1)	
π	True population prevalence of bacteriologically confirmed pulmonary TB (expressed as a proportion).
π_g	Prior guess of the true population prevalence of bacteriologically confirmed pulmonary TB (expressed as a proportion).
p	Survey estimate of the population prevalence of bacteriologically confirmed pulmonary TB.
N	Number of individuals invited to participate in the survey.
t	Number of TB cases found in the survey.
d	Relative precision, where d is a proportion greater than 0 and less than 1.
Design effect (Equation 5.2 and Equation 5.3)	
m	Cluster size – that is, the number of individuals who are invited to participate in the survey from each selected cluster. The cluster size is assumed to be constant – that is, m is the same for each selected cluster.
π_i	True prevalence of TB in the cluster i.
σ_B^2	The variance of the true cluster-level prevalences of bacteriologically confirmed pulmonary TB about the overall population prevalence π. This is the "between-cluster" variation, and the B subscript stands for "between".
σ_B	The standard deviation of the true cluster-level prevalences of bacteriologically confirmed pulmonary TB about the overall population prevalence π.
$k = \frac{\sigma_B}{\pi}$	Coefficient of between-cluster variation. See Section 5.3.6 for further definition. Recommended to assume k is in the range 0.4–0.6. See Section 5.3.6 for guidance on how to estimate k for a particular country.
ρ	Intra-cluster correlation coefficient, assumed in the context of TB prevalence surveys to take a value between 0 and 1. If individuals in the same cluster are no more alike to each other than they are to individuals in a different cluster, then ρ is 0; at the other extreme, if in the same cluster each individual has the same value for TB (yes or no), and if this happens for all the clusters, then ρ is 1. ρ increases with the magnitude of the between-cluster variation σ_B^2 so it also increases as k increases.
Participation in the survey (Equation 5.7)	
x_1	Proportion of eligible individuals who are selected for inclusion in the survey and also participate in the survey.
Missing data on laboratory test results (Equation 5.8)	
x_2	Proportion of survey participants who have sufficient laboratory diagnostic test results.
Statistical theory underlying calculation of sample size for a simple random-sample survey (Annex 5.1)	
σ^2	Variance of the survey estimate p.
σ	Standard error of the survey estimate p.

TB: tuberculosis.
Rows highlighted in grey show the terms entered into one or more of Equation 5.1 to Equation 5.8. The total sample size N is calculated from Equation 5.1 to Equation 5.8 and is highlighted in orange.

5.3.3 Calculation of sample size for a simple random-sample survey

When conducting a TB prevalence survey, the sample size that would be required for a simple random-sample survey should be calculated first. The resulting sample size is then increased by a factor equal to the estimated design effect (see Section 5.3.4).

The method used to calculate the sample size required in a simple random-sample survey is presented in Box 5.1.

5.3.4 How to predict the size of the design effect

The following discussion of the design effect assumes that the number of eligible individuals included in the survey is the same in each cluster (as recommended in Section 5.4), even though in practice there will be some variations.

The design effect can be expressed in one of two ways:

i. using true population TB prevalence π, the coefficient of between-cluster variation k, and cluster size m (i.e. three things); or

BOX 5.1
METHOD USED TO CALCULATE THE SAMPLE SIZE REQUIRED FOR A SIMPLE RANDOM-SAMPLE SURVEY

The sample size N for a simple random-sample survey is calculated as:

$$N = 1.96^2 \frac{(1-\pi_g)}{d^2\pi_g} \qquad \text{(Equation 5.1)}$$

For the derivation of this equation, see **Annex 5.1**.

Thus, the sample size for a simple random-sample survey depends on two things: the required relative precision d, and the prior guess of true TB prevalence π_g.

An important implication of this equation is that the smaller the prior guess of true TB prevalence π_g, the larger is the sample size required to accurately estimate true TB prevalence. This is because the value of $(1 - \pi_g)/\pi_g$ increases as π_g becomes smaller.

Not surprisingly, the sample size also increases as the required relative precision d becomes smaller. This can be seen from **Equation 5.1**, because d is in the denominator. For an illustration of the use of **Equation 5.1**, see **Examples 5.1** and **5.2**.

Example 5.1 National TB prevalence survey of Cambodia, 2010–2011 *(3, 4)*

The prevalence of TB in 2010 was estimated to be 256 per 100 000 population among those aged 15 years and older (i.e. $\pi_g = 0.00256$), assuming that prevalence had fallen by 42% since the 2002 TB prevalence survey. The relative precision required was 25% (i.e. $d = 0.25$). Thus, the sample size N for a simple random-sample survey was calculated as follows:

$$N = 1.96^2 \frac{(1-0.00256)}{0.25^2 \times 0.00256} = 23\,949$$

Example 5.2 National TB prevalence survey of Ethiopia, 2010–2011 *(5, 6)*

The prevalence of smear-positive pulmonary TB in 2010 was estimated to be 200 per 100 000 in the total population (i.e. including children), so $\pi_g = 0.002$ in the total population. This was a "conservative" estimate compared with the one made by WHO for 2008, to allow for potential reductions in TB prevalence in the following years as a result of expansion of the directly observed treatment, short course (DOTS) strategy and other health service interventions. The target population for the prevalence survey was individuals aged 15 years and older, and it was estimated that 55% of the total population was in this age group. The relative precision required was 20% (i.e. $d = 0.2$).

The prevalence estimate of 200 per 100 000 was made using the assumption that the prevalence of TB was 0 in children aged below 15 years. This means that the prevalence of TB in the target population of individuals aged 15 years and older was estimated to be 200/0.55 per 100 000 = 364 per 100 000 (rounded up to the nearest whole number; i.e. $\pi_g = 0.00364$). Thus:

$$N = 1.96^2 \frac{(1-0.00364)}{0.2^2 \times 0.00364} = 26\,289$$

ii. using the intra-cluster correlation coefficient ρ, and cluster size m (i.e. two things).

Using (i), and assuming a constant cluster size m (i.e. the number of individuals from each selected cluster invited to participate in the survey is the same for each cluster), the design effect (DEFF) is calculated as:

$$DEFF = \left[1 + (m-1)\frac{k^2\pi}{(1-\pi)}\right] \quad \text{(Equation 5.2)}$$

Or, using (ii):

$$DEFF = [1 + (m-1)\rho] \quad \text{(Equation 5.3)}$$

For the derivation of these equations, please see **Annex 5.1.**

Although **Equation 5.3** is simpler than **Equation 5.2**, in this document, we will work with **Equation 5.2**. This is because it is easier to make a prior guess for k than it is to make a prior guess for ρ (this is linked to having a binary outcome variable: TB yes or no). When using **Equation 5.2**, we use our prior guess π_g as a substitute for π.

From **Equation 5.2**, it is clear that the larger the between-cluster variation (as measured by k), the larger the cluster size (m), and the higher the true population TB prevalence, the larger is the design effect.

From **Equation 5.3**, it is clear that the larger the intra-cluster correlation coefficient ρ and the larger the cluster size (m), the larger is the design effect.

These observations illustrate a crucial point about the size of the design effect. The design effect will be large if any one or a combination of the following apply:

- the prevalence of TB varies considerably among clusters, such that k is large;
- the number of eligible individuals who are invited to participate in the survey in each cluster is large, so that m is large; or
- the prevalence of TB is expected to be relatively high, so that π is relatively large.

The design effect can be predicted in one or both of two ways:

- from the results of previous surveys; or
- from an assessment of likely between-cluster variation (as measured by k) or an estimate of the intra-cluster correlation coefficient (ρ), and different choices of cluster size.

5.3.5 Estimating the design effect using previous survey results

If a previous survey has been done in the same country, the value of k or ρ from this prior survey can be used to provide an approximate estimate of the design effect, provided that:

- the way in which clusters are defined is the same in both surveys; and
- the magnitude of between-cluster variability has not changed since the first survey.

It is essential to consider whether clusters are defined in the same way whether the assumption about between-cluster variability is realistic. If not, then it is important to consider whether the between-cluster variability is likely to have increased or decreased, based on what is already known about changes in TB epidemiology and control since the first survey.

If there has not been a previous survey in the country, then estimates of k or ρ from surveys conducted in other similar countries, combined with existing knowledge of TB in the country being surveyed, can be used as a guide.

Table 5.2 shows examples of estimated coefficient of between-cluster variation k, estimated design effect and cluster size from national TB prevalence surveys conducted between 2007 and 2016.

5.3.6 Assessment of the likely design effect, given different combinations of the true population TB prevalence, cluster size and coefficient of between-cluster variation

As noted above, the design effect depends on three things: true population TB prevalence (π), the cluster size (m) and the coefficient of between-cluster variation in TB prevalence (k).

True population TB prevalence

A prior guess of the true population prevalence π_g must be made to calculate the sample size for a simple random-sample survey (see **Section 5.3.2**).

Cluster size

The choice of cluster size (i.e. the number of eligible individuals invited to participate in the survey from each selected cluster) and the number of clusters to be sampled must take into account both logistical and statistical issues.

Statistical issues

The number of sampled clusters must be both large enough to expect representative coverage of the total population and sufficient to provide a reliable estimate of between-cluster variation in true TB prevalence. **The number of clusters to be sampled should be no fewer than 30, with a strong recommendation to be at least 50. The cluster size should, in general, be no more than 800 eligible individuals**. In larger clusters, the design effect could be greater than 2 with moderately high TB prevalence (see **Table 5.2**) and/or the number of clusters (the total sample size divided by the chosen cluster size) could be below 50.

Logistical issues

The cluster size should be at least 400 eligible individuals and it should be feasible to complete data

Table 5.2

Estimated coefficient of between-cluster variation k, estimated design effect and cluster size (number of individuals invited to participate) from national TB prevalence surveys conducted between 2007 and 2016 *(7)*

COUNTRY	ESTIMATED k	ESTIMATED DESIGN EFFECT	CLUSTER SIZE
Bangladesh	0.5	1.6	800
Cambodia	0.6	2.5	640
China	0.5	1.4	1500
Democratic People's Republic of Korea	0.5	2.0	700
Ethiopia	0.4	1.3	550
Gambia	0.7	1.6	700
Ghana	0.7	2.0	650
Indonesia	0.5	1.8	500
Kenya	0.7	2.5	720
Lao People's Democratic Republic	0.7	3.2	800
Malawi	1.1	3.2	500
Mongolia	0.6	2.1	600 (city) / 500 (other)
Myanmar	0.7	3.2	710
Nigeria	0.7	2.6	700
Pakistan	0.6	2.4	1400
Philippines (2007)	0.6	2.1	600
Philippines (2016)	0.4	2.0	500
Rwanda	0.7	1.3	610
Sudan	1.1	2.7	800
Thailand	1.0	2.7	900
Uganda	0.8	2.5	580
Viet Nam	0.6	2.6	1500
Zambia	0.7	3.3	825
Zimbabwe	0.3	1.1	600

TB: tuberculosis.

collection for a cluster within a convenient time period (e.g. 1 or 2 weeks). It is **highly recommended to have a constant target cluster size** so that the number of eligible individuals invited to participate in the survey is very similar across the clusters.

A constant cluster size follows from the use of PPS sampling (for further details see **Section 5.4**) and is also the preferred approach from a logistical and analytical point of view. However, in some very specific contexts, the size of the cluster may be decided a priori to vary among strata; for example, if there is substantial variation in population density between urban and rural areas, or between different geographical areas.

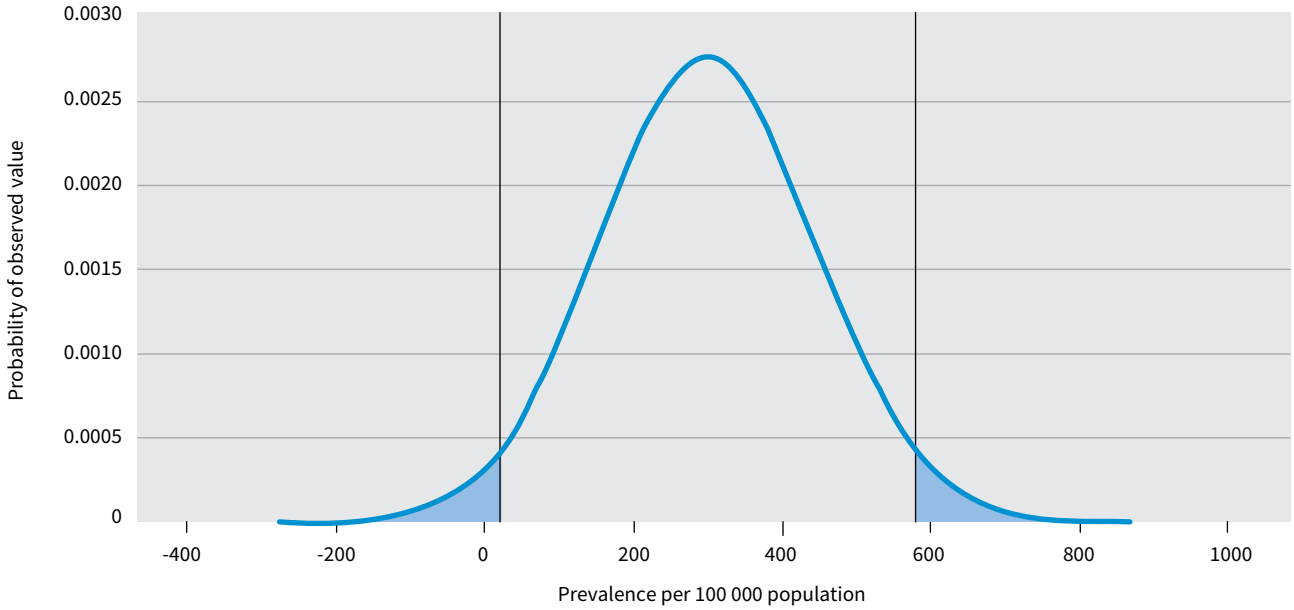
The coefficient of between-cluster variation

We now explain the definition of the coefficient of between-cluster variation k, illustrate it with an example, and then show how we can make a prior guess about its value. Additional mathematical detail is provided in **Annex 5.1**.

Suppose it is assumed that the variation of the true π_i (where π_i is the true TB prevalence in cluster i with the total population partitioned into clusters) follows a normal distribution, centred on the overall true TB prevalence π. Suppose also that the 2.5% and 97.5% centiles of the distribution of π_i, which define the usual 95% confidence interval around the overall true prevalence π, are at 0.2π and 1.8π respectively. If the π_i follow a normal distribution, then the 2.5% and 97.5% centiles are

Fig. 5.2

Normal density graph of true cluster-specific prevalences with mean 300 per 100 000 and standard deviation 0.48×300, for *k*= 0.48[a]



[a] Area under the curve is equal to 1.

at $\pi - 1.96SD$ and $\pi + 1.96SD$ and respectively, where SD is the standard deviation of the distribution. Thus, in this case, we have that $1.96SD = (\pi - 0.2\pi) = 0.8\pi$. If we now use σ_B to denote the standard deviation of the between-cluster variation in true TB prevalence, then $\sigma_B = {}^{0.8\pi}/_{1.96}$, which is approximately ${}^{0.8\pi}/_{2} = 0.4\pi$. We illustrate this idea in **Fig. 5.2**, with an example in which π = 300 per 100 000 population and the 2.5% and 97.5% centiles are at 20 (0.067π) and 580 ($1.933\ \pi$) per 100 000 population, respectively.

More generally and making no assumption about the shape of the distribution of the π_i around the true overall population prevalence π, we can express the standard deviation σ_B as a proportion λ, where $\sigma_B = \lambda\pi$.

The coefficient of variation, *k*, of the cluster-specific TB prevalences is defined as the standard deviation of the cluster-specific TB prevalences divided by the true overall population value. Thus, in the case of a TB prevalence survey:

$$k = \frac{\sigma_B}{\pi} \qquad \text{(Equation 5.4)}$$

Thus, if σ_B is estimated as $\lambda\pi$, then $k = {}^{\lambda\pi}/_{\pi} = \lambda$. This means that the coefficient of between-cluster variation k is simply a proportion (0.4 or 0.48 in the examples above). In particular, with this assumption, the value of k does not depend on the true overall population prevalence.

Based on the results of completed TB prevalence surveys, it is reasonable to assume that *k* will be at least 0.3 and perhaps as high as 0.8 (Table 5.2), and typically between 0.4 and 0.6.

To estimate k for a particular country, it is helpful to consider the plausible range in the true cluster-specific TB prevalence π_i, from the 2.5% centile to the 97.5% centile, and to assume that the variation of the π_i follows a normal distribution centred on the overall true TB prevalence π (even though the actual distribution of true cluster-specific TB prevalences may be more skewed, and not in fact follow a normal distribution).

For example, suppose that a prior guess of the overall true population prevalence of TB π_g is 300 per 100 000 population aged 15 years and older. Suppose also that it is considered that the true cluster-specific TB prevalence ranges from a 2.5% centile of around 20 per 100 000 population – that is, $0.067\pi_g = (1 - 0.933)\pi_g$, to a 97.5% centile of around 580 per 100 000 population – that is, $1.933\pi_g = (1 + 0.933)\pi_g$. This means that the range from the 2.5% centile to the 97.5% centile is from $\pi_g - 0.933\pi_g$ to $\pi_g + 0.933\pi_g$. Thus, assuming a normal distribution, we have that $1.96\sigma_B = 0.933\pi_g$ so that $1.96k = 0.933$, and $k = 0.48$.

In practice, clusters will usually be selected within strata, such as by urban/rural area or by geographical region of the country (see **Section 5.4.2**). This means that the likely between-cluster variation in true TB prevalence, and thus the value of k, could first be considered within each stratum. An average of the values of k across the strata would then give the overall survey k. This average will always be equal to or, most probably, smaller than the value of k calculated ignoring stratification. The latter is the most conservative and hence safest approach.

5.3.7 Final equation for the sample size, corrected for the design effect

Using **Equation 5.2** for the design effect (with prior guess π_g as a substitute for π), the final equation for the sample size corrected for the design effect is:

$$N = \left[1.96^2 \frac{(1-\pi_g)}{d^2\pi_g}\right] \times \left[1 + (m-1)\frac{k^2\pi_g}{(1-\pi_g)}\right]$$

(**Equation 5.5**)

Implications of different combinations of cluster size, true overall TB prevalence and coefficient of between-cluster variation for the magnitude of the design effect

Fig. 5.3 and **Table 5.3** illustrate the implications that different combinations of the true TB prevalence π, cluster size m and coefficient of between-cluster variation k have on the design effect. **The values of k (k = 0.4 in Fig. 5.3 and k = 0.6 in Table 5.3) have been chosen as two plausible values between 0.3 and 0.8.**

BOX 5.2
ESTIMATES OF BETWEEN-CLUSTER VARIATION k FROM THE NATIONAL TB PREVALENCE SURVEYS OF THE PHILIPPINES, 2016, AND KENYA, 2016

The Philippines, 2016 *(8, 9)*

In the analysis of the 2016 TB prevalence survey conducted in the Philippines, the design effect for bacteriologically confirmed was 2.0. The average number of participants per cluster who were aged 15 years and older was 500. Among individuals aged 15 years and older, the prevalence of bacteriologically confirmed TB was 1159 per 100 000 population. The value of k was estimated to be 0.4.

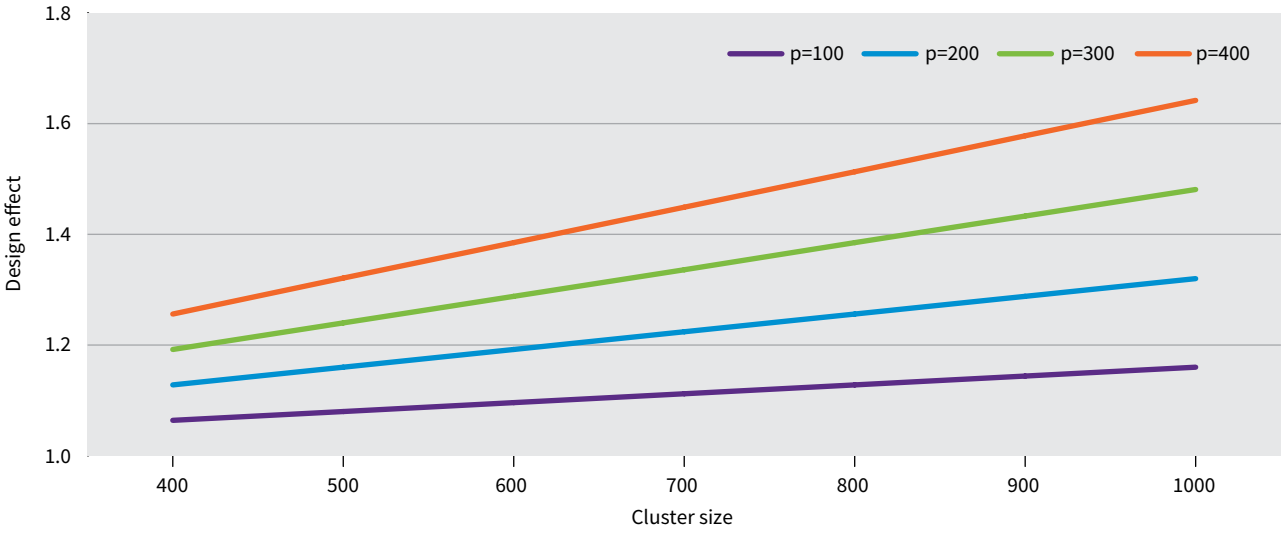
Kenya, 2016 *(10)*

In the analysis of the 2016 TB prevalence survey conducted in Kenya, the design effect for bacteriologically confirmed TB was 2.5. The average number of participants per cluster aged 15 years and older was 630, and the prevalence of bacteriologically confirmed TB was 558 per 100 000 population. From the formula relating the design effect to population TB prevalence, cluster size and k, the estimated value of k was 0.70.

Based on the results of completed TB prevalence surveys, it is thus reasonable to assume that k will be at least 0.3 and possibly as high as 0.8. In planning the sample size for new TB prevalence surveys, we recommend assuming that k will be between 0.4 and 0.6; that is, between the two extremes illustrated here.

Fig. 5.3

Design effect for different combinations of TB prevalence p (per 100 000 population aged ≥15 years) and cluster size m when k = 0.4



TB: tuberculosis.

Table 5.3

Design effect for different combinations of true TB prevalence π (per 100 000 population aged ≥15 years) and cluster size m when $k = 0.6$

CLUSTER SIZE	TB PREVALENCE (PER 100 000 POPULATION)					
	100	150	200	250	300	400
400	1.144	1.216	1.288	1.360	1.432	1.577
500	1.180	1.270	1.360	1.450	1.541	1.721
600	1.216	1.324	1.432	1.540	1.649	1.866
700	1.252	1.378	1.504	1.631	1.757	2.011
800	1.288	1.432	1.576	1.721	1.866	2.155

TB: tuberculosis.

5.3.8 Examples of how to predict the design effect based on (i) π_g, m and k, and (ii) m and ρ

In 2010, the design effect was predicted for two surveys due to be implemented in 2010–2011: one in Ethiopia *(5, 6)* and one in Cambodia *(3, 4)*. The prediction of the design effect in these two surveys, based on cluster size and assumptions about π_g and either k or ρ, is illustrated in **Box 5.3**.

5.3.9 Finite population correction

Having adjusted the sample size for the design effect, strictly speaking the next step in the calculation of the final sample size should be to account for the fact that, in a national-level population survey, sampling is being done from a finite (although very large) population of eligible individuals in the country. This correction is done because sampling from a finite population results

BOX 5.3
PREDICTING THE DESIGN EFFECT FROM NATIONAL TB PREVALENCE SURVEYS OF ETHIOPIA AND CAMBODIA, 2010–2011

Ethiopia, 2010–2011 *(5, 6)*

The prevalence of TB was estimated to be approximately 364 per 100 000 population among adults aged 15 years and older in Ethiopia. The cluster size was planned as 550. With k assumed to be 0.5, the design effect (DEFF) was estimated, using **Equation 5.2**, as:

$$DEFF = 1 + (550 - 1)\frac{0.5^2 \times 0.00364}{(1 - 0.00364)} = 1.5014$$

Assuming a simple random-sample survey, the sample size required was 26 289 (see **Box 5.1**). With a design effect of 1.5014, the sample size needed to be increased to 26 289 x 1.5014 = 39 471.

Note that this calculation of the estimated design effect should be repeated for a range of plausible values of k – for example, for each of $k = 0.4$, $k = 0.5$ and $k = 0.6$; $k = 0.5$ is used here for illustration.

Cambodia, 2010–2011 *(3, 4)*

From the analysis of the 2002 TB prevalence survey, the intra-cluster correlation coefficient (ρ) was estimated to be 0.000342. For the 2010–2011 TB prevalence survey, a conservative assumption was made that the intra-cluster correlation coefficient would be approximately two times higher. This assumption was made after careful consideration of likely changes in TB epidemiology and variation in TB prevalence across the country since 2002. With an estimated prevalence of TB of 256 per 100 000 individuals aged 15 years and older, and with a cluster size of 640 individuals aged 15 years and older, the design effect (DEFF) was estimated, using **Equation 5.3**, as:

$$DEFF = 1 + (640 - 1) \times 0.00075 = 1.4793$$

Thus, the sample size needed to be increased from 23 949 (as estimated in **Box 5.1** assuming a simple random-sample survey) to 23 949 x 1.4793 = 35 428.

in less uncertainty about the estimate of true population TB prevalence, compared with a situation in which the survey estimate is to be used to make a prediction about TB prevalence in another setting or in the future.

However, although the so-called "finite population correction" is a standard and well-established method in the theory of sample surveys, in practice it makes only a very small difference to the total sample size in the context of a national TB prevalence survey. Thus, we recommend that, for simplicity, the finite population correction is **not** made. However, for completeness we show here the formula that can be used to make this correction:

$$N_{FPC} = \frac{N}{1 + \frac{N-1}{T}} \quad \text{(Equation 5.6)}$$

where N is the number of people to be sampled as calculated from **Equation 5.5**, T is the total population of eligible individuals in the country, and N_{FPC} is the sample size if the finite population correction is made.

5.3.10 Allowing for the participation rate (or non-participation rate)

In a field survey, it is expected that some people will either not attend the initial screening at all or will drop out during the survey. The next step in the sample size calculation, after adjusting for the design effect, is to increase the sample size to allow for non-participation in the survey. The calculation is straightforward. If the proportion of eligible individuals who participate in CXR screening and symptom screening in each of the sampled clusters is expected to be a proportion x_1, and the sample size after allowing for the design effect is N, then the sample size must be increased to:

$$\frac{N}{x_1} \quad \text{(Equation 5.7)}$$

For TB prevalence surveys, the value of x_1 is typically assumed to be 85–90% (i.e. 0.85–0.90 if expressed as a proportion). In other words, it is assumed that 10–15% of eligible individuals will not participate in the symptom screening survey and/or will not attend for CXR screening.

Two examples that illustrate how to adjust the sample size for the expected participation rate are provided in **Box 5.5**.

5.3.11 Allowing for missing laboratory diagnostic test results

It is expected that laboratory diagnostic test results will not be available for all survey participants who screen positive and are thus eligible to submit sputum samples for TB diagnosis. This could be due to sputum samples not being collected or being lost, Xpert test results being invalid, or culture test results being contaminated. Even though missing data can be handled at the analysis level (**Chapter 17**), such analysis requires assumptions and it is important to limit the amount of missing data on diagnostic test results. The final step in the sample size calculation is to increase the sample size obtained in **Section 5.3.10** to allow for missing diagnostic test results among survey participants who screen positive on TB symptom or CXR screening. This calculation is also straightforward and similar to the participation rate adjustment. If the proportion of screen-positive survey participants with sufficient Xpert and culture test results is expected to be a proportion x_2, and the sample size obtained in **Section 5.3.10** is N, then the sample size must be increased to:

BOX 5.5
ADJUSTING FOR THE EXPECTED PARTICIPATION (OR NON-PARTICIPATION) RATE: EXAMPLES FROM THE NATIONAL TB PREVALENCE SURVEYS OF ETHIOPIA AND CAMBODIA, 2010–2011

Ethiopia, 2010–2011 ***(5, 6)***

It was assumed that 85% of eligible individuals would participate in the survey. From **Box 5.3**, the total sample size required was 39 471 not allowing for non-participation. Thus, the target sample size of eligible individuals, assuming that 85% of eligible individuals participate in the survey, is 46 435 (39 471/0.85).

With the target cluster size for eligible individuals aged 15 years and older kept at 550, this means that 85 clusters (46 435/550, rounding up to the nearest whole number) need to be selected.

Cambodia, 2010–2011 ***(3, 4)***

It was assumed that 90% of eligible individuals would participate in the survey, based on a very high participation rate of 96% in the 2002 TB prevalence survey. From **Box 5.3**, the total sample size required was 35 428, not allowing for non-participation. Thus, the target sample size of eligible individuals, assuming that 90% of eligible individuals participate in the survey, is 39 364 (35 428/0.90).

With the target cluster size for eligible individuals aged 15 years and older kept at 640, this means that 62 clusters (39 364/640 clusters, rounding up to the nearest whole number) need to be selected.

$$\frac{N}{x_2} \quad \text{(Equation 5.8)}$$

For TB prevalence surveys, we assume that the value of x_2 is typically 85–90% (i.e. 0.85–0.90 if expressed as a proportion). In other words, it is assumed that 10–15% of sputum-eligible individuals (those who screened positive on TB symptom or CXR screening) will not have sufficient Xpert or culture test results for them to be classified as a survey case (prevalent TB=Yes) or not a survey case (prevalent TB=No).

5.3.12 Final calculation of sample size

All of the prior guesses made to plan the total sample size (anticipated TB prevalence, design effect and proportion of eligible individuals who participate fully in the survey) may be wrong to a greater or lesser degree. The important thing is always to err on the side of caution. If the sample size is too big, it will cost more, but a good result will be obtained; if the sample size is too small, it will cost less, but the resulting estimate may be too inaccurate to be of any use.

It is always important to consider different scenarios; that is, different combinations of the prior guess of true TB prevalence π_g, required precision d, the coefficient of between-cluster variation k, cluster size m, the participation rate x_1 and the complete laboratory test results rate x_2.

In conclusion, sample size should be determined following a feasible scenario for which there is a high level of confidence that true population TB prevalence will be estimated with a relative precision of between 20% and 25%.

In Table 5.4 we illustrate different plausible scenarios using the example of the 2010–2011 national TB prevalence survey of Ethiopia *(5, 6)*. We show the required sample size for each of d = 0.20 and d = 0.25; for three values of the prior guess of true TB prevalence π_g – 300, 364 and 400 per 100 000; and for three values of the prior guess of k – 0.4, 0.5 and 0.6.

In this example from Ethiopia, cluster size is considered fixed at 550 (from a logistical perspective, this cluster size can be completed in 1 week); this cluster size means that even with a true TB prevalence of 400 per 100 000 population and k = 0.6, the design effect is still less than 2 (from Table 5.3).

The prior guess of the participation rate is also fixed at 85%, as assuming a value any higher than this could be overly optimistic.

5.4 Selection of clusters and individuals within clusters

Once the total sample size has been calculated and the size of each cluster defined (as explained in Section 5.3), the sample size is divided by the assumed cluster size to calculate the total number of clusters to be sampled.

The clusters to be sampled then need to be selected. Cluster selection requires three major steps. The first is to decide on a locally appropriate definition of a cluster. The second is to consider whether or not to stratify the country into a limited number of strata (e.g. urban/rural; north/south). The third step is to select clusters, either from within each stratum (if applicable) or from the whole country. These steps are explained in the next three subsections.

5.4.1 Definition of a cluster

The definition of cluster needs to be adapted for each country. In all cases, however, **a cluster is any well-defined geographical area of similar population size**. Clusters typically use as their building blocks census EAs, villages or towns.

5.4.2 Stratification

If the prevalence of TB can be assumed to be similar across a country, then the sampling of clusters can be done randomly from all over the country. In practice, however, there will usually be geographical variation in

Table 5.4

Sample size required for different scenarios according to various values of true TB prevalence, the coefficient of between-cluster variation k and choice of relative precision d, and assuming a cluster size of 550 individuals aged 15 years and older, national TB prevalence survey of Ethiopia, 2010–2011 *(5, 6)*

TB PREVALENCE (PER 100 000 POPULATION)	RELATIVE PRECISION					
	d = 0.20			d = 0.25		
	k = 0.4	k = 0.5	k = 0.6	k = 0.4	k = 0.5	k = 0.6
300	47 475	53 057	59 881	30 384	33 957	38 324
364	40 853	46 435	53 259	26 146	29 719	34 086
400	38 059	43 642	50 465	24 358	27 931	32 298

TB: tuberculosis.

the prevalence of TB. For example, the prevalence of TB can be different in urban and rural settings or between the northern and southern areas of a country. If geographical variation is thought to exist, a "stratified" design should be used to increase the precision of the overall national estimate of prevalence.

In a stratified design, the number of clusters allocated to each stratum should be proportional to the share of the national population accounted for by each stratum. For example, if the country is stratified into urban and rural areas, and 40% of the country's population live in urban areas and the remaining 60% in rural areas, then 40% of the total number of clusters required should be sampled from urban areas and the remaining 60% from rural areas. A word of caution: the prevalence estimates for each stratum will not be as accurate as the eventual overall estimate and should be interpreted with caution. The only objective of calculating sample size should be to achieve a reliable (precise and representative) estimate of the overall true population prevalence of TB, and not to also obtain reliable estimates of prevalence within each stratum.

The use of a stratified design is encouraged even for countries where small differences among geographical regions are anticipated, or when little information is available about regional variability in TB prevalence.[1] When clusters are allocated to strata in proportion to the size of each stratum, a stratified design ensures a balanced and fair geographical coverage of the country.

5.4.3 Selection of clusters

Once a decision is made about whether to use stratification, determining which clusters are selected requires a formal approach.

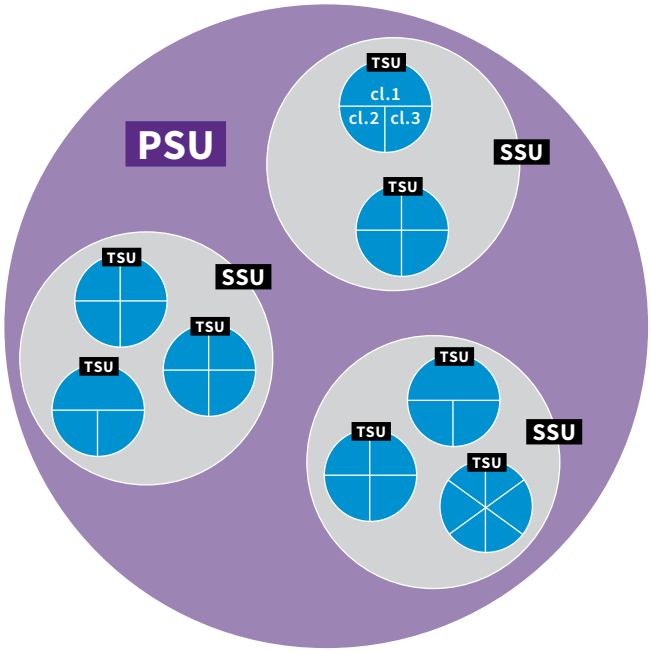
In the first instance, survey teams should identify any areas of the country that are not reachable; for example, areas where security is a concern, remote islands or areas where roads are nonexistent. It is then advisable to exclude these areas from the original sampling frame (see **Example 5.3**). This approach does, of course, limit the representativeness of the sample, and **should be reserved only for situations in which there are serious safety or feasibility concerns**. The larger the population in these excluded areas, as a proportion of the total population, the less representative the survey estimate will be of the country as a whole. The larger the excluded areas become, the more the survey estimates describe subnational estimates of TB disease prevalence and should be disseminated as such.

Clusters are selected at random from larger areas such as cities or local geopolitical units (these have different names in different countries – e.g. zones, states, regions, districts and departments). Cluster selection is typically a multistage process, particularly in large countries (see **Fig. 5.4**). It may start with the selection of large primary sampling units (PSUs), followed by smaller secondary sampling units (SSUs), and so on until the level of geographical areas comprising only clusters is reached (see **Example 5.3**). The number of stages will vary by country and will depend on how the country is divided administratively and the smallest administrative level for which data on population size are available to use as the PSU.

Survey teams can also be faced with a situation where some selected clusters are not reachable, for reasons which were unknown at the time of cluster selection. Survey protocols should clearly state how the selection of further clusters to replace the unreachable clusters will be done. One suggestion is to replace a cluster with another that is selected from the same "next-higher-level" sampling unit. For example, in the Cambodia 2010–2011 *(3, 4)* prevalence survey, the PSU was a district and the SSU was a commune. Thus, if a commune

Fig. 5.4

Schematic representation of multistage sampling[a]



cl: cluster; PPS: probability proportional to size; PSU: primary sampling unit; SSU: secondary sampling unit; TSU: tertiary sampling unit.

[a] Assume we selected the PSU (in **purple**) according to PPS (see **Example 5.3** for how to do this), from which we would like to select one cluster. Within this PSU, we first need to select an SSU (in **grey**) according to PPS. Within the selected SSU, we need to select a TSU (in **blue**) according to PPS. We have data on how many clusters there are within the selected TSU. From these, we randomly select a single cluster (e.g. one of cl.1, cl.2 or cl.3). The cluster is selected using simple random sampling when clusters are of approximately equal size, or using PPS when clusters differ greatly in size. From the selected cluster, the "target" number of eligible individuals, equal to the selected cluster size, is included in the survey.

[1] It should be highlighted that even if notifications are similar across regions, use of stratified sampling is still advisable. Geographical variation in notifications will be an inaccurate reflection of geographical variation in TB prevalence when there is variation in factors such as access to care and reporting quality.

was not reachable, it was replaced with another commune (selected at random) from the same district.

Population data, typically collected during nationwide censuses, are critical for setting up the sampling frame. At each stage when a sampling unit is selected, the probability of a unit being selected should be proportional to its population size. This is termed PPS sampling. **A major advantage of using a fixed cluster size in conjunction with PPS is that, at the analysis stage, it is possible to use a self-weighting approach without any need to apply population weights** (see also **Chapter 17**). However, to ensure buy-in from local governments and political leaders, as well as cover all areas in a country, clusters are sometimes allocated to, as opposed to sampled from, large geopolitical units, ensuring all these units are represented in the survey (see **Example 5.4**). During the last stage of selecting a cluster, all possible clusters within the sampling frame are listed, and one cluster is randomly selected. At this last stage, if the clusters vary considerably in their population size, which might be the case with towns and villages, then the cluster is selected with PPS. If the clusters are similar in their population size, which is expected if EAs are used as the clusters and may also be the case with villages, then one cluster is selected with simple random sampling – that is, each cluster has the same probability of being selected at the final stage.

5.4.4 Selection of individuals within clusters

After a cluster is selected, cluster areas in which, for example, schools, military barracks or prisons are located must be immediately identified and excluded according to the survey protocol (see **Chapter 2** and **Chapter 13**). Once this is done, the target number of eligible individuals per cluster (as decided previously in the sample size calculation) needs to be identified and invited to participate in the survey. The actual number identified and invited to participate in the survey needs to be as similar as possible for each cluster.

The total number of eligible individuals identified within each cluster could be either lower or higher than the target cluster size selected for the sample size calculation. The following is advised:

a. If the cluster size is lower than the target size, then a neighbouring cluster must be randomly selected and combined with the one initially selected in order to reach the target size.

b. If the cluster size is only slightly higher than the target size (as a rule of thumb, 10% of the selected cluster size could be allowed), the survey team might need to include the few extra individuals in the survey to ensure buy-in from the local community.

c. If the cluster size is much higher than the target size, then a subset of cluster individuals equal to the target number must be randomly selected.

In scenarios a) and c), a subset of eligible individuals from a cluster should be selected, either from a neighbouring cluster (in addition to the cluster originally selected), or from within the original cluster. This can be done by dividing a cluster into household groups using existing divisions between households, such as paths, roads or natural boundaries. Household groups should then be selected at random until the target cluster size is reached. One way to do this is to select the first household group at random, and then subsequent household groups can be added in a randomly selected direction (e.g. clockwise from the first household group), until the target size is reached. It is recommended that this random selection is fair and transparent and involves the community by means of an open meeting at which the household groups will be selected. Inviting community members to participate in this selection process, and explaining the random (and hence fair) aspect of it, helps to ensure community buy-in.

Example 5.3 and **Example 5.4** include all aspects of the sampling approach used in TB prevalence surveys, as outlined in this chapter: stratification, multistage sampling, PPS and selecting individuals within clusters.

Example 5.3. PPS multistage cluster sampling in Cambodia, 2010–2011

Cambodia conducted a repeat prevalence survey in 2010–2011 *(3, 4)*; the first survey was conducted in 2002 *(11)*. In the repeat survey, 62 clusters were sampled from across the country. Clusters were stratified into 13 from urban areas and 47 from rural areas selected from districts included in the 2002 survey *(11)*, plus two clusters from the remaining areas of the country. These last two clusters were sampled from districts that were excluded from the 2002 survey because of security concerns. Cambodia has four administrative geopolitical levels: provinces, districts, communes and villages. Districts were selected as the PSUs, to be consistent with the first survey, and they were sampled by PPS. Communes were selected as the SSUs and were sampled from within each district by PPS. Finally, villages within each of the selected communes were selected with simple random sampling, on the assumption that villages within the same commune are similar in terms of their population size. Therefore, a village was the sampling unit (cluster) in the Cambodian survey *(3, 4)*.

The steps required to select the 13 districts from urban areas using PPS are listed below. They refer to **Table 5.5** at the end of this example. **Exactly the same logic applies every time PPS is used**.

Steps in applying PPS sampling

1. List all urban districts in random order, (Column A) with their population aged 15 years and older (Column B).
2. Calculate the cumulative population (Column C). The number in the final row of this column is the total

population aged 15 years and older of the urban areas. In this example, the total urban population aged 15 years and older is 1 909 749.

3. Determine the number of districts that will be sampled, in this example 13.
4. Divide the total population (1 909 749, the final figure in Column C) by the number of districts to be sampled (in this case 13). The result (146 903) is called the "sampling interval" (SI).
5. Choose a number between 1 and the SI at random. This is the random start (RS). In this example, the RS was 127 785. Choosing the RS can be done in a number of ways; for example, with the RANDBETWEEN function in Microsoft Excel – RANDBETWEEN(1,146903) will return a randomly chosen number between 1 and the SI. The equivalent function in Stata is runiformint(1,146903), and in R is sample(1:146903,1).
6. Calculate the following series of 13 cumulative population points: RS; RS + SI; RS + 2SI; RS + 3SI; RS + 4SI; RS + 5SI; RS + 6SI; RS + 7SI; RS + 8SI; RS + 9SI; RS + 10SI; RS + 11SI; RS + 12SI.
7. For example, RS + 2SI = 127 785 + 2 × 146 903 = 421 591.
8. Each of these 13 numbers corresponds to a district on the list. The districts selected are those for which Column C, the cumulative population, contains the numbers in the series calculated in Step 6.

With a starting point of 127 785 and an SI of 146 903, we identified cumulative population points and their corresponding districts as described in Step 6 and, continuing in this manner, the desired number of districts was selected.

Selected cumulative population points

1. Cumulative population point included in 1st selected district:
   RS = 127 785 → district 5
2. Cumulative population point included in 2nd selected district:
   RS + SI = 274 688 → district 9
3. Cumulative population point included in 3rd selected district:
   RS + 2 × SI = 421 591 → district 16
4. Cumulative population point included in 4th selected district:
   RS + 3 × SI = 568 494 → district 23
5. Cumulative population point included in 5th selected district:
   RS + 4 × SI = 715 397 → district 29
6. Cumulative population point included in 6th selected district:
   RS + 5 × SI = 862 300 → district 30
7. Cumulative population point included in 7th selected district:
   RS + 6 × SI = 1 009 203 → district 30 (note district 30 has been selected twice, which means two clusters will be sampled from it)
8. Cumulative population point included in 8th selected district:
   RS + 7 × SI = 1 156 106 → district 32
9. Cumulative population point included in 9th selected district:
   RS + 8 × SI = 1 303 009 → district 34
10. Cumulative population point included in 10th selected district:
    RS + 9 × SI = 1 449 912 → district 35
11. Cumulative population point included in 11th selected district:
    RS + 10 × SI = 1 596 815 → district 36
12. Cumulative population point included in 12th selected district:
    RS + 11 × SI = 1 743 718 → district 41
13. Cumulative population point included in 13th selected district:
    RS + 12 × SI = 1 890 621 → district 46

Example 5.4. Multistage cluster sampling in Nigeria, 2012 *(12)*

Nigeria conducted a national prevalence survey to start in 2012. They sampled 49 000 individuals to achieve a relative precision of 20% for the actual population prevalence. Seventy clusters of 700 participants each needed to be selected. The country is split into six geopolitical zones. The 2006 national population census estimated the total population as 140 million in 37 states, 774 local government areas (LGAs) and about 89 280 EAs. On average, a state has a population of 3.8 million, an LGA about 188 000, and there are about 1568 people in an EA. A single EA comprises a cluster.

A multistage sampling approach was used:

- Stratification: The first stage involved stratifying the country into the six geopolitical zones. The 70 clusters were divided into the six geopolitical zones proportional to population size. Eighteen clusters were allocated to Zone A, 10 to Zone B, 9 to Zone C, 11 to Zone D, 8 to Zone E and 14 to Zone F.
- Stage 1: To facilitate nationwide participation and support, at least one cluster was chosen from each of the 37 states. The remaining 33 clusters were chosen from each state according to population size. This approach approximates PPS sampling.
- Stage 2: In each state, all available LGAs were listed and the required number of them were sampled using PPS sampling.
- Stage 3: In each selected LGA, all available EAs were listed. Since EAs are defined to have similar population sizes (EAs are equivalent to the clusters in **blue** shown in **Fig. 5.4**), one of them was selected using simple random sampling. The EA is then the "clus-

Table 5.5

Selected districts from urban areas using PPS sampling, for the national TB prevalence survey of Cambodia, 2010–2011

In this example, the number of districts to be sampled is 13, the sampling interval was 146 903 and the random start was 127 785.

COLUMN A	COLUMN B	COLUMN C	COLUMN D
DISTRICT	DISTRICT POPULATION AGED ≥15 YEARS	CUMULATIVE POPULATION	CUMULATIVE POPULATION POINT SELECTED FOR SAMPLING
1	15 598	15 598	
2	5 621	21 219	
3	61 372	82 591	
4	43 075	125 666	
5	86 189	211 855	127 785
6	15 139	226 994	
7	27 057	254 051	
8	16 230	270 281	
9	9 326	279 607	274 688
10	12 933	292 540	
11	34 628	327 168	
12	10 356	337 524	
13	30 630	368 154	
14	5 504	373 658	
15	32 595	406 253	
16	22 550	428 803	421 591
17	6 513	435 316	
18	22 197	457 513	
19	6 074	463 587	
20	28 240	491 827	
21	44 411	536 238	
22	9 073	545 311	
23	60 187	605 498	568 494
24	3102	608 600	
25	8 285	616 885	
26	15 724	632 609	
27	4 608	637 217	
28	20 034	657 251	
29	146 651	803 902	715 397
30	206 103	1 010 005	862 300, 1 009 203
31	89 208	1 099 213	
32	91 961	1 191 174	1 156 106
33	128 334	1 319 508	
34	101 328	1 420 836	1 303 009
35	137 411	1 558 247	1 449 912
36	74 527	1 632 774	1 596 815
37	10 587	1 643 361	
38	13 073	1 656 434	
39	15 044	1 671 478	
40	3 411	1 674 889	
41	117 627	1 792 516	1 743 718
42	3 966	1 796 482	
43	65 045	1 861 527	
44	12 498	1 874 025	
45	10 260	1 884 285	
46	11 663	1 895 948	1 890 621
47	3 156	1 899 104	
48	10 645	1 909 749	

PPS: probability-proportional-to-size.

ter", from which a target number of individuals were included in the survey.

- Stage 4: In each EA, all households were visited, and eligible individuals invited to participate in the survey.
  - In situations where the population of eligible participants was less than 650, a part of the next adjoining EA was included in the cluster to reach the target of 700.
  - In situations where the population of eligible participants was up to 750, all these participants were included in the survey.
  - In situations where the population of eligible participants was greater than 750, the target of 700 was randomly selected using blocks of household groups.

5.4.5 Subnational estimates

Countries that implement a national TB prevalence survey are also likely to want to obtain subnational estimates; for example, at the provincial or regional level.

It is important to highlight that the primary objective of a national TB prevalence survey is to obtain a reliable estimate of the prevalence at national level. Any steps in the design of the survey, as previously described, should apply at national level only.

In countries where subnational estimates are part of the secondary objectives of the national TB prevalence survey, additional clusters could be included in one or more specific subnational levels to increase the precision of the subnational estimates. It is important to note that this should be done only after all the steps described above, including the sample size calculation and the selection of the clusters, have been completed for the primary objective.

The number of clusters to be added at the subnational level (based on the number of individuals who will be invited to participate in the survey) could be determined using **Equation 5.1** to **Equation 5.8** to obtain a reasonable level of precision around the subnational estimate. The level of precision for the subnational estimate will be lower than for the national estimate (so the value of the relative precision will be higher for the subnational estimate than for the national estimate).

It is important to keep in mind that adding more clusters will increase the cost and the logistical requirements of the survey. In addition, the increased complexity at the subnational level that this secondary objective will bring may also have a detrimental impact on the quality of the national survey and so have a detrimental effect on the overall estimate of TB prevalence. For example, the increased number of samples to be collected, transported and tested, and the increased amount of data to be collected and entered, may lower the overall quality of the survey.

In conclusion, subnational estimates can be considered as a secondary objective of a national prevalence survey, but the feasibility, risks and higher costs must be considered carefully when writing the protocol.

5.5 Definition of the eligible survey population

A very important aspect of sampling design for prevalence surveys is the definition of the eligible population that contributes towards the target cluster size. As described in **Chapter 3**, the eligibility of an individual is based on two things:

- age (aged ≥15 years); and
- residency status in the household (e.g. people living in the household for the past 4 weeks or a period equal to the time window between the pre-census and census visits – see **Chapter 13**). The definition of residency status ensures that individuals who move into the household because of the survey, in anticipation of receiving access to health care, are excluded.

Eligible individuals (the ideal survey population representative of the target population) can be divided into two groups: those who actually participate (the observed survey population), and those who do not participate in the survey. The closer the *participant* population is to the *eligible* population, the better the inference on TB disease prevalence that can be drawn from the survey.

All eligible individuals should be invited to participate in the survey. It is likely that some people will not be found at home at the time of the mini-census; that is, the census of the population in the selected cluster (see **Chapter 13**). Furthermore, of those found and invited, some will not attend for screening and some will not give their consent to participate in the survey. **It is imperative to enumerate all eligible individuals and classify them as "survey participant", "absent" or "did not consent to participate"**. This will allow the survey team to identify any systematic biases in the sampled population (e.g. young men of working age who are away at work during survey operations). It is essential that biases are documented so that the results of the survey can later be interpreted in the context of these biases.

It is also important to enumerate and collect basic demographic information from both children aged below 15 years and individuals who do not meet the definition of residency. The former will allow the survey team to adjust the TB prevalence estimate for demographic changes in the population compared with the last available demographic data, while the latter allows an insight into the mobility of the population in the country.

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Annex 5.1 Sample size calculation for a simple random sample survey, and definition and estimation of the design effect

This annex is designed for readers who would like to have a deeper understanding of the mathematical principles that underpin calculation of the sample size for a simple random sample survey, and the size of the design effect.

1. Sample size calculation assuming a simple random sample survey is to be done

If the number of people included in the survey is denoted by N and the number of TB cases found in the survey is t then: The point estimate of the true prevalence of TB will be estimated from the survey as:

$$p = \frac{t}{N} \qquad (1)$$

and the variance of the survey estimate p is given by the usual binomial expression

$$\sigma^2 = \frac{\pi(1-\pi)}{N} \qquad (2)$$

And the standard error by

$$\sigma = \sqrt{\frac{\pi(1-\pi)}{N}} \qquad (3)$$

The 95% confidence interval for the prevalence of TB is calculated as:

$$[p - 1.96\sigma; p + 1.96\sigma] \qquad (4)$$

It is thus clear that, the greater is the required precision (i.e. the narrower is the required width of the 95% confidence interval), the bigger must be the sample size N.

The next step is thus to define the relative precision that is required. We can denote this as $d\pi$, where d is a proportion and π is the population prevalence of TB. For example, if the required relative precision is 0.2 (20%) then $d\pi = 0.2\pi$; if the required relative precision is 0.25 (25%) then $d\pi = 0.25\pi$.

We are then requiring that:

$$1.96\sqrt{\frac{\pi_g(1-\pi_g)}{N}} = d\pi_g \qquad (5)$$

Where π_g is our "prior guess" of the true TB prevalence. If we re-arrange this equation, we obtain

$$N = 1.96^2 \frac{(1-\pi_g)}{d^2\pi_g} \qquad (6)$$

as the required total sample size, depending on the required d and prior guess of TB prevalence π_g.

2. Design effect correction to sample size calculation, due to cluster sample survey design

In a cluster sample survey, the total population is partitioned into "clusters" of individuals, for example into towns and villages. As explained in Section 5.3, "clusters" are selected at random from the total population of clusters, usually in a multistage process, and then a random sample of individuals from each selected cluster is included in the TB prevalence survey.

The extra uncertainty about the true prevalence of TB due to a cluster sample survey design, compared with a simple random sample survey design, is called the "design effect".

It is assumed in the following discussion of the design effect that the number of eligible individuals included in the survey is the same in each cluster, though in practice some clusters may include a higher number of individuals than the target. A constant cluster size (in terms of eligible individuals included in the survey) follows from the use of PPS sampling and is the preferred approach from a logistical (and analytical) point of view.

To estimate the design effect, an estimate of either:

i. The between-cluster variation in true TB prevalence σ_B^2,

   or

ii. The correlation between individuals in the same cluster for whether or not they have TB, i.e. the intra-cluster correlation coefficient ρ.

is required. Technically, they are equivalent but one (σ_B^2) is an absolute measure and the other (ρ) is relative and constrained to be between 0 and 1. If individuals in the same cluster are no more alike to each other than they are to individuals in a different cluster, then ρ is 0; at the other extreme, if in the same cluster each individual has the same value for TB (yes or no), and this occurs for all clusters, then ρ is 1.

From the perspective of (i), we are considering that the true prevalence of pulmonary TB varies among clusters, and thus that observed variation in the prevalence of pulmonary TB between clusters is not just due to sampling variation. We can represent this by assuming that the true prevalence in cluster i is π_i, that the true prevalence averaged over all clusters in the country's population is π, and that the variation of the π_i about the overall prevalence π is σ_B^2. Such variation in the true prevalence of TB between clusters is termed "over-dispersion".

In the literature on how over-dispersion can be modelled, the simplest way in which this can be done is to assume that

$$\sigma_B^2 = \Phi\pi(1-\pi) \quad (7)$$

where Φ is an unknown scale parameter that takes a value ≥0 and π is the true overall prevalence, averaging across all clusters in the population [Collett, 2003]. With this framework, and with all clusters having the same number of eligible individuals included in the survey, it can be shown that the variance of the survey estimate p is equal to:

$$\frac{\pi(1-\pi)}{N}[1+(m-1)\Phi] \quad (8)$$

where m is the number of eligible individuals included in the survey from each cluster (cluster size) and N is the total sample size. Comparing this with equation (2), we can see that the variance of the survey estimate p is increased by a factor of $[1+(m-1)\Phi]$, and it is this factor that is termed the "design effect".

From the perspective of (ii), the intra-cluster correlation, the variance of the survey estimate p can be shown [Collett, 2003] to be:

$$\frac{\pi(1-\pi)}{N}[1+(m-1)\rho] \quad (9)$$

Thus ρ can be equated to Φ, and so we can also represent the between-cluster variation as:

$$\sigma_B^2 = \rho\pi(1-\pi) \quad (10)$$

Or, equivalently

$$\rho = \frac{\sigma_B^2}{\pi(1-\pi)} \quad (11)$$

and the design effect as:

$$DEFF = [1+(m-1)\rho] \quad (12)$$

3. Estimation of the design effect in terms of k, the coefficient of variation

From section 2. above, an estimate of ρ or σ_B^2 is required to make a "prior guess" about the value of the design effect. With a binary outcome, such as TB yes or no, it is easiest to think in terms of σ_B^2, the between-cluster variation. It also turns out to be easiest to make a prior guess as to the value of σ_B^2 in terms of the coefficient of variation k, because k (like ρ) is a relative measure (although it is not constrained to be less than 1).

The coefficient of variation, k, of the cluster-specific TB prevalences is defined as standard deviation (SD) / true overall population value, and thus in the case of a TB prevalence survey,

$$k = \frac{\sigma_B}{\pi} \quad (13)$$

Thus, for example, if σ_B is estimated as 0.4π, then we have that $k = 0.4\pi/\pi = 0.4$.

Because $k = \sigma_B/\pi$, we can substitute k into equation (11) to obtain

$$\rho = \frac{(k\pi)(k\pi)}{\pi(1-\pi)} \quad (14)$$

Which simplifies to

$$\rho = \frac{k^2\pi}{(1-\pi)} \quad (15)$$

We can then express the design effect in terms of cluster size, k and π:

$$DEFF = \left[1+(m-1)\frac{k^2\pi}{(1-\pi)}\right] \quad (16)$$

We thus have 2 ways to estimate the design effect, using (16) or using

$$DEFF = [1+(m-1)\rho] \quad (17)$$

If we use equation (16) to predict the value of the design effect, then for π we substitute the value of our "prior guess" π_g. Thus our equation for the sample size, corrected for the design effect and using equation (16) for the design effect, becomes:

$$N = \left[1.96^2\frac{(1-\pi_g)}{d^2\pi_g}\right] \times \left[1+(m-1)\frac{k^2\pi_g}{(1-\pi_g)}\right] \quad (18)$$

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CHAPTER 6

Interviews and data collection tools

In national tuberculosis (TB) prevalence surveys, it is important to collect information carefully from all survey participants, using standardized data collection tools to ensure that the data are comparable across data collection sites and teams. Also critical is the way questionnaires are designed and administered, to ensure that the data collected are accurate and meet the survey objectives.

This chapter first describes the purpose of the interview, types of data collection tools, the design and content of the questionnaire and the tools used. It then provides guidance on how to administer a questionnaire and the type of assurance measures required to ensure the quality of the information that is collected. This chapter should be read in conjunction with the chapter on data management (**Chapter 16**).

6.1 Purpose of the interview

In a TB prevalence survey, the interview comprises a set of standardized questionnaires that collect data to answer specific questions. Interview data are collected at households and the field site, with answers recorded using standardized forms or tools.

At the household level, the **enumeration or census form** makes it possible to capture the demographics (e.g. age and sex) of all members of a community, and to identify those who are eligible to participate in the survey. Generally, one person from each household helps the team member to complete the form. Additional information to be collected can include residency status, education level and occupation. Household socioeconomic status is often determined using an asset scoring list or some other method that is already in use in-country *(1)*. These data allow the survey team to understand whether those individuals who participate in the survey are representative of the whole population in terms of age and sex when compared with the latest national census. Also, these data can be used to determine whether the population who participate are different from those that do not participate based on sociodemographic characteristics, and whether there could be a bias.

At the field site, the one-to-one interview will be the first screening tool of the survey (i.e. **screening questionnaire**) and will provide information about the prevalence of symptoms suggestive of TB. The interview also asks about health care seeking practices for those with symptoms in the population being studied. The interview can assist in answering the following questions:

- What is the prevalence of symptoms suggestive of TB in the population?
- How many people diagnosed with TB in the survey reported symptoms suggestive of TB?
- What are the health care seeking practices in the population overall and among individuals reporting symptoms suggestive of TB?

Such questions can provide insight into whether the current symptom-screening algorithm in routine practice would be able to identify people with TB diagnosed during the survey and, if not, which type of cases the screening algorithm would miss. This information can also help to inform programmatic policy discussions about screening algorithms, where people with TB-suggestive symptoms seek care (e.g. in public, private or informal health facilities), and whether those with symptoms suggestive of TB who sought care were sufficiently investigated for TB. This could provide further insight into where and how many people with TB may be missed by health service providers, and thus could be used to optimize case-finding strategies.

To assist with the analytical models that estimate the burden of TB (see **Chapter 17**), two other questions should also be asked at the first interview:

- How many participants have a prior history of TB?
- How many participants are currently receiving treatment for TB?

The screening questionnaire can also collect information on risk factors for TB, such as HIV, diabetes mellitus, alcohol use disorders and tobacco use (see **Chapter 10**).

The questions to be asked will vary from survey to survey, depending on the population being studied and the specific objectives of the prevalence survey; however, it is important to formulate a clear list of questions before the questionnaire is designed. Although it can be tempting to try to answer many different questions within one survey, the questionnaire should be kept as brief and concise as possible. This will help to maintain quality and allow time to complete all the procedures necessary for the survey. It is unethical and wasteful to ask questions that will not be used in analysis; hence, each survey question should be deemed necessary

Table 6.1

List of data collection tools in a national TB prevalence survey (for about 50 000 invited individuals enumerated from a population of 70 000)

	DATA COLLECTION TOOL	ESSENTIAL OR OPTIONAL	APPROXIMATE NUMBER OF INDIVIDUALS COMPLETING EACH TOOL
1	Enumeration forms[a]	Essential	70 000
2	Invitation card[b]	Essential	50 000
3	Informed consent forms and information sheets	Essential	42 500[d]
4	Screening questionnaires (including health care seeking behaviour questions)	Essential	42 500 (3400[e])
5	Chest X-ray forms	Essential	42 500
6	Questionnaires for a subset of participants[c] – e.g.: – screen positive – risk factors (case–control)	Optional	 6375[f] 1200[g]
7	Sputum collection register	Essential	6375[h]
8	Laboratory results register	Essential	6375[h]
9	Clinical management and referral register	Essential	500[i]

TB: tuberculosis.

[a] Also known as the census form or register.

[b] Invitation cards are given to those who are 15 years and older, and fulfil the residency criteria.

[c] Specific questions can be asked of participants who screen positive based on specific survey objectives.

[d] Assumes an 85% participation rate.

[e] Assumes that 8% are symptomatic and are asked about health care seeking behaviour.

[f] Assumes a 15% screening positivity rate.

[g] Questions could be asked as part of a nested case–control study (e.g. 200 cases and 1000 controls).

[h] Assumes a 15% screening positivity rate. The numbers registered could be by sample, so this can increase 3–4 fold depending on the diagnostic algorithm used and the number of sputum samples collected and tested.

[i] Assumes that 200 people are defined as survey cases and a further 300 have a positive laboratory or chest X-ray result that does not meet survey case definitions or are new non-TB diagnoses that warrant further investigation and follow-up.

to answer a specific research question, and thought should have been given as to how the question will be analysed.

6.2 Types of data collection tools

Table 6.1 provides an example of a standardized set of data collection tools recommended for use at different stages of the survey. The tools marked as essential are those that are needed in all prevalence surveys. For the tool marked as optional, its inclusion will depend on the specific objectives defined in the survey protocol. **Table 6.1** also indicates the approximate number of individuals who would complete forms using each of the different tools in a typical survey with about 50 000 invited individuals. Depending on additional objectives outlined in the survey protocol, the standardized set may be further expanded.

All forms, in paper or digital format,[1] containing personal identifiers (e.g. first name, last name, date of birth, address and mobile phone number) should be kept confidential. At least one form must link the personal identifiers with a unique survey identification (ID) number, to allow for identification of the participant if follow-up activities are required. Survey IDs should appear on all survey forms from each participant. It is up to each country to decide whether to include the participant's name on some or all survey forms, depending on what is deemed acceptable. When using paper forms in particular, the use of additional identifiers could offer an extra cross-check; however, it would also require enhanced confidentiality measures to be in place. If a relational database is used, a unique survey ID number may be sufficient, but if a non-relational database is used, additional identifiers may be necessary to accurately link individual records.

Data collection templates and tools should be drafted on paper and included in the protocol for approval by the research ethics committee (REC). Subsequently, they can be used to design the digital data collection tool (see **Chapter 16**).

6.3 Questionnaire design

It is essential to collect survey information in a standardized and unbiased manner. To ensure the quality of the information collected, the questionnaire must be carefully designed, the procedure for completing the questionnaire must be clearly described and staff must be well trained.

[1] Ideally, all forms should be in digital format; however, they could initially be created in paper format and then converted as per the data management plan. Paper versions of each form may be needed in case the digital data collection system fails during field operations.

Each person who participates in a prevalence survey is assigned a unique survey identification number[1] which is used to link each participant to their questionnaire and forms, chest X-ray (CXR) and, if required, sputum and blood samples (see **Chapter 16**).

6.3.1 Principles of questionnaire design

The key principle in designing a questionnaire is that the questionnaire should be as clear, simple and precise as possible.

The exact questions to be asked in the questionnaire will vary among surveys, depending on the population being studied and the specific objectives set for the prevalence survey. However, a clear list of questions to be answered should be formulated before the questionnaire is designed. It may be tempting to try to include many different questions within one survey, but care should be taken to keep the questionnaire as brief and concise as possible, to maintain quality and to allow time to complete all the procedures necessary for the survey. Each interview question should be deemed necessary to address a specific research question that the survey seeks to answer; therefore, **any question that does not have a clear purpose and plan for analysis should be removed**. It is unethical and wasteful to ask participants questions if the responses are not going to be used in analysis. For example, some questions that do not have a direct impact on the survey findings are those concerning marriage status and religion.

A short questionnaire can be completed within a reasonable timespan, whereas if the questionnaire is too long, people may lose patience and attention. A good strategy is to go through a proposed questionnaire asking the following about each question:

- Why is this question being asked?
- What are the likely possible answers?
- How will this question be analysed?

Questions should be worded simply and be intelligible to the general population. They should be precise in meaning and should not be open to ambiguous interpretation. For example, the question, "Do you sweat at night?" is ambiguous because if people sweat in hot weather they may answer "yes". A better formulation for this question would be, "Do you have drenching sweats at night, so much that you have to get up and change the bedclothes or your nightwear?".

It is best to avoid wording that implies expectation of a particular answer (i.e. leading questions). Also, to obtain high-quality responses, the questionnaire should begin with easy, straightforward questions, keeping complicated or sensitive questions for later. Questions about symptoms should be asked before those about possible causes (e.g. questions about respiratory symptoms should precede those about tobacco smoking). Questionnaires should be translated into the local languages used by the survey population. A translated questionnaire must be translated back into the original language and be checked by a different person who understands both languages, to ensure that the meaning of the questions has been properly understood and is the same in all languages that are used.

The interview questions should be written and spoken in a way that is unambiguous, non-leading, and culturally and linguistically appropriate for the intended target population. Before the survey, questions should be tested for readability, comprehension and flow, using a sample of the population who represent the community being surveyed but are not actual survey participants. Questionnaires and forms should first be developed on paper and tested before being programmed into an electronic data management system. Subsequent testing of questions via a tablet computer is still necessary because it may bring up other issues that are not apparent when testing with paper (e.g. illogical answers and skip patterns[2]).

To help standardize the outcome of surveys within and across countries, and to optimize the benefits of such surveys, it is vital to **collect crucial information in a standardized way**. Therefore, it is recommended that a minimum set of questions is asked of all survey participants to ensure that the same basic set of indicators is obtained from all surveys (see **Table 6.2**).

6.3.2 Questionnaire layout

The layout of the questionnaire is important to ensure data accuracy, quality and efficiency; the actual layout used will depend on whether a paper or electronic version is used to collect data. Paper-based questionnaires should be laid out in a manner that is easy for the data collector to both complete and enter into the computer. Good spacing is essential, and it is best to have all the answers in a single column so that they can be easily checked for completeness; this also makes data entry easier. Electronic data capture versions of the questionnaires should mirror any paper versions and follow recommendations on good design of data forms *(2–4)*.

It is best to avoid open-ended questions and free text answers unless they are required, and instead provide likely options. For example, the question "Do you currently have a cough?" should not have an empty data field for the interviewer to complete but rather should have the possible options to be ticked or circled (i.e. Yes and No). If possible, coded numerical answers should

[1] The identifier is a unique number assigned to all enumerated individuals. Some surveys may wish to use an additional number which is assigned at reception known as the participant serial number. This is a sequential number based on when a participant arrives at the field site; it can aid in such things as participant flow and verifying forms (see **Chapter 16**).

[2] A skip pattern refers to the situation where the sequential flow of a survey is changed, based on answers to one or more previous questions in the survey.

be used throughout. All questions should have an "unknown" and "no response" option, so that all questions can be completed by the data collector; if this is not the case, it will be unclear whether a blank response means "unknown" or "not asked". If all likely options are not known, it may be necessary to have a response category of "other", with space to specify the answer. Pilot testing can help to prevent this scenario by ensuring that the most likely options have been included.

In many questionnaires, some questions are only asked of those participants who answered the previous question in the affirmative (e.g. if the response to "Do you have a cough?" is yes, the next question is "For how long have you been coughing?") – such questions are called "skips". In electronic data collection devices, skips should be built in automatically; for example, using drop-down lists for the answer options, to minimize errors. Thorough testing is required to ensure that skips are structured correctly, so that quality data are collected and missing data are avoided. In paper format questionnaires, logical and appropriate layout combined with clear instructions for skips will help to ensure data quality.

Most recent surveys have used electronic data capture. At a bare minimum, surveys should use a barcoding system to ensure that the unique personal identifier for each participant correctly links information (e.g. from forms, CXRs and samples). More considerations on electronic data capture are outlined in **Chapter 16**.

6.4 TB prevalence survey data collection tools

6.4.1 Enumeration form

The enumeration form, sometimes known as the census form or register, is intended to:

- collect baseline information about the survey population, to identify individuals who are eligible to participate in the survey;
- collect identifiers that allow for the follow-up of survey participants[1] (e.g. for clinical purpose); and
- identify potential biases among those who consent to participate in the survey but also to identify differences between those who participate and those who do not.

The enumeration form, conducted at the household level, is necessary for all surveys. It collects census-type data from all individuals in the survey area or sampling frame (adults and children[2]), and records name, address, age, sex and residency status.[3] The enumeration data serve to:

- list the population from which eligible individuals are invited to participate in the survey;
- ascertain that individuals included in the survey are representative of the eligible population when compared with the national census (any differences can be taken into account in the data analysis, see **Chapter 17**); and
- provide the linkage with the unique survey ID number and individual personal identifiers (e.g. names and addresses).

The data collected in the enumeration form allow for the calculation of consent rates; information about non-consent and how it may affect the result of the survey can be taken into account during data analysis (see **Chapter 17**). Many surveys have found that men, especially younger men and those of working age groups, are underrepresented because, compared with women, they are more often absent during the survey implementation. The enumeration form allows this potential bias to be identified.

The enumeration form will contain personal identifiers (e.g. names and addresses), because these are required for follow-up of individuals who need further investigation or treatment for TB. The data capture system should be designed in such a way that data confidentiality is always maintained (**Chapter 16**). Examples of a survey team member conducting a census (enumeration) of the household is shown in **Fig. 6.1**.

Socioeconomic data may be collected from all survey participants at the household level. Collecting data on socioeconomic status may allow countries to assess whether the prevalence of symptoms and signs suggestive of TB, and ultimately TB, varies by socioeconomic groups. There are standardized tools for collecting basic household-level data on socioeconomic status. If established national tools are used to determine socioeconomic status, the data collected can also help in ascertaining the representativeness of the sampled population and in other in-depth analysis of, for example, risk groups and health care seeking behaviour. However, an analysis of eight prevalence surveys found that, given the relatively small number of TB cases identified in prevalence surveys, the data collected may not be the most efficient way to assess the relationship between household socioeconomic level (both relative and absolute) and individual TB disease *(1)*. Examples of a generic enumeration form and of household-level data forms are shown in online supplementary material.

[1] A survey participant is someone who is eligible to participate, has provided consent and has undergone a symptoms-based questionnaire. Ideally, all participants will also have a CXR; however, some people may refuse or may be exempted.

[2] It is important to collect information about children (i.e. those aged <15 years for survey purposes).

[3] Eligibility to participate is based on age (≥15 years) and residency status (as defined by the survey).

Fig. 6.1

Enumerating the number of people in a household, national TB prevalence surveys of a) Myanmar, 2017–2018 and b) South Africa, 2017–2019

a)

b)

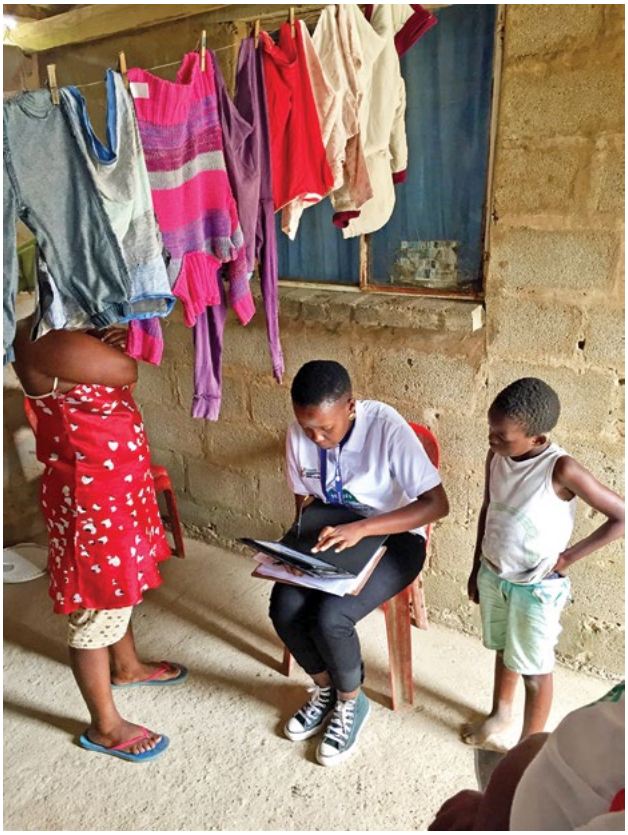

Photo credit: a) WHO Myanmar country office, b) WHO/Irwin Law.
TB: tuberculosis.

6.4.2 Invitation card

People who are eligible to participate in a survey, based on age and residency, are given an invitation card during the household enumeration (**Fig. 6.2**). Name, age, sex and details of date, time and location of the field site are recorded. Each card is labelled using a barcode representing the unique personal identifier, which includes the cluster number, household number and individual number (see **Chapter 16**). Only one card is provided per invitee, but if the invitees are not present at the time of enumeration, then the cards could be left with someone in the household. The invitation card can also be used to track completion of survey procedures onsite, by ticking a box on the card at each workstation completed. This helps to ensure that all procedures are completed and to guide participants within the field site. Eligibility to submit sputum samples can also be marked by circling sputum to be done, making tracking even more straightforward.

6.4.3 Informed consent and information sheet

Informed consent

When an invitee arrives at reception at the field site, the person's invitation card should be checked, and their identity verified. Next, the invitee should be registered, and their informed consent must be obtained before they take part in the prevalence survey (see **Chapters 11** and **13**). It is an ethical requirement to obtain consent from all survey participants.

Informed consent is a two-way process that requires the provision of relevant information (verbal and written) to a competent individual, ensuring that they have understood the facts and have decided (or refused) to participate without having been subjected to coercion, undue influence or deception *(5)*. The process should also allow for potential participants to ask questions of the interviewer.

Particular care should be taken when "vulnerable groups" are being asked for informed consent. A vulnerable group is defined as any group with diminished autonomy; this could include women, poor people, illiterate individuals or any group in a dependent relationship with the researchers. For prevalence surveys in high TB burden settings, many communities will be "vulnerable" owing to poverty and illiteracy and, if the ministry of health or health care staff are conducting the survey, these communities could be in a dependent relationship with the researchers.

Consent must be obtained in writing. If a participant is illiterate then a fingerprint can be used, witnessed and countersigned by an independent witness (e.g. by another family or community member who was present at the time of information giving). Each consent form must also be signed by the person who conducted the informed consent process. It is usual for the participant to keep a copy of the information sheet (see below) and

Fig. 6.2

An invitation card from the national TB prevalence survey of the Philippines, 2016

National TB Prevalence Survey 2016
Department of Health
Philippine Council for Health Research Development
Foundation for the Advancement of Clinical Epidemiology, Inc.

NTPS 2016

Cluster Number:
Household Number:
Line Number:

(For household members 15 years and above AND residing in village for ≥ 14 days)

1. Region	4. Stratum	Survey Barcode
2. Province	5. Barangay	
3. City/Municipality		
Name:	Age (years):	
Last Name First Name Middle Name	Sex:	

INVITATION

Please come and participate in the National TB Survey on _____ at _____
(Date: MM/DD/YY) (Time: HR/MIN)

at the survey site located in _____

If in case you cannot come on the scheduled date above, please come to the survey site between _____ and _____
(Date: MM/DD/YY) (Date: MM/DD/YY)

from 8:00 A.M. to 5:00 P.M.

PLEASE BRING THIS CARD WITH YOU. THANK YOU!

Source: National tuberculosis prevalence survey 2016, Philippines – Annexes. Foundation for the Advancement of Clinical Epidemiology, Inc. (2017) Manila, Philippines (reproduced with permission).

Fig. 6.3

Participant watching a short instructional video on a tablet computer describing the survey as part of the process of obtaining informed consent from the individual, national TB prevalence survey of the Philippines, 2016

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

a signed copy of the consent form. Individuals under the age of consent (this varies from country to country but is usually 16 or 18 years of age) will need to provide assent and must have the consent form signed on their behalf by a parent or legal guardian. Cultural sensitivity must be used when assessing who is appropriate to sign; in some societies, a father rather than a mother may have to sign, or both parents may be required to sign.

Information sheet

Information is usually given in the form of a plain language written document called the information sheet; however, it may also be given using posters, songs, talks, live presentations or video (see **Fig. 6.3**). The essential elements of the information sheet are:

- a description of the research and the procedures involved;
- risks of taking part in the survey;
- benefits of taking part in the survey;
- alternatives to taking part in the survey;
- confidentiality;
- compensation;
- contact information for the investigators or researchers and ethical boards; and
- a statement that participation is voluntary and there will be no penalty for refusal to participate

A potential risk of taking part in a TB prevalence survey is psychological distress while waiting for results or when receiving the results of investigations (especially

sputum and HIV tests). Also, there may be stigma associated with being diagnosed with TB or HIV. Since CXRs are used as a screening tool, participants should be advised about radiation safety and associated risks (see **Chapter 7**).

The potential benefit from participating in a survey includes diagnosis of TB (or other comorbidities if these are included) and access to treatment. All survey participants should be informed that, as an alternative to taking part in the survey, they can attend a health care facility if they are concerned about symptoms or signs suggestive of TB.

Any data collected from a participant are confidential. Processes taken to maintain this confidentiality (e.g. use of survey numbers rather than names) should be explained. Access to data and the use of the data to be collected should be explained to the participants, including how the results will be disseminated (e.g. via reports, publications or presentations). TB prevalence surveys pose particular challenges for informed consent because TB is a notifiable disease in many countries meaning that a diagnosis of TB must be reported to public health officials. The information sheet must state that any individual found to have TB will be followed up by a public health official. Participants must understand that confidentiality will be breached for any individual found to have TB in the prevalence survey; this is different from other research settings.

Compensation includes any payments made to participants to compensate them for their time, travel or inconvenience. It is unreasonable to expect participants to pay out of pocket for travel or to take time off work to participate in the survey. However, any compensation should be reasonable so that it does not induce someone to take part in the survey simply for financial gain. The survey steering and technical committees will decide whether compensation will be provided and, if so, the amount, which should be clearly stated in the information sheet.

Phone numbers for the investigators (e.g. survey team leader, principal investigator, the national TB programme) and REC should be provided on the information sheet so that participants can contact someone if they have any questions about the survey or would like to report a concert.

The information sheet should clearly state that participation in the survey is entirely voluntary, and the individual will not lose any access to healthcare or privileges by not participating. Also the sheet will state that a participant can withdrawal from the survey at any time and that there are alternative options for seeking treatment (e.g. through the regular health services).

In additional to covering all the areas discussed above, the information sheet must be culturally sensitive and readable by the target population; thus, the wording should be kept simple. It is a good idea to check readability by engaging community members to help refine the wording. The information sheet must be translated into the appropriate languages for the survey population and should then be independently backtranslated to ensure that the meaning has not been altered in translation.

Examples of consent forms and information sheets that have been used in specific surveys are given in online supplementary material. The examples may provide useful ideas for the design of the forms; however, each country and REC will have its own standards and layout.

6.4.4 Screening questionnaires

The objectives of the individual screening questionnaire are to:

- identify survey participants who have symptoms suggestive of TB, and should have sputum samples collected for further investigation;
- obtain information about previous and current TB treatment; and
- collect information on health care seeking behaviour among participants who report symptoms suggestive of TB.

The screening questionnaire may include details about occupational status, ethnicity or racial origin if these are considered important factors for the epidemiology of TB in the country. Some surveys may already collect such information during enumeration, making it unnecessary to collect it here.

All participants should be asked for symptoms that could be related to TB. The questions about symptoms used for screening (see **Chapter 3**) must be simple, unambiguous and culturally appropriate. Questions on symptoms should be hierarchically ordered; that is, the first question about the symptom should ask whether the interviewee has the symptom, and if the response is "yes", the second question should be about duration of the symptom. As a minimum, the symptom-screening questions should contain those questions used by the national TB programme's screening algorithm. In countries with a high prevalence of HIV, screening questions should align with the national HIV programme guidance (see **Chapter 10**). Examples of a survey team member conducting an interview at the field site are shown in **Fig. 6.4**.

Screening algorithms from surveys conducted between 2007 and 2016 can be found in **Table 2.2** in the World Health Organization (WHO) publication *National tuberculosis prevalence surveys, 2007–2016 (6)*.

The TB screening questionnaire is used to reduce the number of individuals who are eligible for sputum examination, which in turn reduces the number of sputum samples that need to be collected and examined by the laboratory. In surveys conducted between 2007 and

Fig. 6.4

Survey participants being interviewed in the field, national TB prevalence surveys of a) Bangladesh, 2015–2016, and b) Lesotho, 2019

a)

b)

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

2016, about 6.5% of survey participants from Africa and 5.7% from Asia were symptom-screen positive *(6)*.

The questionnaire must include details from all participants on their current or past history of TB treatment and the timing of their most recent treatment episode. Such information is critical for the mathematical models used to estimate the burden of TB. These details could be verified via the participant's TB registration number or prescription register. Questions could also be asked about where they received treatment, and what procedures were undertaken.

A minimum set of questions that would need to be asked is provided in **Table 6.2** but can be adapted by countries to fit with their screening strategy. Examples of other screening questionnaires that have been used in specific surveys are given in online supplementary material.

Health care seeking behaviour

For participants reporting symptoms suggestive of TB, the screening questionnaire can be extended to inquire about health care seeking behaviour. In electronic data systems, participants reporting symptoms can be automatically selected and asked additional questions; for example, whether they sought care for the symptoms they reported and, if so, where they sought care (e.g. public or private sector) and at which level (e.g. pharmacy, health centre or hospital). If no care was sought, another question is the reason for not seeking care (see **Chapter 20**). A summary of health care seeking behaviour outcomes from surveys conducted between 2007 and 2016 can be found in **Table 3.5** in the WHO publication *National tuberculosis prevalence surveys, 2007–2016 (6)*. A few countries have extended the questionnaire to ask those who sought care about what processes were involved; for example, were sputum samples collected, was a CXR done, and was TB treatment or TB preventive medicine provided.

Prevalence surveys have resulted in some important insights into health care seeking behaviour for TB-suggestive symptoms (see **Box 6.1** and **Chapter 20**).

Questionnaire to ascertain HIV status and comorbidities

HIV is a major factor in the spread of TB in certain settings. It is important to understand the burden of HIV-associated TB in all settings. TB prevalence surveys are ideally suited for obtaining information about HIV status, history of HIV testing and uptake of HIV treatment. Also, in accordance with WHO guidance *(8, 9)*, such surveys are ideal for providing access to HIV testing for all survey participants. Questions on HIV can be asked at the screening interview or via a dedicated HIV testing station at the field site. Training in good interview technique is critical for this aspect of the interview, to align with best practice, and with principles of confidentiality and consent. A minimum set of questions to be asked of

Table 6.2

A minimum set of questions to be asked to all survey participants during the screening interview

	QUESTIONS	ANSWERS
1	Interview date	Day / month / year
2	Survey number / barcode	
3	Are you currently on TB treatment now?	1. Yes 2. No
4	Have you been on TB treatment before?	1. Yes 2. No 3. Don't know
5	If yes, how long ago was this?	…….. (months/years)
6	Do you currently have a cough?	1. Yes 2. No (go to Question 10)
7	If yes, how many days (or weeks) have you been coughing?	…….. (days/weeks)
8	Are you coughing up sputum?	1. Yes 2. No
9	Are you coughing up blood?	1. Yes 2. No
10	Do you currently have a fever?	1. Yes 2. No (go to Question 12)
11	If yes, for how many days (or weeks) have you had this fever?	…….. (days/weeks)
12	Do you have night sweats?	1. Yes 2. No (go to Question 14)
13	If yes, for how many days (or weeks) have you been experiencing night sweats?	…….. (days/weeks)
14	Do you have chest pain?	1. Yes 2. No (go to Question 16)
15	If yes, for how many days (or weeks) have you been experiencing chest pain?	…….. (days/weeks)
16	Have you had unexpected weight loss in the last month?	1. Yes 2. No (go to Question 18)
17	If yes, for how many days (or weeks) have you had (unexpected) weight loss?	…….. (days/weeks)
For participants reporting symptoms suggestive of TB (i.e. answering yes to questions 6, 8, 9, 10, 12, 14 and 16)		
18	Thinking about your current symptoms, did you consult with someone for help?	1. Yes 2. No (go to Question 20)
19	If yes, where did you first seek care?	*Outline options as per country needs*
20	If you did not seek care for these symptoms, why not?	*Outline options as per country needs*

TB: tuberculosis.

all survey participants and strategies for HIV testing are provided in **Chapter 10**.

In addition to HIV, a substantial proportion of TB globally is associated with undernutrition, diabetes mellitus, alcohol use disorders and tobacco use (see **Chapter 10**). Prevalence surveys offer an opportunity to collect more data on these other comorbidities, and to provide additional testing or measurement in some settings.

Questionnaire for a subset of participants (optional)

A separate questionnaire could be administered to a select group of participants to fulfil a secondary objective of the survey. For example, this questionnaire could be for those who screen positive, or for a selection of survey cases with matching controls (i.e. case–control study). It could be a continuation of the previous screening questionnaire for those individuals who screen positive or it could be a separate questionnaire. Further questions could be asked about the presence of additional symptoms and actions taken by the individual in response to their symptoms (e.g. seeking health care), if not already included. Each interview question should be deemed necessary to address a specific research question that the survey seeks to answer, so **any question for which the purpose and analysis plan are not clear should be removed**.

6.5 Administration of questionnaires

A standard operating procedure (SOP) should be adopted for how, where and by whom each questionnaire is administered, because any of these factors may influence the responses given. Training must be conducted on the questionnaire, especially with respect to the language and words used, and any questions that may cause difficulty. During the training, data collectors should practise the questionnaires on each other and in simulated households, to ensure that they are familiar with the questions and responses.

How to ask questions

All interviewers (including those conducting the enumeration or census) must be trained in interview skills. Important areas in this training are as follows:

BOX 6.1
HEALTH CARE SEEKING BEHAVIOUR, NATIONAL TB PREVALENCE SURVEY OF ZAMBIA, 2013–2014 *(7)*

The first nationally representative population-based survey of Zambia documented health care seeking behaviour among participants with symptoms. Only 35% of participants sought care for their symptoms, with older people more likely to seek care than younger ones. Males and urban residents were less likely to seek care than their female and rural counterparts.

Of those seeking care, most (81.8%) chose a government facility for their first visit. Other findings were that males were less likely than females to use a government health facility; those aged 25 years and older were more likely to use a government health facility than those aged 15–24 years; urban residents were less likely than their rural counterparts to use a government facility; individuals from the highest wealth quintiles were less likely to choose a government facility for their first visit than those from the lowest wealth quintile; and educated people were less likely than uneducated people to use a government health facility.

Even for patients who do seek care, the opportunity to make a TB diagnosis at the health facility can be missed. Of participants who sought care, only 14% reported having received a CXR and only 12% reported having had a sputum smear examination. The average time (in weeks) from the onset of symptoms to first seeking care was 3 weeks, irrespective of the nature of the symptoms.

Various supply and demand factors affect health care seeking for TB in Zambia. Many people delayed seeking care for their symptoms but there were still many missed diagnostic opportunities even when care was sought.

- introduction of interviewer and the survey to the participant;
- assessment of eligibility for inclusion in the survey;
- informed consent process, which must include:
  - information giving (e.g. full survey procedures, including collection of information and biological specimens);
  - participant's ability to give consent;
  - for participants under the age of consent (typically, 15–17 years), ability to give assent and their parent or legal guardian's ability to sign the consent form;
  - explanation that participation is voluntary;
  - confidentiality of information;
- ability to put the participant at ease, and to ensure a comfortable and private environment in which to ask questions;
- understanding that questions must be asked in the order in which they are written on the questionnaire, using the same wording as on the questionnaire or as has been discussed in training (certain questions may need further explanation using different wording if the interviewee cannot understand the question, but these should also be discussed in training);
- understanding the need to avoid influencing the answers to questions by:
  - using the same tone of voice for each interviewee and question, and ensuring that the tone is conversational, friendly and courteous;
  - keeping facial expressions friendly and interested but neutral;
  - never showing surprise, shock or approval in response to the interviewee's answers;
  - avoiding unconscious reactions (e.g. nodding the head, frowning or raising the eyebrows);
  - never giving one's own opinions or advising the interviewee;
  - not attempting to educate the interviewee while conducting the interview, to avoid interviewees saying what they think should be said rather than answering the actual question;
  - not making interviewees feel as if they are taking an examination or are being investigated;
- ensuring that all questions are answered – if a participant refuses to answer a question or cannot give an answer, the appropriate field (e.g. "unknown" or "no response") should be completed;
- being familiar with the questionnaire so that the questions can be asked conversationally rather than being read stiffly;
- ensuring that interviewers are well versed (or know who to ask) in responding to questions they may receive from the interviewee;
- understanding how to keep control (and manage the length) of the interview, including how to deal with situations where interviewees go off into irrelevant conversation and how to bring them gently back to the interview (includes understanding how to allow enough time for interviewees to answer and how long to allow silences before repeating questions); and
- being familiar with the data collection tools, and knowing how to troubleshoot issues related to information technology (IT).

6.6 Quality assurance of questionnaires

Training and clear instruction are essential to ensure the quality of the data collected. The number of interviewers should also be kept to a minimum, to reduce the magnitude of interpersonal variation.

Pretesting and piloting of the questionnaire provide an opportunity to identify any problems. Trained interviewers should be commissioned to perform pilot testing. The wording of questions, their sequence, and the structure and overall length of questionnaires can be improved in response to the findings of the pretesting and piloting. Once there is agreement on the questions to include, questionnaires should be designed and tested before they are built into an electronic data capture system. Once developed in the electronic system, extensive testing should also be done to identify wrong skips, missing data fields and IT-related issues such as the time it takes to load a page, and to ascertain how devices function in the heat, how often devices need to be charged and whether it is possible to see the screen under sunlight.

Monitoring in the field

Monitoring visits to the field should be scheduled at regular intervals throughout the course of the survey, especially during the initial phase. Core survey staff (e.g. survey coordinator, central-level coordinators and the quality assurance [QA] officer, see **Chapter 12**) should undertake the visits, focusing on all aspects of the survey process to identify problems and remedy them, especially in the enumeration and interview process. Close monitoring will help to ensure that SOPs are adhered to and that the data collected are accurate.

It is important to assess the progress of the survey using a set of standardized QA indicators, so that results can be comparable across survey sites (see **Chapter 14** for a list of key monitoring indicators). Such visits are particularly important at the beginning of data collection, to ensure that logistics are running smoothly and that field staff are well prepared.

Subsequent field visits should focus on the quality of data recorded in the field, and on survey process issues (e.g. procedure for selection of clusters or households, selection of eligible invitees, and response rates). During such visits, supervisors can observe the administration of the questionnaires to check whether field staff are using the formal translation of questions (if required) or are paraphrasing questions, which may alter their meaning. Team supervisors should continuously check that data have been accurately captured and are legible and complete, and that consent forms have been signed appropriately.

It is also important to perform QA on the data collected, to ensure that the data collectors are accurately recording genuine information and that data are not being fabricated. Supervisors should plan to re-interview a random sample of participants using data variables that are unlikely to change (e.g. age and history of previous TB) rather than more fluctuating variables such as symptoms. The number of re-interviews will vary, depending on the specific survey protocols and the availability of staff.

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CHAPTER 7

Chest radiography

Chest X-ray (CXR) is an essential screening tool in national tuberculosis (TB) prevalence surveys. Important determinants of the effective use of CXRs in prevalence surveys are careful equipment choice, timely procurement, meticulous planning, optimum staffing, adequate training, radiation safety, and adherence to regulations on use of CXRs. The increasing use of computer-aided detection (CAD) software to read CXRs has its benefits and limitations.

This chapter describes the role of CXR as a screening tool in TB prevalence surveys, the different kinds of equipment in use (with the main focus on digital technology), the recent developments and applications of CAD software for TB screening with digital CXR, and aspects related to chest radiography that need to be considered during survey preparation and implementation, both at the field and central levels (e.g. quality assurance [QA] process). Some practical tips and lessons learned from previous surveys are also described.

7.1 Overview

Chest X-ray (CXR) is a rapid imaging technique that allows lung abnormalities to be identified. CXR is used to diagnose conditions of the thoracic cavity, including the airways, ribs, lungs, heart and diaphragm *(1)*.

The primary purpose of using chest radiography (the term referring to the procedure that provides the CXR) in national TB prevalence surveys is as a screening tool, together with the questionnaire for symptoms, to identify participants eligible for bacteriological examination.

According to the World Health Organization (WHO) recommended screening strategy in TB prevalence surveys, all participants with an "abnormal" CXR are categorized as "eligible for sputum examination", regardless of the presence of symptoms (see below for the definition of "abnormal"). CXR can also provide supportive evidence to refer survey participants to the health system for follow-up and further investigations when bacteriological results are inconclusive. Nevertheless, CXR can identify conditions other than TB that may require attention or referral. Therefore, CXR must be interpreted as both a screening tool for the survey and as a potential clinical tool to benefit survey participants. CXR results may also provide an indirect measure of bacteriological examinations and data management quality (e.g. a normal CXR result in a participant with positive bacteriological tests is unlikely and should therefore prompt a check of the participant's identity, barcode, ID number, etc.).

In TB prevalence surveys, CXRs are read at the field level to determine, together with symptom screening, which participants are eligible for sputum examination. They are then re-read at the central level by expert radiologists for more sophisticated image interpretation (also known as "central reading"), quality control and clinical management.

During the 1950s, CXR (mostly mass miniature radiography) was the only screening tool used in TB prevalence surveys led by WHO *(2)*. However, in the 1990s and 2000s, CXR found little favour with public health programmes for diagnosis and case detection of TB, given its poor specificity and significant variation within and between observers in the reading of CXRs. Additional barriers to promoting large-scale programmatic use of CXR were poor access to high-quality radiography equipment and expert interpretation, plus the widespread use of low-quality radiography and the challenge of maintaining equipment *(1)*.

More recently, evidence from national TB prevalence surveys has demonstrated that CXR is the most sensitive screening tool for pulmonary TB, and that a significant proportion of people with TB did not report symptoms suggestive of TB *(3–6)*. For these reasons, in 2021 WHO published guidance on systematic screening for tuberculosis (TB) disease that included CXR among the three approaches recommended for screening in the general population and high-risk groups, together with symptom screening and molecular WHO-recommended rapid diagnostic tests (mWRDs) for TB and C-reactive protein for screening of people living with HIV *(7)*.

However, CXR requires considerable equipment and resources; therefore, programmatic use of CXR for TB screening might be more challenging. In addition, CXR has several limitations:

- it is a two-dimensional representation of a three-dimensional structure;
- parts of the lung fields are not visualized due to overlapping structures;
- there is no universally accepted reporting system;
- it can be difficult to ascertain disease activity;
- it involves exposure to ionizing radiation; and
- it requires skilled technicians to implement and read the CXRs.

These limitations have been partially addressed by modern digital CXR technology, which is much improved when compared with conventional systems, as explained later in this chapter.

In TB prevalence surveys from 2007 onwards, there was a transition from cumbersome conventional methods to digital CXR imaging systems, which improved the quality of images, simplified the flow of participants and improved the efficiency of the reading process. Other advantages of digital systems include no requirements for removal of chemicals (unlike conventional methods); immediate availability of the images for CXR reading in the field; more efficient online transmission of images via the internet, with the possibility of real-time remote CXR reading and quality monitoring; and simpler image archiving and retrieval. In addition, ultra-portable equipment can be installed much more quickly than conventional systems, and can be easily transported from one site to another, which has clear advantages under field conditions. Radiation exposure has also decreased with technological improvements.

Chest radiography is now considered a safe and sensitive screening tool for use in national TB prevalence surveys because it is used for active case-finding activities. In addition, CXR does not only investigate the presence or absence of pulmonary or pleural lesions suggestive of TB, but can also identify other conditions affecting the lungs or other structures (e.g. heart, mediastinum and ribs), or sequelae of past TB. However, in many settings, CXR is not easily accessible, especially outside a formal health setting and at the peripheral level. For these reasons, the possibility of having a CXR as part of a population-based survey is usually much appreciated by the community and may be a factor in achieving high survey participation rates.

In recent years, computer-aided detection (CAD) software based on artificial intelligence (AI) has been developed to interpret CXRs for signs of TB. After reviewing these CAD products, WHO recommended their use in 2021, having found them to have the same or higher accuracy than human reading *(7)*. These products have already been used in several TB prevalence surveys in combination with human readers, as illustrated later in this chapter. TB screening through use of CXR and CAD only (i.e. without human readers) has been done in the TREATS (TB Reduction through Expanded Antiretroviral Treatment and Screening for Active TB) project *(8)*[1] (see **Box 7.1**).

This chapter provides information on the use of X-rays in national TB prevalence surveys. Although most of the relevant issues will be addressed, a detailed analysis of all technical aspects of X-ray use is beyond the scope of this handbook and can be consulted elsewhere *(9)*.

7.2 The epidemiological value of CXRs in TB screening activities

CXRs have shown good sensitivity in identifying individuals with the highest risk of having TB, particularly when the criteria of "any lung abnormality" and "intentional over-reading"[2] are used. A Cochrane systematic review published in 2022 (largely based on national TB prevalence surveys[3]) described the sensitivity and specificity of symptom screening and CXR as screening tools to detect bacteriologically confirmed pulmonary TB disease in HIV-negative adults and adults with unknown HIV status *(12)*. The summary sensitivity was 94.7% (95% confidence interval [CI]: 92.2–96.4%, very-low-certainty evidence) for any CXR abnormality (23 studies) and 84.8% (95% CI: 76.7–90.4%, low-certainty evidence) for CXR abnormalities suggestive of TB (19 studies). Specificity was 89.1% (95% CI: 85.6–91.8%, low-certainty evidence) for any CXR abnormality and 95.6% (95% CI: 92.6–97.4%, high-certainty evidence) for CXR abnormalities suggestive of TB. Sensitivity[4] was more heterogeneous than specificity and could be explained by regional variation *(13)*.

The primary aim of including CXR as a screening tool in TB prevalence surveys is to identify participants with any lung abnormality that might be related to TB (i.e. one of the criteria that make participants eligible for bacteriological examination) rather than to make a diagnosis of TB based on the CXR. A secondary aim of using CXR is to help make a diagnosis of TB for those with inconclusive bacteriological findings. In addition, CXR can provide useful information about the prevalence of inactive TB or fibrosis.

To increase sensitivity when identifying individuals with the highest risk of having TB, intentional over-reading of the X-rays should be encouraged; that is, participants with any suspicious lung abnormality (even one that may not be considered typical of TB) should be referred for sputum examination. Similarly, if CAD is used for CXR reading, a carefully selected "abnormality" threshold is recommended, to increase sensitivity (see **Section 7.5.2**).

[1] The TREATS project is measuring the success of a "universal test and treat" project called PopART in reducing the prevalence and incidence of TB in South Africa and Zambia, 2019–2021. The project includes a TB prevalence survey to compare TB disease burden in intervention and control trial arms, and is led by a consortium of 10 institutions.

[2] To increase the sensitivity of screening, people reading CXRs in prevalence surveys have been trained to assume that there is a CXR abnormality if there is doubt.

[3] In the Cochrane review, all participants who screened negative by CXR and symptom screening were assumed to be TB-negative. The estimate of CXR accuracy, especially specificity, may therefore be inflated.

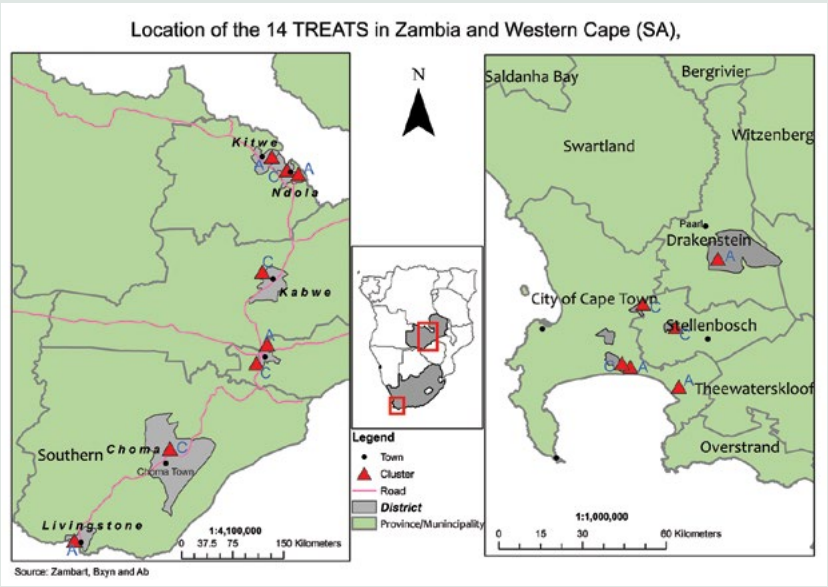
[4] High sensitivity of a screening test is useful only for deciding that a negative screening test outcome is so unusual that it strongly indicates the absence of the target condition. It means that people can be confidently regarded as not having a condition if their screening test yields a negative result; that is, they can be "ruled out". However, positive and negative predictive values (PPV and NPV, respectively) should be retained as the metrics of choice in screening contexts.

BOX 7.1
AUTOMATED X-RAY READING USED AS THE MAIN CXR IMAGE-READING TOOL: THE EXPERIENCE OF THE TREATS TB PREVALENCE SURVEY RESEARCH PROJECT

As part of the TREATS project *(8)*, which was funded by the European and Developing Countries Clinical Trials Partnership (EDCTP), subnational TB prevalence surveys were conducted in 21 communities in South Africa and Zambia (**Fig. B7.1.1**) during 2019–2021 *(10, 11)*.

Fig. B7.1.1

TREATS project: location of the 21 communities in South Africa and Zambia, 2019–2021



As per WHO recommendations, all participants were screened by symptoms and chest X-ray to determine eligibility for sputum examination. X-rays taken for screening purposes were read in the field only using CAD4TB (version 5). CAD scores guided an automated decision on sputum eligibility with a score of 50 or more as eligible.

Eligible participants submitted two sputum samples on the spot (Day 1) and were asked to return on Day 2 to collect the result of testing on those two samples; based on that result, participants could be asked to provide additional samples. During the Day 2 visit, a medical officer would review the X-ray and inquire (again) about symptom occurrence, and review all information available for each participant (e.g. Xpert® MTB/RIF Ultra (Xpert Ultra) results, symptoms and CXR image) to decide whether referral or additional samples were needed to decide the participant's TB status (**Fig. B7.1.2**). *Continued*

Fig. B7.1.2

Radiographer explaining the CXR to the participant (left); OneStopTB truck with X-ray at the mobile field site of the TREATS project (right), 2019–2021

Photo credit: Eveline Klinkenberg.

BOX 7.1

AUTOMATED X-RAY READING USED AS THE MAIN CXR IMAGE-READING TOOL: THE EXPERIENCE OF THE TREATS TB PREVALENCE SURVEY RESEARCH PROJECT

Automated reading of the X-ray using CAD software CAD4TB simplified the participant flow for screening purposes. It also reduced the workload for the medical officer in the in-depth review of all sputum-eligible participants on Day 2 without the risk of missing critical abnormalities on the X-ray.

To ensure that participants with unexplained high CAD scores would receive care if needed, all participants with a CAD score of 70 or higher were reviewed by the medical panel, irrespective of bacteriological findings. Where needed, participants were referred or further followed up.

CXR sensitivity to detect bacteriologically confirmed pulmonary TB does not reach 100%; hence, some TB cases may be missed by CXR. Potentially the only way to detect all TB cases would be to perform sputum culture for all participants; however, this approach is neither feasible nor cost-effective, and is therefore not recommended.

7.3 X-ray techniques in TB prevalence surveys

For national TB prevalence surveys, a single posteroanterior view of the chest in an erect position is required (see **Figs. 7.1**).

Although lateral views (right or left lateral, or both) are sometimes added in health screening programmes, there is no evidence that this helps to identify TB cases in surveys of TB in the community, and the required time (for the procedure as well as interpretation) and radiation dose increase significantly *(14)*. For these reasons, TB prevalence surveys usually do not include lateral views.

7.4 X-ray technology and equipment

Two types of X-ray technology are in use: conventional (analogue, non-digital) and digital.

1. conventional X-ray systems with manual or automatic film processing;
2. digital systems:
   a. indirect digital X-ray systems – computed radiography (CR); and

Fig. 7.1

Example of a digital posteroanterior CXR being taken during the national TB prevalence survey of South Africa, 2017–2019

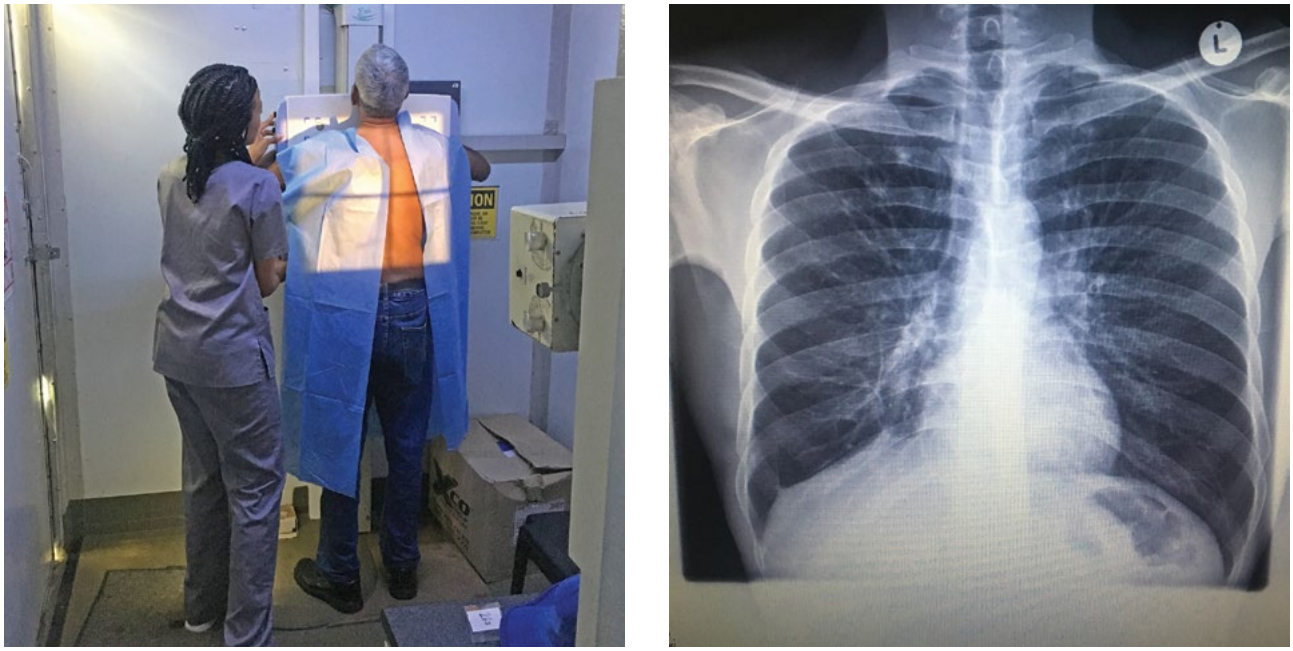


Photo credit: Marina Tadolini.

b. digital radiography or direct digital radiography (DDR).

Both technologies use the same principle of X-ray production by interaction of accelerated electrons with tungsten nuclei within the X-ray tube anode; the difference between conventional and digital technologies is the method of recording the result. In conventional systems, the result is recorded and displayed on an X-ray film, whereas in digital systems the result is recorded on a detector and displayed in a digital format on a computer screen (and can also be printed on an X-ray film or paper).

The two basic methods of film processing in conventional X-ray systems are manual and automatic. In the manual processing method, film is manually moved from one chemical (i.e. developer, fixer) to the next until processing is complete. In automatic processing, an electromechanical device (referred to as an automatic film processor) transports the film from one solution to the next without any manual labour other than placing the film into the device.

Digital radiography is an advanced form of X-ray that uses X-ray-sensitive plates to capture data during object examination; these data are immediately transferred to a computer without the use of an intermediate cassette. Digital radiography is divided into indirect and direct radiography systems. Indirect systems uses a cassette-based phosphor storage plate to capture the image. This plate is scanned with a laser scanner and then captured to create the digital image. Direct systems use flat panel detectors that convert X-rays to charge, which is then processed to produce the digital image.

Digital radiography is increasingly becoming the preferred modality of radiographic imaging because it involves fewer steps in image processing; hence, it delivers high throughput with excellent image characteristics (contrast and resolution) and a lower dose of radiation.

The following section mainly focuses on digital CXR. For conventional technology, please refer to the previous version of this guidance *(15)*.

Box 7.2 summarizes the advantages of digital systems over conventional CXR technology. A modern digital radiography set-up usually comes as an integrated package comprising a calibrated X-ray generator, a sensitive detector and an electronic workstation with the required software, including anatomically programmed radiography (a series of anatomy-specific predetermined settings) that reduces manual steps for the radiographer during the process of image acquisition. Digital radiography provides all the benefits of digital images, such as archiving, sharing via a local picture archiving and communication system (PACS) network for onsite reporting, and the option to include CAD screening or teleradiology. However, considerable capital investment is needed because of the cost of the detector and calibrated X-ray generator. Also, the detectors are fragile and need to be handled with care during radiography or transportation because even minor mechanical damage can mean total malfunction, large financial implications and disruption to the survey.

From 2007, there was a transition from conventional to digital CXR imaging systems in TB prevalence surveys. In only nine of 36 surveys implemented between 2007 to 2024, film images were developed using an automatic film processor (a standard practice in surveys before 2007); the last two surveys to use conventional CXR were in Uganda (2014–2015) and the Democratic People's Republic of Korea (2015–2016). All other surveys thereafter have used digital X-ray systems. CR with an imaging plate and image reader was used in the surveys in Nigeria (2012) and the United Republic of Tanzania (2012), whereas DDR with a flat panel detector subsequently became the standard technology for other countries.

Technical aspects and differences between conventional X-ray systems are summarized in online supplementary material.

BOX 7.2
ADVANTAGES OF DIGITAL SYSTEMS OVER CONVENTIONAL CXR TECHNOLOGY

Digital technology has multiple advantages over conventional CXR, which further enhance its role in TB case detection:

- reduced procedure time;
- improved image quality;
- greater image versatility (i.e. image can be manipulated as needed, lightening or darkening, zooming in or out, rotating, flipping or inverting);
- lower radiation dose;
- immediate availability of the images for CXR reading;
- no requirement for removal of chemicals (more environmentally friendly);
- simpler image archiving and retrieval;
- possibility of electronic transmission of images (e.g. for expert opinion, QA and real-time remote support);
- possibility of using CAD in combination with human readers; and
- availability of portable and ultra-portable equipment.

7.4.1 Direct digital radiography

In DDR systems, image capturing and read-out are combined using special detectors; no X-ray film or imaging plate is required. The results are recorded and displayed almost simultaneously, because no separate image processing or reading is required. More recently, X-ray detector technology has progressed significantly, with the production of sensitive, lightweight, wireless detectors with extended battery power supply leading to a greater degree of portability.

Depending on the use, size, required infrastructure and portability, the X-ray equipment needed for TB programmes can be classified into stationary, portable and ultra-portable X-ray equipment.

Portable radiographic systems are defined as a subset of "mobile" radiographic equipment, with specific physical and technological characteristics that mainly affect the system's portability, management and clinical applications. Portable X-ray systems are designed to be used mainly when planned diagnostic or screening activities are located far from health structures, or when multiple outreach interventions are socially or economically convenient and are considered an advantage. Minimum technical specifications for ultra-portable digital X-ray systems were developed in 2020–2021 to support decision-making on selection, regulation, incorporation, allocation and use of ultra-portable equipment *(16, 17)*.

Portable equipment used in TB prevalence surveys must be easy to be moved and transported to the field (see **Fig. 7.2**). In contrast, mobile X-ray equipment used in hospitals (e.g. in intensive care units, emergency and operating theatres), although often called portable, is much heavier.

CXR equipment can also be installed in a truck (see **Fig. 7.3**). In this case, the type of CXR unit can vary; some surveys have used high-specification stationary units in the truck whereas others have installed a portable unit. Depending on the accessibility of cluster sites and available funding, countries have used a variety of CXR delivery options, including X-ray trucks, X-ray containers loaded on a truck, portable X-ray units or combinations of these options. Not all trucks can access all terrains, so a presurvey assessment of the cluster sites, and roads to get to them, will be required.

Ultra-portable equipment is battery operated, generally emits lower doses of radiation, and can be packed into backpacks and thus can easily be transported into the field. The X-ray generator (with battery) typically weighs less than 20 kg, whereas the X-ray detector (with battery) generally weighs less than 5 kg and can be carried in a small case or backpack or even handheld (see **Fig. 7.4**). This cuts the high overhead costs incurred for previous X-ray systems that required a large vehicle. Perhaps more importantly, the ultra-portable design and low weight reduce physical strain on medical staff who need to carry and set up the equipment. When combined with a high-sensitivity digital radiography unit with advanced noise-reduction technology, an ultra-portable X-ray system can capture high-quality images despite the use of low-dose radiation. The reduced radiation exposure particularly benefits groups such as pregnant women, who may have been excluded from surveys in the past because of the risks associated with the level of radiation exposure during a CXR *(18)*. Ultra-portable devices can be safely used in the community provided basic safety measures are adhered to *(19)*.

Ultra-portable equipment may change the strategy used in TB prevalence surveys to make the cluster size smaller and survey operations shorter as less time is

Fig. 7.2

Portable CXR equipment used in the national TB prevalence survey of Eswatini, 2018–2019

Photo credit: Eveline Klinkenberg.

Fig. 7.3

CXR vehicle used in the national TB prevalence survey of Mozambique, 2018–2019

Photo credit: Eveline Klinkenberg.

Fig. 7.4

Ultra-portable CXR equipment used in a follow-up study as part of the TREATS project, 2019–2021

Photo credit: Eveline Klinkenberg.

required for setting up. While portable radiographic systems have been used extensively in national TB prevalence surveys, ultra-portable equipment with digital technology or an integrated package has only been used in some research projects (e.g. the TREATS project; see Fig 7.4).

The comparative analysis of stationary, portable and ultra-portable digital radiography X-ray equipment against various consideration parameters (e.g. throughput, setting, vehicle installation, CAD integration, life of equipment) are provided in online supplementary material.

7.5 Computer-aided detection (CAD) for TB

In recent years, numerous AI-based CAD software products have been developed for automated interpretation of CXRs for screening or triage for pulmonary TB, with the express purpose of determining the likelihood of TB disease. CAD offers the potential to overcome several of the implementation challenges inherent in human interpretation of CXRs. Several independent evaluations of commercially available CAD products have demonstrated that the accuracy of these products in screening activities is comparable or sometimes even superior to experienced, certified radiologist readings *(20, 21)*. Among other benefits are the improved accessibility of CXR in areas where trained personnel are scarce, reduction in variability within and between readers, quick turnaround time of CXR results, removal of human reader error, and consistency and relative standardization across teams and clusters of a TB prevalence survey.

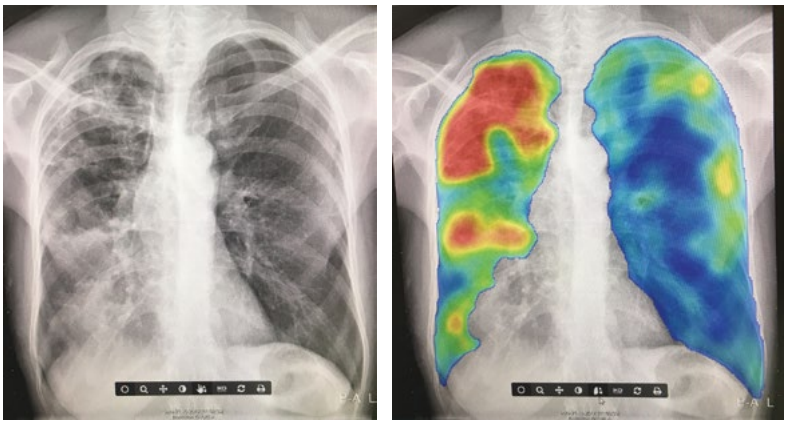
Based on the available evidence, in March 2021, WHO recommended for the first time that CAD may be used **in place of human readers** to interpret digital CXRs for screening and triage for TB disease among individuals aged 15 years and older in populations in which TB screening is recommended *(7)*.

Use of CAD is not essential in prevalence surveys but can be an option to assist with interpreting CXRs, either as a replacement of or an accompaniment to human reader interpretation, and it can reduce the required workload and time required for initial screening. Although CAD offers a valuable support for CXR interpretation, CAD alone cannot be considered as a diagnostic tool; rather, it is used as a screening or triage tool to identify individuals who should receive confirmatory bacteriological testing for TB. Although CAD products can provide high accuracy and consistency in reading of CXRs, false negative readings by CAD are still possible for very early or minimal TB among participants being screened. False positive readings for non-TB lung abnormalities are also possible, as with human reading of CXRs and with all screening methods. Furthermore, if there are enough qualified personnel to read CXRs and CAD is not already used in a particular country, there may be no immediate requirement to use it for surveys. However, purchase of CAD with the appropriate licence schedule and duration, and affiliated resources (via a survey) could make a lasting contribution to strengthening programmatic capacity once a survey is completed.

There are various CAD products on the market, and new developments and updates in AI-powered products for TB detection are relatively frequent. Information on available and upcoming CAD products can be accessed at the regularly updated website *(22)*. Most CAD providers regularly update their products. Although changes made to the CAD product are limited compared with the already marketed version approved by Conformité Européenne (CE) or the United States Food and Drug

Fig. 7.5

A CXR (left) being interpreted by CAD (right) from the national TB prevalence survey of Namibia, 2018



Red areas show greater likelihood of abnormality than the blue.

Photo credit: Marina Tadolini.

Administration (FDA), the updated version does not require a new CE or FDA assessment. In most instances, software updates are included in the maintenance and support contract for the product.

The technical requirements of CAD must align with best regulatory practice and with WHO's aims to support its disease programmes for TB in low- and middle-income countries, and to ensure programmatic suitability of the software. WHO prequalification has recently published technical specifications for CAD products and is expected to subsequently launch a process for evaluation of CAD products *(23)*.

CAD products are designed to read CXR images in common image file formats, including DICOM® (Digital Imaging and Communications in Medicine), JPEG and PNG. Most TB CAD products can read either anteroposterior or posteroanterior CXRs; lateral CXR is not often included in TB CAD products. CAD software analyses CXR images and produces an output highlighting where chest abnormality is present ("detection"), a number (the score) ranging from 0 to 100 (or from 0 to 1), or dichotomous classification of TB-related abnormalities "present" or "absent" (see **Figs. 7.5–7.6**). The score conveys the likelihood that the image being analysed contains abnormalities associated with TB. The higher the score, the higher the likelihood that the model assigns the image to this category.[1] The abnormality score is a continuous numerical output that can be translated into a binary classification by selecting a cut-off point (or threshold) on the abnormality score, above which the "TB-suggestive abnormalities are present" classification is assigned.

When using CAD products, internet availability is an important implementation factor to consider. A strong and stable internet connection is required for online mode because X-ray files are large (roughly 10–30 MB). If it is anticipated that CAD will be used in remote areas without reliable internet access, it is important to purchase a CAD product that can analyse CXR images and generate results locally offline.[2]

Fig. 7.6

CXR and use of CAD shown on a tablet in the field, from the national TB prevalence survey of Lesotho, 2018

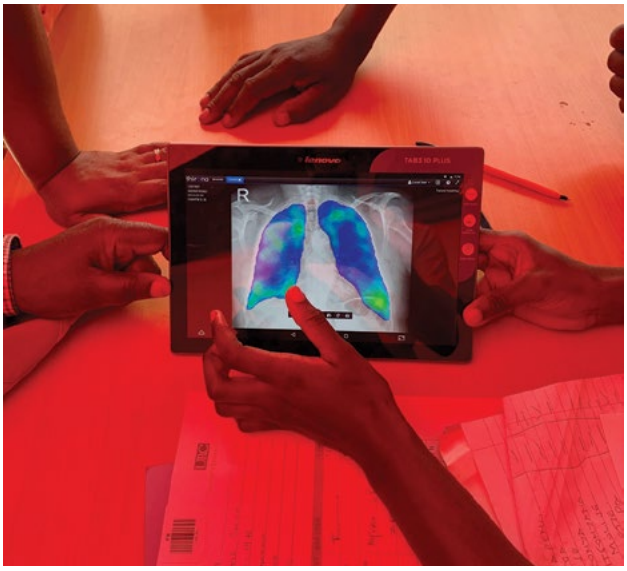


Photo credit: WHO/Irwin Law.

7.5.1 Use cases of CAD for screening in national TB prevalence surveys

Two use cases describe how CAD can be integrated into a CXR screening workflow within a national TB prevalence survey (**Fig. 7.7**):

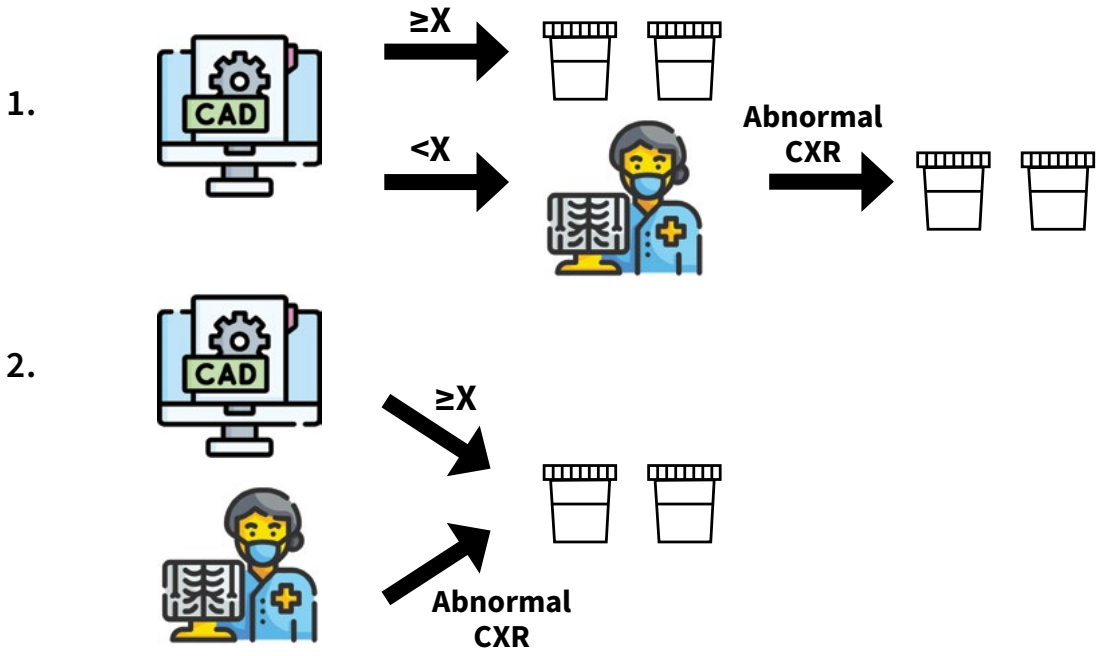
[1] It is essential to emphasize that likelihood is not proportionally related to probability. In other words, an abnormality score of 80 does not signify twice the probability a CXR contains TB abnormalities compared to an image with a score of 40. Additionally, it is crucial to understand that when two different CAD software products yield the same abnormality score, it does not imply that the probability a CXR contains TB abnormalities is identical. Furthermore, even when comparing the same abnormality score from different versions of the same CAD software, it does not necessarily indicate the same probability of TB abnormalities being present.

[2] Currently, all manufacturers offer offline solutions, which generally require an external processor like a laptop or other device. However, efforts are underway to integrate CAD software directly with the X-ray machine's computer or laptop, which would simplify the installation and set-up process. A hybrid version allows data to be synchronized with a cloud server when an internet connection becomes available, offering instant results and data backup.

Fig. 7.7

Use cases of CAD in a national TB prevalence survey

1. CAD with human reading of CAD-negative CXRs; 2. Parallel CAD and human reading



CAD, computer-aided detection. CXR, chest X-ray.
X is the number which represents the CAD threshold.
Images: Flaticon.com

- CAD with human reading of CAD-negative CXRs
- Parallel CAD and human reading

CAD with human reading of CAD-negative CXRs

For the first use case, CAD is used as an initial screen and all participants with a score equal to or above the determined threshold are referred for diagnostic evaluation for TB (confirmatory testing with an mWRD). All CXRs below the threshold are re-read by the human reader in the field who decides whether the participant is eligible for diagnostic evaluation for TB. The human reader will be able to review all CXRs but ensure that all those above the threshold are automatically screened in.

Some of the advantages of this use case include high sensitivity with the use of the human reader to capture those that are less than the threshold, the human reader will also be able to identify CXRs with any pathology which require further management, and less work wil be required of the human reader compared with use case #2. A disadvantage includes a lower sensitivity than use case #2.

Parallel CAD and human reading

For the second use case, CAD is used as an initial screen and all participants with a score equal to or above the determined threshold are referred for diagnostic evaluation for TB (confirmatory testing with an mWRD). In addition, the human reader in the field reads all CXRs (not necessarily blinded by the CAD score) and decides whether the participant is eligible for diagnostic evaluation for TB.

Advantages of this use case include higher sensitivity than use case #1, and the human reader will also be able to identify CXRs with any pathology which require further management. Disadvantages include more intensive work required by the human reader compared with use case #1, and the higher sensitivity of the use case will mean additional workload for the field laboratory.

The interpretation of CXR screening based on the use cases of CAD are shown in **Table 7.1**.

Can CAD be used without a human reader?

Another possible use case is the complete replacement of the human reader with CAD. That is, all participants with a score equal to or above the determined threshold are referred for diagnostic evaluation for TB with no human reading of any CXRs as part of the screening process. Although this use case is less intensive than use cases mentioned above, sensitivity is restricted to the performance of CAD and, most critically from an ethical viewpoint, there is no human reader to identify false negative CXRs (i.e. those below the threshold score), and CXRs with non-TB abnormalities (irrespective of the threshold score) that require further clinical

Table 7.1

Sputum eligibility based on the CAD use case to screen participants

CAD USE CASE	CAD THRESHOLD	HUMAN READER IN THE FIELD	ELIGIBLE FOR SPUTUM COLLECTION BY CXR SCREENING[a]
CAD with human reading of CAD-negative CXRs	Above threshold score	N/A	Yes
	Below threshold score	Abnormal	Yes
	Below threshold score	Normal or other abnormality	No[b]
Parallel CAD and human reading	Above threshold score	Abnormal	Yes
	Below threshold score	Abnormal	Yes
	Above threshold score	Normal or other abnormality	Yes
	Below threshold score	Normal or other abnormality	No[b]

CAD: computer-aided detection; CXR: chest X-ray; N/A: not applicable; TB: tuberculosis.

[a] This is independent of parallel symptom screening by interview. Irrespective of the CAD use case, if a participant acknowledges the presence of screening symptoms, the participant is eligible to submit sputum samples.

[b] Although participants are not eligible for sputum collection by CXR screening, they could be eligible if they were screen positive by symptom questionnaire.

management. Furthermore, **CAD is currently only recommended to replace a human reader for screening of TB and *not* for other lung, cardiac or upper gastrointestinal diseases**. Although the primary aim of a survey is to identify individuals with TB, other more common lung and cardiovascular pathologies are likely to be identified during screening *(24–26)*, thus requiring the interpretation of certified radiologists (or medical officers) and further clinical assessment (**Chapter 9**). Therefore, given the current limitations of CAD and given there will always be a person to discuss, inform and manage screening results with survey participants, there is currently greater utility for a human reader to be part of the overall screening and quality assurance process.

Which use case should be chosen?

The decision on which use case is chosen should be discussed with people experienced in conducting surveys, and should take into account the available technical and human resources. **In an ever-evolving environment, the use of CAD for TB screening will undoubtedly change with new versions of software and hardware, and with more in-country experience**.

7.5.2 CAD threshold

There is no single "correct" threshold (e.g. between 0 to 100) **that can be used across all CAD products to determine which individuals need further confirmatory testing**. The threshold varies across the different technologies, settings, populations being screened and purposes of screening.[1] In addition, evaluations of the different commercially available CAD solutions certified by the CE or FDA showed some variation in the diagnostic accuracy between use cases and settings, and between different versions of the same software *(27)*. Some important changes between versions of the software may significantly affect the performance of the algorithm if the same threshold scores are used. Therefore, users should contact the manufacturer to understand updates related to the TB algorithm. **In addition, manufacturer-recommended thresholds (e.g. 60) are currently based on limited data and (at the time of writing) may appear to be too high for use in community-based screening populations like those in prevalence surveys.** It has also been reported that the diagnostic accuracy may also vary between different CXR equipment using the same software *(28)*.

Selecting the threshold score involves an inherent trade-off between sensitivity and specificity. A lower threshold score will maximize sensitivity of the tool to detect true TB cases among the population being screened, but the reduced specificity will result in additional costs related to unnecessary follow-on diagnostic testing. On the other hand, a higher threshold score will reduce the volume, and thus the costs, of follow-on diagnostic testing owing to higher specificity, but the reduced sensitivity will result in missed cases of TB, as shown in **Fig. 7.8** *(29)*. In TB prevalence survey settings, a lower (more sensitive) CAD threshold will result in more survey participants being eligible for sputum collection and therefore will require a higher volume of laboratory testing in the field and centrally, whereas a less sensitive threshold will screen in fewer participants for sputum collection and may miss some people with TB.[2] Hence, careful consideration is needed to determine the most suitable threshold in TB prevalence survey settings, given the cost and logistical implications.

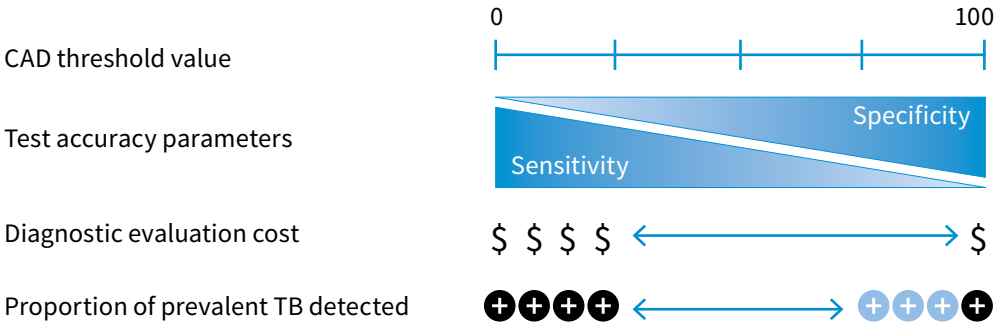
For these reasons, it is essential to **calibrate CAD**

[1] The objective of screening in a prevalence survey is to increase the chance of identifying the greatest number of people with TB in the community. This can be achieved by increasing the sensitivity of the screening tool; however, due consideration should be given to the resources available to confirm TB disease, such as laboratory capacity and human resources.

[2] Symptom screening in addition to CXR screening will increase sensitivity, but the overall yield of TB cases from symptom screening is generally much lower than from CXR screening alone *(6)*.

Fig. 7.8

Sensitivity versus specificity across the spectrum of CAD threshold values *(29)*



CAD, computer-aided detection; TB: tuberculosis.

products before implementation and use in a new setting or population *(7)*. Calibration of CAD requires analysing its diagnostic accuracy against a validated means of detecting TB or interpreting CXR images that can act as a reference standard (e.g. an experienced human reader). A user can then determine the most appropriate abnormality threshold score for their setting and use case, above which a confirmatory diagnostic test will be conducted. Calibration of CAD will help the user to estimate the accuracy, predictive values, overall yield and requirements for further diagnostic testing expected from the product.

As an example, **Table 7.2a** shows how many CXRs would have been considered abnormal by modifying the threshold in Mozambique's national TB prevalence survey (where a threshold of 40 was used, Delft CAD4TB version 5) and how that would have changed the volume of participants eligible for sputum collection based on abnormal CXR (and therefore the total number of sputum samples to be collected for bacteriological investigations). **This example is specific to the software and hardware products used and the population being screened, so the values shown are for illustration only**. By way of comparison, **Table 7.2b** highlights the imperfect sensitivity (and therefore number of false negative CXRs) if only the human reader in the field were used to screen in participants. In this example, the sensitivity of the human reader approximated a CAD score between 60 and 70 even with intentional over-reading.

Table 7.2a

Example of impact of CAD4TB (version 5) threshold on workload, based on data from the national TB prevalence survey of Mozambique, 2018–2019 *(30)*

CAD THRESHOLD[a]	NUMBER OF ABNORMAL CXRS (BASED ON CAD ONLY)	NUMBER OF SPUTUM-ELIGIBLE PARTICIPANTS (BY SYMPTOMS OR CXR BY CAD)	NUMBER OF SPUTUM SAMPLES TO BE COLLECTED FOR LABORATORY INVESTIGATIONS (2 SAMPLES PER PARTICIPANT)	NUMBER OF TB CASES DETECTED[b]	SENSITIVITY (%)	SPECIFICITY (%)
40	4 561	6 840	13 680	74	96.1	83.7
50	2 345	4 914	9 828	69	89.6	91.7
60	1 113	3 864	7 728	62	80.5	96.2
70	542	3 406	6 812	51	66.2	98.2

CAD: computer-aided detection; CXR: chest X-ray; TB: tuberculosis.

[a] The selected CAD threshold for the survey was 40.

[b] Twelve cases were excluded because they did not have an X-ray taken; 3 cases had a CAD4TB score <40 (n=74 cases for CAD4TB score >40).

Table 7.2b

Sensitivity and specificity of the human reader *in the field*, based on data from the national TB prevalence survey of Mozambique, 2018–2019 *(30)*

CXR READER	NUMBER OF ABNORMAL CXRS ELIGIBLE FOR SPUTUM SUBMISSION (BASED ON HUMAN READER ONLY)	NUMBER OF SPUTUM-ELIGIBLE PARTICIPANTS (BY SYMPTOMS OR CXR BY HUMAN READER)	NUMBER OF SPUTUM SAMPLES TO BE COLLECTED FOR LABORATORY INVESTIGATIONS (2 SAMPLES PER PARTICIPANT)	NUMBER OF TB CASES DETECTED	SENSITIVITY (%)	SPECIFICITY (%)
Human reader	746	2 740	5 480	51	67.1	97.5

CXR: chest X-ray; TB: tuberculosis.

Setting a CAD threshold in a national TB prevalence survey

It is necessary to calibrate the CAD threshold before starting field operations. There is likely to be a level of uncertainty at the start of the survey given the limited data to inform the initial threshold. Therefore a degree of flexibility allows for the threshold to be adjusted with the availability of more CXRs and corresponding CAD scores. Although other methods have previously been described *(29)*, a more practical and less costly suggestion is described in **Box 7.3**.

7.6 CXR interpretation by a human reader

7.6.1 Human reading of CXRs in the field

No CXR abnormality is specific enough on its own for a definitive diagnosis of TB. Some past surveys have adopted "TB-suggestive CXR findings" as a screening criterion. However, experience has shown that a variable proportion of bacteriologically confirmed TB cases were among individuals with "non-TB-suggestive CXR abnormality" or "minimal lesions". Therefore, individuals with any abnormality in the lung should be considered "eligible for sputum collection". This criterion should be applied irrespective of the HIV burden in the population.

If a human reader is used at the field level, the recommended CXR classifications are:

- normal;
- abnormal (pulmonary or pleural); or
- other abnormality (non-pulmonary pathologies).

Normal CXR

A normal CXR means lung fields are clear and no abnormality is detected. Participants with a normal CXR have no radiological basis for undergoing bacteriological examination. However, if the participant reports screening symptoms, then sputa should be collected for bacteriological examination.

Abnormal CXR

An abnormal CXR means a lung abnormality of any kind (including pleura) is detected on interpretation by the medical officer (e.g. opacities, cavitation, fibrosis, pleural effusion, calcification, or any unexplained or suspicious shadow, including findings not suggestive of TB). **Participants with an abnormal CXR, irrespective of symptoms, are asked to submit sputum samples for bacteriological examination**. Across implemented surveys, about 10% of survey participants were categorized as having "any CXR abnormality", making them eligible for sputum examination, although the proportion varied across different surveys *(6)*. Participants presenting with severe pathology on CXR may require immediate follow-up and referral (**Chapter 9**).

Other abnormality on the CXR

Congenital abnormalities, normal variants and bony abnormalities (including fractures) are excluded by definition, as are findings such as increased heart size and other heart-related abnormalities. These findings should be categorized as "other abnormality". Participants with *only* these abnormalities do not need to submit sputum samples for bacteriological examination unless they report screening symptoms. However, participants with severe pathology on CXR may require immediate follow-up and referral (**Chapter 9**).

Intentional over-reading by the human reader should be encouraged so that no suspected TB cases are left out; that is, if in doubt, the reader should classify the CXR as "abnormal, eligible for sputum collection". The purpose of over-reading in field sites is to not miss opportunities to diagnose TB among survey participants.

If the field reader identifies CXRs that show any abnormality that requires urgent or expert medical care or medication (e.g. pneumothorax, pneumonia, large pleural effusion or suspicion of malignancy), they should inform the team leader so that such participants can be counselled and referred to an appropriate health care facility. A hardcopy CXR film[1] may need to be provided to such participants together with a referral form (**Chapter 9**). If such an abnormality is detected at the central level (after fieldwork is completed), the survey coordinator should ensure that such participants are informed and guided towards appropriate health care.

7.6.2 Human reading of CXRs at the central level

At the central level, a more detailed CXR interpretation can be performed. The central CXR team should comprise one or more radiologists (with or without a chest physician), with the radiologist being the overall person in charge (this may be a legal or regulatory requirement in some countries).

To ensure quality control of the performance of human readers in the field, it is important for a certain proportion of normal and abnormal CXRs to be re-read by the central radiology team (**Chapter 14**). Similarly, a predefined proportion of CXRs that were ruled in or out by CAD should also be re-assessed. Ideally, all CXRs should be re-read to precisely quantify the level of under-reading or over-reading that happened in the field. **If reading 100% of images at the central level is not feasible owing to human resources or financial constraints, re-reading of all field abnormal CXRs plus at least 10% of randomly selected normal CXRs is recommended**.

The central team should classify X-rays based on a three-category classification similar to that used by the field reader, or a more detailed classification. An exam-

[1] A digital CXR image could be transferred to a portable storage device and given to the participant, or directly emailed to the treating officer.

BOX 7.3
SUGGESTED METHOD: HOW TO SET THE CAD THRESHOLD IN A NATIONAL TB PREVALENCE SURVEY

The method aims to match the CAD score to the screening positivity rate of a central CXR reader[1] for TB. In general, it is better to start with a low CAD score, and adjust up rather than the other way around.

1. A central CXR reader(s) should read CXRs from **two pilot clusters**[2] (or about 1000 CXRs) that use the same X-ray equipment and CAD software (and version) as the survey itself. The population being screened in the pilot should also be similarly representative of the survey population. The central CXR reader(s) should be blinded to the CAD score, field reader reports and any Xpert Ultra results. A CXR reader should screen in those eligible for sputum examination.
2. Calculate the referral rate of the central reader i.e. number of those screened in divided by number of CXRs read e.g. 250/900 = 0.28.
3. Collect all the CAD scores from the same CXRs read by the central CXR reader, and rank them from highest to lowest.
4. The initial CAD threshold is the Nth ranked CAD score where N is the referral rate mutiplied by the number of CXRs with an available CAD score. e.g. 0.28x900 = 252nd CXR.
5. After the first 5 clusters (approx. 2500 CXRs), ideally the same central CXR reader(s) should again review all the CXRs and repeat the same process as above. As before, the reader(s) should be blinded to the CAD score, field reader reports and any Xpert Ultra results. This method can be redone after the first 10 clusters (and possibly again after the first 15 clusters) until the threshold is deemed to be stable.
6. Calculate the maximum number of Xpert tests that can be done in one day per cluster (also see **Chapter 8**). This is the rate limiting step[3]. For example, based on a screen-positive rate of 15% and various assumptions (shown below in the table), the maximum number of Xpert tests per cluster that can be done in a 12-hour day is 48. After each cluster, review the number of Xpert cartridges used for testing. If the overall screening rate is consistently higher than 15%, then assess if the number of Xpert tests can be increased per cluster. Also assess if symptom screening is contributing to the higher rate; additional training may be required to ensure staff are interviewing in a standardised way.

CATEGORY	NUMBER
Number of participants per cluster	500 participants
Estimated screen positive (symptom and/or CXR)	15% (75 participants)[a]
Number of screening days	5
Estimated number of participants that screen positive per day	15
Number of Xpert Ultra tests required per day using diagnostic Option 1[b]	30
Number of Xpert machines (4 module) per cluster[c]	2
Number of tests per 12-hour day	48[d]

[a] Typically 5–10% of participants are screen positive by CXR only, and 5% are symptom positive only, and 5% are both CXR and symptom positive.
[b] Based on diagnostic Option 1, each screen positive participant should submit 2 sputum samples for Xpert testing.
[c] It takes approximately 2 hours per test to be completed.
[d] More samples can be tested if hours are extended. The priority is for the participant to receive results the next day thus facilitating clinical management but also to collect further samples for culture if Xpert positive.

This method of setting the threshold will be reviewed by WHO and may vary once there is more experience with its use in TB prevalence surveys. Please discuss threshold selection with survey experts as there may be new insights following publication of this guidance.

[1] The central reader(s) should ideally be a local radiologist with extensive experience of reading CXRs and tuberculosis. If a person is not available, then a specialist external reader (which could be based remotely) could also serve the function.
[2] For a pilot cluster, an arbitrary threshold can be used for testing and training purposes only e.g. 30 out of 100 (or 0.3 out of 1).
[3] Compared with diagnostic Option 1, Xpert testing capacity is less of a concern if Option 2 is selected because only 1 Xpert will be conducted.

ple of the latter, developed specifically for the Myanmar survey (2017–2018), is provided in **Annex 7.1**. In the case of an inconclusive result, an opinion from a "neutral" expert should be sought.

Central reading of CXRs may find a certain level of **under-reading** by the field reader. That is, an image is erroneously classified as "normal" (or "other abnormality") in the field but central readers detect some abnormalities (i.e. eligible for sputum collection). Under-reading should be minimized as much as possible. It is also expected that there will be some CXRs that are labelled "abnormal" at the field level but "normal" at the central level; that is, **over-reading**. A small percentage (i.e. <5–10% classified as abnormal at the field level are read as normal at the central level) is acceptable. However, if the proportion of over-reading is excessive, this will have implications for laboratory workload, owing to the collection of a high number of samples from subjects with no CXR abnormalities. In both situations, where there is excessive under-reading or over-reading of CXRs, further training and supervision of field readers is highly recommended.

With digital radiology and internet connectivity now allowing for remote CXR consultation, central reading of CXRs by a human reader can happen simultaneously with, or soon after, reading by the field reader. This provides opportunities to change the CXR interpretation and collect sputum samples from participants who have a centrally read abnormal (eligible for sample collection) CXR, but a normal field reading (and no reported screening symptoms). If applicable, the change in the screening outcome should also be reflected in the data collection system; that is, "not eligible" should be changed to "eligible for sputum". This QA process allows for more immediate retraining of specific field readers, and adopting this in the first few clusters or days of field operations can improve screening quality and limit the risk of missing people with TB. However, this process requires the availability of central readers and reliable information technology (IT) support, and it can be a challenge to re-contact participants and collect specimens for the central laboratory once the survey team has left the field site.

In circumstances where there are no in-country central readers, digital transfer of CXRs to colleagues in other countries has been undertaken in some surveys; for example, CXRs from Lesotho (2019) were sent to South Africa, and those from Eswatini (2018–2019) were sent to Japan.

The central team may also undertake post-survey evaluations; for example, re-analysis of cases showing radiological–bacteriological mismatches through to quality-related issues in X-ray, data management and laboratory work. This may include examination of CXRs where the CAD score was high but there was no bacteriological confirmation, and re-assessing all those who were classified as survey cases to ensure their CXR is in agreement with other data.

7.7 Choice of equipment

The choice of which equipment to use for chest radiography depends on cost, procurement versus leasing, field conditions, radiation safety, workload and long-term use. This section discusses each of these factors.

7.7.1 Costs

Resources are often limited, and appropriate choices need to be made. This is not easy, given considerable variation in the price (and fluctuations over time) of various X-ray technologies.

The unit cost for one set of X-ray equipment is approximately US$ 95 000 (2024) if direct digital radiography is used.[1] Updated costs can be found in the Global Drug Facility health products catalogue *(31)*. Cost may vary depending on choice of detectors and countries of shipment. Considerable reductions from the official list price may be possible after negotiation, especially if items are ordered in volume. The number of CXR machines to be procured depends on the number of field teams used during the survey (i.e. one CXR machine per field team is required). However, having one or two backup CXR machines is usually recommended because breakdowns due to bad road conditions or overheating can happen.

Apart from the initial costs of equipment, installation and training, warranty extension, maintenance and spares must also be considered, which may add significantly to the total costs.

A good practice is to assess costs based on the life cycle concept, whereby costs are calculated for the life cycle of the equipment (usually taken as 8 years), including initial investment, maintenance, operational costs, inflation and depreciation. If X-ray units are to be mounted on trucks or vans, or housed in lead-shielded containers, these need to be included in the total costs. X-ray vans can also be equipped with a small laboratory with Xpert machines (see **Fig. 7.9**).

When selecting a CAD supplier, performance and price are fundamental criteria, but there are other vital considerations such as the availability of internet connectivity, the portability (of hardware), compatibility with X-ray systems, and integration with any existing radiology information system or PACS.[2] At present, some data suggest that the use of CAD as a screening tool

[1] The unit cost includes hardware, CAD software, installation, training and warranty (1 year) based on the Global Drug Facility catalogue for diagnostics, medical devices and other health products (2024).

[2] The Stop TB Partnership and Foundation for Innovative New Diagnostics (FIND) have developed a resource to compare different CAD products *(22)*. The Stop TB Partnership's Global Drug Facility also provides more details in its diagnostics catalogue *(31)*.

Fig. 7.9

Interior of a van equipped with a digital X-ray and GeneXpert machines used in the TREATS project, 2019–2021

Photo credit: Eveline Klinkenberg.

could be a cost-effective and efficient way to improve TB diagnosis *(32, 33)*.

In addition to the cost of CXR equipment and consumables, the cost of CXR reading at the field and central levels should also be budgeted. Field reading could include human reading or CAD, according to the survey protocol, whereas central reading relies on senior radiologists' expertise. If radiologists are not available at the local level, remote (i.e. distant, in-country or international) radiologists might be invited to collaborate (provided that digital technology is used and images are transmitted electronically), and this should be included as a specific budget line. As an example, Eswatini's survey (2018–2019) involved radiologists in Japan reading some CXRs, and radiologists from South Africa read CXRs for Lesotho's survey (2018).

Considering the advantages of DR, it is recommended that future surveys make more frequent use of digital rather than conventional technology, even though conventional equipment is less costly than digital technology.

7.7.2 Procurement versus leasing

An alternative to the procurement of a full range of equipment is to lease equipment for the duration of the prevalence survey. Among recently completed surveys, South Africa opted for CXR leasing, which included equipment servicing, cloud storage of CXRs, and provision of human resources such as drivers, radiographers, offsite radiologists and vehicles (see **Fig. 7.10**). Leasing may be less expensive and more convenient for countries that already have sufficient radiology infrastructure; however, considering that leased equipment has to be returned at the end of the survey, there will be no future benefit like the investment of new CXR equipment which could be repurposed after the survey e.g. for TB screening or diagnostic purposes.

Fig. 7.10

Leased X-ray van used in the national TB prevalence survey of South Africa, 2017–2019

Photo credit: Marina Tadolini.

If mobile CXR equipment is already available in the country (i.e. used for active case-finding activities), a temporary allocation of some of that equipment to the survey might be explored. An added advantage may be the addition of an in-country service contract.

7.7.3 Field conditions

Field and road conditions play an important role in decision-making about what type of equipment to use. For example, DR systems are heavy and require good transportation facilities. Portable equipment might be transported with vehicles (e.g. 4-wheel-drive cars) and installed once at a cluster site, or installed on specific vans or trucks, which might also accommodate the reading station for the medical officer (see **Figs. 7.11–7.12**).

It is also possible in a specific country to procure a

Fig. 7.11

CXR container on the back of a truck used in the national TB prevalence survey of Lesotho (2018)

Photo credit: WHO/Irwin Law.

Fig. 7.12

Interior of the X-ray van used in the national TB prevalence survey of South Africa, 2017–2019

Photo credit: Marina Tadolini.

variety of equipment, and allocate the most convenient piece of equipment to particular types of terrain (e.g. Eswatini and Lesotho had both CXR vans and portable equipment).

Powerful X-ray units require greater input power, which thus requires a more powerful electric generator. However, the imaging power of these units is offset by the extra weight that needs to be transported.

Ambient temperature is another factor to be considered in the field. High temperature (i.e. >40°C) can affect the radiology equipment (X-ray generator), and also the quality of images owing to the specific characteristics of flat panel detectors. It is therefore important to consider the technical specification of the equipment's flat panel (i.e. lower and upper limits of the temperature), or choose a cooler room for the X-ray site, to guarantee quality images and avoid image deterioration.

Recent ultra-portable units are operated with lithium batteries. Some caution should be taken with lithium batteries because they may deteriorate quickly when instructions are not strictly followed (e.g. over-charging and high temperatures, during both operation and storage and transportation, can accelerate the deterioration of lithium batteries). The number of CXRs that can be taken by one battery may change quickly due to deterioration of the battery, which has serious consequences for active case detection activities and prevalence surveys. Therefore, if a backup of all equipment cannot be guaranteed, at least a backup battery is essential.

7.7.4 Radiation safety

X-rays are ionizing radiation and can potentially cause biological damage, especially in vulnerable populations such as children and pregnant women. This can lead to legal and ethical issues in using X-rays for screening in the community. Therefore, radiation risks to survey participants and, in particular, to survey staff (whose risk is greater considering the prolonged and high workload) must be mitigated in national TB surveys by conformity to radiation safety standards and good practices guidance *(34)*.

CXR is largely considered safe, with a radiation dose of 0.1 mSv, which corresponds to 1/30 of the average annual radiation dose from the environment (3 mSv) and 1/10 of the annual accepted dose of ionizing radiation for the general public (1 mSv). Pregnant women are especially vulnerable to ionizing radiation from radiography, and children have a longer life expectancy and, therefore, more time to develop radiation-induced health effects. However, CXR has been deemed to not pose a significant risk for a pregnant woman and her foetus or for children, provided that good practices are observed, as the primary beam is targeted away from the pelvis.

In most countries, use of X-rays is regulated by gov-

ernment authorities. The radiation regulatory body should be engaged during the survey planning stage to understand whether a specific approval (e.g. clearance from the radiation authority) is required to conduct the study, and a copy of the survey protocol and the X-ray reference guide should be submitted. Technical specifications of the X-ray equipment and radiation safety measures (e.g. adherence to the ALARA [as low as reasonably achievable] principle, use of radiation caution signs, use of lead aprons for staff and monitoring devices such as dosimeters) should also be mentioned clearly and submitted. Precautions are needed to ensure the safety of health care workers and survey participants (e.g. marking areas with exposure risk and making sure that unauthorized people do not stray any closer to the detector area than is safe). Protective gowns, or curtain-style protective shields or partitions, and regular use of personal dosimeters to measure ionizing radiation exposure, are recommended for X-ray technicians throughout field operations. Pre-testing of X-ray machines (for radiation leakage) may be mandatory in some countries.

The X-ray reference manual should contain guidance on the radiation safety practices being adopted during fieldwork. Any advice from the radiation regulatory body should be incorporated in the reference manual and followed during fieldwork. Application to the ethics review committee (or other equivalent body) should cover all aspects of survey field radiography. Supervisory visits should be made by the central team to see that radiation safety is being observed in the field.

Some areas that influence radiation safety, as well as relevant suggestions for each area, are listed in **Fig. 7.13**.

Informed consent for X-rays must be obtained from all participants (see **Chapter 11**); this may be part of the overall consent, but use of X-ray should be specifically mentioned. Good communication is important in allaying public anxiety. An X-ray fact sheet (translated into the local language) can be used for this purpose (see **Annex 7.2**).

7.7.5 Workload

To provide an idea of the workload in prevalence surveys, the average workloads handled in some previous surveys are provided in **Table 7.3**. These figures can vary significantly: usually the number of X-rays to be taken per day is expected to be between 110 and 200 (i.e. the number required to complete a cluster of 500–700 people in 4–6 days). The total number of CXRs that will be taken per day depends on participant attendance, and the indicated figures can only be reached if the attendance during survey activities is high. A day in a TB prevalence survey spans from early morning to late evening (which may account for 12–14 hours in total) – it is not limited to the average 8 working hours of routine activities.

Fig. 7.13

Radiation safety: considerations and suggestions

REGULATORY	• Ensure that survey radiography conforms to the existing national laws and regulations for X-rays • Engage the national radiation authority during protocol development and maintain communication
PROCUREMENT	• Procure from manufacturers with a good track record • Pre-test equipment before actual use (may be mandatory in some countries) • Procure radiation protection devices (refer to the X-ray reference manual for details) • Ensure there is a service contract and in-country servicing to maintain safety and quality of equipment
PROTOCOL	• An X-ray reference manual should contain details of radiation safety measures to be employed in the field • Ensure the protocol is cleared by the research ethics committee (REC) • Submit a copy of the protocol to the national radiation authority
PRE-SURVEY	• Employ qualified personnel only • Include radiation safety in training
FIELDWORK	• Apply the ALARA principle (i.e. radiation is as low as reasonably achievable) • Ensure adherence to standard operating procedures • Obtain informed consent from all participants

ALARA: as low as reasonably achievable.

Table 7.3

Average expected CXR workload in selected national TB prevalence surveys

COUNTRY	SAMPLE SIZE	AVERAGE EXPECTED NUMBER OF CXRS PER DAY[a]	CXR TECHNOLOGY USED
Kenya, 2015–2016	72 000	200	Direct digital
Myanmar, 2009–2010	49 690	175	Conventional and AFP
Myanmar, 2017–2018	69 000	150–160	Direct digital
Nepal, 2018–2019	57 610	100–120	Direct digital
Philippines, 2007	21 960	110	Conventional
Philippines, 2016	54 000	200	Direct digital
South Africa, 2017–2019	55 000	100	Direct digital
Viet Nam, 2006–2007	105 000	175	Conventional and digital

AFP: automatic film processing; CXR: chest X-ray; TB: tuberculosis.

[a] Excluding mop-up day, where workload is generally lower.

The time taken for an X-ray includes explaining the procedure to the participant, the participant changing clothes, taking the image and awaiting the (CAD or human reader) result. Survey experience has shown that the average time taken for each X-ray is longer initially and then decreases as the process is streamlined and staff become experienced in handling the process. It is crucial in this phase to also involve local volunteers who can assist by explaining the process in local language to facilitate participants' understanding and help older people to dress or undress. Usually, gowns or T-shirts are provided to participants to avoid artefacts due to clothes.

Daily CXR capacity varies depending on the type of CXR equipment being used. Although portable equipment has a throughput of 100–300 CXRs per day, ultra-portable equipment has a limited daily capacity of less than 100 per day, although this might improve with the recent development of new battery systems and use of a charger during operation.

7.7.6 Long-term use of X-ray equipment

Another important factor in the choice of equipment is the potential use of X-ray equipment after the survey is completed; for example, for outreach activities not necessarily related only to TB. Although CXRs can be done with a low-rating X-ray generator, general radiography (e.g. X-ray of the lumbar spine) requires use of a high-power X-ray generator (i.e. higher power rating of the X-ray generator and X-ray tube). If, at the end of the survey work, the X-ray unit is to be used for chest radiography only, the configuration may not be important. However, if the equipment may be later used for general radiography work in a health care facility, it is practical to buy a higher configuration machine (if possible, one with a flexible arm). Long-term use is of course not possible in the case of leasing.

Some examples of long-term use of CXR equipment after the survey are provided below:

- the Philippines (direct digital for 2016 survey) used CXR facilities for active case-finding activities;
- Rwanda (direct digital) used equipment for TB screening in prisons;
- Thailand (direct digital) used equipment for active case-finding activities and occupational health[1] in industrial settings;
- Myanmar (direct digital) used equipment for active case-finding activities and in coronavirus disease (COVID-19) fever clinics; and
- multiple countries have used equipment for periodic active case-finding visits to prisons.

7.8 Human resources

Digital systems are more user friendly and require fewer human resources than conventional systems, because there is no need for film development. CR and conventional systems are more labour intensive and time consuming.

Human resources may not be an important issue if adequately skilled personnel are available, and the employment costs are not prohibitive. If local human resources or CXR reading skills are limited, CAD systems alone could be used for field CXR reading with no human readers, as per the recent WHO guidance *(7)*. However, this approach has never been implemented in national TB prevalence surveys (although it has been used in research prevalence surveys such as TREATS) (see **Box 7.1**).

Human resources involved in the survey X-ray activities may be part of a central X-ray team or a field X-ray team.

The **central X-ray team** includes expert radiologists who work at the central level, starting from survey preparation then throughout the entire duration of the survey. The number of involved radiologists may vary

[1] It is not always necessary to buy X-ray equipment for the prevalence survey because X-ray vans for occupational health can be mobilized for the survey, and equipment might be borrowed or leased.

from one to three or four depending on availability and the number of CXRs expected to be read centrally. Central X-ray team members are also part of the medical panel (see also **Chapter 9**).

The main responsibilities of the central X-ray team are:

- developing the X-ray reference manual (e.g. standard operating procedures [SOPs] and interpretation method);
- developing standard training methodology (e.g. standard CXR image set);
- performing a threshold calibration if a CAD system is used;
- training of the field X-ray team (e.g. medical officer, radiographer, data manager and field team leader);
- monitoring and QA of pilot clusters and survey fieldwork;
- classifying and reporting results as per the adopted interpretation method;
- undertaking final case ascertainment; and
- undertaking post-survey assessment (including re-analysis of radiological and bacteriological mismatch cases, if required).

In some recent surveys, where in-country human resources for central CXR reading were limited, remote reading was implemented in a different country after survey CXR digital images were uploaded to the cloud. Although cloud-based options will be increasingly used, they might not be an option in every country; for example, confidentiality issues (especially when images are transmitted out of the country) might be raised.

Each **field CXR team** typically includes at least one radiographer and one assistant, and a medical officer in charge of reading the CXR in the field during screening operations. These staff members usually work hand in hand with the team leaders and field data managers.

The main responsibilities of the **field X-ray team** are:

- installing and uninstalling X-ray equipment at the survey site;
- carrying out X-ray fieldwork as per the X-ray reference manual;
- ensuring radiation safety for themselves, participants and the general public;
- overseeing (by medical officers) CXR interpretation, to identify participants eligible for sputum examination, and recording CXR interpretation in the data collection system;
- operating CAD (if applicable);
- providing feedback (from medical officer) to all survey participants about CXR results;
- referring (by medical officer) participants with severe conditions that may need immediate care; and
- ensuring maintenance of CXR equipment.

The two main aspects of managing X-ray-related activities are operation and interpretation, as discussed below.

7.8.1 Operation

The field X-ray team should comprise one or (if possible) two radiographers[1] who report to a medical officer.[2] The radiographers are responsible for setting up the X-ray unit; carrying out the CXR procedure; ensuring radiation safety for the field teams, participants and general public; archiving X-ray images and documents related to X-ray work; maintaining the X-ray equipment and ensuring QA; uninstalling the X-ray equipment at the end of fieldwork; performing routine maintenance; and basic troubleshooting. An assistant should be available in the X-ray area (preferably a female, for the comfort of female participants) who can help with tasks such as briefly explaining to the participants the procedure and what they are expected to do, allaying any anxiety they may have and guiding them to a changing area; a local volunteer can suffice for this purpose. A technician or a driver attached to each field team is also advisable to maintain the electric generator, ensure fuel supply and assist the X-ray team with daily maintenance of the X-ray machine.

7.8.2 Interpretation

Interpretation of CXRs should be in two stages – field and central. Field-level interpretation is done during the screening process at the field site, whereas the central X-ray team is responsible for quality control of the field-level results and carrying out a detailed interpretation (e.g. classification of X-rays into the adopted classification system).

- Field-level interpretation can be done by a medical officer (usually one per field team), with or without a CAD reading system.
- Central-level interpretation is done after the end of fieldwork at a survey site (or in real time if images are transmitted electronically immediately after processing). The X-ray images are reviewed at the central level by a senior radiology team (i.e. one or more

[1] Some ambiguity surrounds use of the term "radiographer". In some countries, "radiographer" and "X-ray technician" are different cadres, while in others the terms are used interchangeably. Sometimes the term "radiological technologist" is also used. For survey purposes, a radiographer is a skilled individual who by qualification or training can perform X-rays.

[2] For the sake of simplicity, the term "medical officer" is used in this chapter. Depending on country-specific scenarios, the person may be an adequately trained health worker or radiologist or physician or any other individual approved for the purpose of field-level interpretation and for supervising the field X-ray team. Although such a person is not required to provide a written X-ray opinion (since this is community work and not clinical practice), it should be remembered that X-rays are medical diagnostic procedures. Adequate training of such individuals on interpretation of CXRs is a prerequisite. Depending on the composition of the field team, the medical officer may also act as an onsite physician or team leader.

radiologists, depending on the country's decision). **Ideally, all CXRs should be centrally reviewed** (both for quality control issues and for data analysis), **although some countries may only review all field abnormal CXRs and at least 10% of randomly selected normal CXRs, depending on the number of central readers**. It is assumed that the central-level CXR reader has more experience than the field reader and is thus the reference standard. The sooner the central reading is done, the better, to ensure QA of field reading (i.e. if there is too much deviation, especially if abnormal CXRs are being missed by field readers, then action needs to be taken).

The reporting terms and classification of findings should be based on a standardized set of X-ray images, developed specifically for this purpose (an example is shown in **Annex 7.1**). A document containing guidelines on interpretation (or the country-specific X-ray reference manual) should be available for all X-ray team members and the team leader, and guidelines should be discussed during training and pilot clusters.

Clinical management and referral of people with severe pathology identified through CXR is described in **Chapter 9**.

7.9 Training

Training of X-ray personnel should be performed by a radiologist. A radiographer who has experience or training in using the particular X-ray technology to be used in the survey should assist the radiologist. If a radiologist is not available, a chest physician (with experience in radiography practice and CXR interpretation) can provide the training.

Radiographers should receive a minimum of 5–6 days training, including hands-on experience of equipment to be used in the survey (operation, routine maintenance and basic troubleshooting), QA and radiation safety. Training in use of the equipment should be provided directly by the manufacturer; this should be included in the procurement contract.

Medical officers should receive at least 3 days training, including orientation to the X-ray technology being used, and practice sessions on classifying normal and abnormal CXRs using a standardized image set.

The training should include a practice session that simulates field conditions; this can be carried out, for example, in a factory setting. A pilot study (with the entire survey team) should be carried out before the actual survey work commences.

The number of X-rays to be taken per hour depends on the sample size, the radiography technology being used and, of course, the number of participants attending the field site. Some extra time needs to be allowed for repeat X-rays. The average time taken per participant can be calculated based on the pilot survey.

Based on specific conditions and requirements, each country should develop their own X-ray reference manual (containing SOPs, equipment details, practical advice, interpretation and training methodology) for use during their prevalence survey.

7.10 Field operations

Once the survey team arrives at the survey site, the X-ray room or area is prepared for fieldwork. The radiographer unpacks the equipment and installs it at a proper place and in a proper manner, to ensure safety for participants, the field team and the public; privacy for participants; and maintenance of a smooth workflow. Once installation is complete, the equipment is checked for proper functioning. The X-ray area or room is then clearly marked, and radiation hazard signs are displayed at appropriate places. A restricted-entry zone is created around the area such that only X-ray personnel and the participant undergoing CXR (sometimes with an attendant if the participant needs physical support) are allowed inside. If the X-ray equipment is pre-installed on an X-ray bus or van with lead shielding, preparation of the area is not required. A restricted-entry zone around the X-ray bus helps maintain privacy and smooth participant flow.

On survey examination days, participants come to the X-ray area at a scheduled time (appointments are given to households during enumeration (census) day) after their symptom screening interview. **If a participant is not physically able to have a CXR or refuses for any reason, sputum samples should be collected from that person**. Once the participant is received in the X-ray area, a volunteer (or assistant) checks the survey identification number and ascertains that consent has been obtained. Some surveys may require a separate X-ray data sheet to be used and the receptionist can start the process at that point. An explanation is given to the participant about what they should expect during the X-ray procedure (e.g. breath-holding) – visual aids and fact sheets should be used for this purpose. A local health worker can perform this task and a female assistant or volunteer should be used for the comfort of female participants. Once the participant has put on the participant gown or T-shirt (in the designated changing area), they are guided to the X-ray procedure area. Privacy must be ensured for survey participants who need to remove any clothing with metallic components or accessories.

In the meantime, the X-ray assistant (or radiographer) prepares the X-ray unit for the new participant. Demographic data of the participant are also recorded and entered into a computer; most demographic data would have already been collected and if a barcode from the invitation card is used for identification, scanning the barcode can be sufficient (after confirming identity by checking the name and age) without the

need to re-enter data (see **Chapter 16**). It is critical that the correct demographic data and survey ID are also recorded in the system being used. Data management errors can occur given the number of daily CXRs undertaken; for example, a CXR of a female participant could be mixed up with a male participant, or a son and father with similar names could be interchanged.

In the procedure area, the radiographer confirms the participant's identity, positions the participant for the CXR, applies the protective gonadal gowns to the participant and performs the CXR. The participant is then asked to wait in the waiting area while the X-ray image is processed. The radiographers can swap their roles during the day, to reduce radiation exposure.

Once the image is ready, a medical officer inspects it and carries out basic QA and field reading (unless CAD is used alone). The officer then records the findings on the X-ray data sheet or directly in the CXR system in the case of digital collection; recording may be automated if the system in use allows. If the CXR findings suggest that the participant needs urgent medical intervention, the team leader is informed so that appropriate action can be taken (see **Chapter 9**).

If the CXR procedure does not need to be repeated (which may be necessary if the image quality is not good enough for interpretation), the participant is asked to change back into their clothes (ideally in a second changing area) and proceed to the screening verification personnel, who guide the participant towards the next step, which will depend on the screening result (see **Fig. 7.14**). For example, a person with an abnormal CXR would be asked to proceed for sputum examination. Participants should be reassured that going for sputum examination does not mean that they have TB, and that, based on the CXR (or symptom screening), a sputum examination will help in further evaluation. If the participant does not qualify for a sputum examination, a data clerk checks that all documentation is complete before the participant leaves the survey site (or goes to the HIV station if this is part of the survey process). At the final exit, participants are thanked and a token of appreciation may be provided.

If a CXR shows some abnormality that needs medical attention, a referral letter should be drafted by the medical officer and the participant referred to the nearby clinic (see **Chapter 9**). A written opinion on the CXR is usually not provided at this stage because the medical officer is only trained for survey-related X-ray interpretation and not for making a detailed radiological assessment. However, an online or over-the-phone consultation between the field team and the central unit to manage some urgent cases is now more feasible thanks to digital technology and the ability to transmit images from the field with a good internet connection.

Fig. 7.14

Medical officer explaining the CXR result to a participant in the national TB prevalence survey of Eswatini, 2018–2019

Photo credit: Marina Tadolini.

7.11 Practical issues and tips

7.11.1 Procurement of equipment, accessories and consumables

X-ray equipment forms a considerable part of the total survey costs, and experience shows that procurement of such equipment is a frequent bottleneck. Countries have their own procurement processes and rules, and it helps to initiate the process early so that the equipment is available in good time. This means that the choice of X-ray equipment should be finalized as early as possible. Depending on the type of X-ray technology chosen, a list of all items needed with the X-ray unit should be prepared, so that these items are procured well in advance of the actual fieldwork. (An example of an X-ray equipment checklist is shown in **Annex 7.3**.)

If sufficient equipment is already available in the country and can be temporarily devoted to the prevalence survey, it might not be necessary to procure new items. A comprehensive checklist in this regard should be prepared ahead of time, to ensure that all the equipment, software and consumables needed to carry out the survey are available, or to plan procurement of only the necessary or missing equipment. This may represent a considerable cost saving.

A third option, besides procurement or use of existing equipment, is equipment leasing (with or without service) from the X-ray company. South Africa made use of this option for their prevalence survey (2017–2019); the package arranged included radiographers and maintenance in addition to the equipment itself.

Technical partners and mechanisms, such as WHO, the Global Fund and others, can assist country experts in choosing appropriate equipment for survey purposes and preparing procurement lists. International agencies

including the United Nations Children's Fund (UNICEF) and the United Nations Office for Project Services (UNOPS) have facilitated the procurement process in several countries.

7.11.2 National authority authorization

Laws applicable to the purchase of X-ray equipment in each country should be respected; for example, in some countries the national radiation authority must be informed before the equipment is purchased or imported. Also, approval of use from the radiation authority might be required in addition to market authorization. Such authorization might be different for indoor use and outdoor use.

7.11.3 Transportation

Since prevalence surveys are carried out in the community, equipment must be transported to field sites. Often, sites have poor road connectivity and conditions; therefore, equipment may have to be transported by other means (e.g. by boat or manually carried). Rarely, even this may not be possible, in which case the X-ray equipment may have to be set up at another centre and participants transported to and from that centre.

The weight and dimensions of the equipment are thus critical factors in assessing the suitability of transportation (see **Fig. 7.15**). Trucks or vans are the usual mode of transportation. Special X-ray machine-mounted trucks or vans can be made available by many manufacturers. These are custom-made, and the X-ray area is lead shielded to provide radiation safety. Another option is a lead-shielded container fitted with an X-ray machine, which can be transported to and deposited at the survey site. A limitation with these options is that reasonably good road connectivity and conditions are essential.

Fig. 7.15

X-ray equipment transported by boat during the national TB prevalence survey of the Philippines, 2016

Photo credit: Raldy Benavente/FACE Inc (Philippines).

In general, digital CXR equipment is heavier (except for ultra-portable units) and more delicate than conventional systems. Four- or six-wheel-drive vehicles are better suited for transporting heavy equipment and for rugged terrain. Costly and delicate equipment (e.g. DDR) usually requires more sophisticated means of transport such as air suspension vehicles. Fuel for CXR transportation also needs to be included in the survey budget.

7.11.4 Total weight

Total weight should include the weight of the X-ray equipment, consumables, electric generator and other accessories (as per the equipment checklist). Although the weight of the X-ray machine is almost always mentioned in the specifications provided, the weight of the chosen electric generator (depending on the total power requirement and availability) is also a critical factor. High-power electric generators are heavy and may need separate transportation.

7.11.5 Space or housing

Given that many X-ray items are to be taken to the survey site, the X-ray unit in the field must be housed in such a way as to ensure radiation safety and smooth flow of participants. A walled room such as a community hall or school classroom can be used for housing the portable X-ray unit. WHO recommends 230 mm baked clay brick walls as adequate for radiation protection *(35)*. There should be no obvious sources for radiation leaks (e.g. open windows), at least in the direction of the primary X-ray beam. The radiographer should make sure there is no public waiting area in the direction of the primary beam. A water-level meter should be used to confirm that the X-ray machine is placed on a flat surface; this ensures that the X-ray beam is horizontal. The entire radiography unit can also be mounted on a truck or in a 20-foot container cabin. If a walled area is not available for radiography, open radiography can be considered. An example of the flow of participants and data in the CXR area, showing requirements at each point in the flow, is given in **Fig. 7.16**.

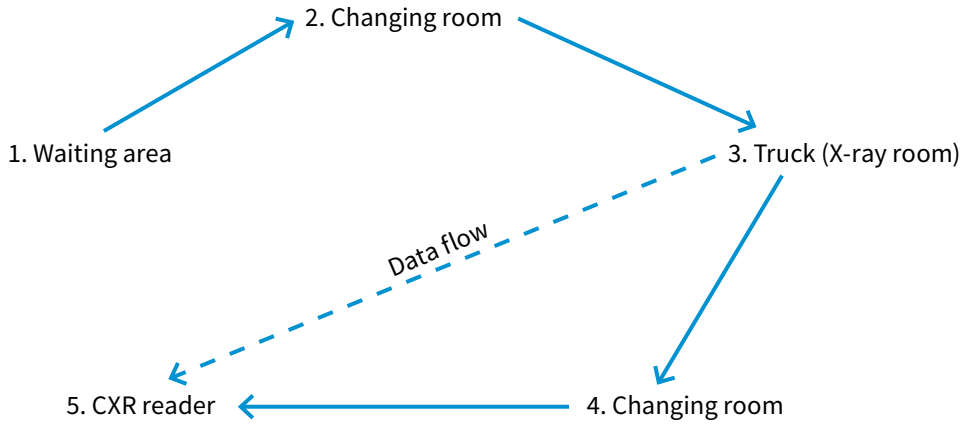
Compliance with the national laws governing radiation is essential. The International Commission on Radiological Protection and the National Council on Radiation Protection and Measurements recommend a safe distance of 2 m from the source of radiation in image intensifier fluoroscopy set-up. The exposure cord should therefore be at least 2 m long, or a remote control switch should be used for exposure. An adequate distance from the X-ray source should be measured and the areas cordoned off *(36)*.

7.11.6 Installation

Installation of CXR equipment and CAD (if used) is a delicate process that is usually managed by the equipment suppliers (at least in the first instance), and the presence

Fig. 7.16

Participant and data flow at the CXR station in the national TB prevalence survey of Eswatini, 2018–2019



CXR: chest X-ray; TB: tuberculosis.

of a survey team IT specialist during equipment installation is recommended.

If CAD is to be used, a local area network is required if CAD software is installed on a different computer from the one linked with the CXR machine used for screening (two-device mode). A network connection is then required to transmit digital CXR images from the X-ray system workstation to the CAD laptop. A static IP address should be assigned to both computers so that a DICOM node for image transfer can be set up on the X-ray system workstation to ensure transmission of images to the CAD laptop.

7.11.7 Storage (consumables, hardware)

Participant and personnel gowns, data sheets, CXR SOPs or other documents, lead markers and other consumables, and CXR viewers, barcode readers and other equipment (e.g. CAD software) will need to be safely stored throughout the field operations.

7.11.8 Generator

In general, digital X-ray systems require more power than conventional systems. The power required can be estimated by adding up the power requirements of various equipment to be used (e.g. X-ray machine, autoprocessor, workstation, view box, lights, fans, air-conditioning and CAD). Procurement of a generator should be considered after this has been done. A sufficient fuel supply for the generator must be ensured – the engineer or technician can be put in charge of this.

7.11.9 Breakdown of equipment

The malfunction of CXR machines can happen during field operations, often due to high ambient temperature. If a breakdown occurs and is not rapidly repaired, it will slow down and delay the ongoing cluster operations (and subsequent clusters). X-ray breakdown can represent a critical bottleneck for the survey and for the laboratory in particular, as all participants are asked to submit sputum samples (regardless of symptoms) if CXRs cannot be performed. In cases of CXR breakdown, reception can be temporarily closed while the issue is fixed; processing of participants already in line could be completed by making them sputum eligible. If the breakdown cannot be solved in a short time frame, the decision can be made to complete the current cluster without CXR but delay the next cluster. This may affect the survey schedule and delay the following clusters. Hence, regular maintenance of X-ray equipment (including preventive maintenance) is crucial. A comprehensive maintenance contract with the supplier reduces the breakdown time of equipment.

7.11.10 Spare equipment

If possible, it is good practice to keep at least one X-ray unit available as backup, such that it can be mobilized quickly in case of breakdown during fieldwork.

Adequate spare equipment should be provided to field teams. An example is the collimator bulb in the X-ray machine, which sometimes fuses and can be changed immediately by the radiographer in the field. It is advisable to include spare parts provision in the leasing contract if leasing is the chosen approach.

Sometimes, the field teams will need to be innovative when equipment is not readily available (see **Fig. 7.17**).

7.11.11 Checklist

A checklist containing the names and quantity of the equipment required for fieldwork should be prepared (see **Annex 7.3**). Checklists to assess site suitability and site readiness can also be prepared.

Fig. 7.17

Reading a CXR image in the field using a cardboard box to prevent excessive glare during the national TB prevalence survey of Mozambique, 2018

Photo credit: Eveline Klinkenberg.

7.11.12 Instructions

Many survey participants may be undergoing CXR for the first time; hence, it is essential to instruct them properly. Visual aids such as charts and fact sheets should be used for this purpose. A local health worker or volunteer can explain in detail what the participants are expected to do (e.g. changing, positioning and breath-holding) in the local language or dialect. Given that most participants are healthy individuals, CXRs can be taken much faster in prevalence surveys than in clinical settings, provided participants are instructed properly. Even with a single conventional unit, several surveys have managed to perform 30–40 CXRs per hour during a busy period.

7.11.13 Recording of CXR findings

CXR results should be recorded by the field reader into the data collection system, and if used on the individual tracking form to allow determination of sputum eligibility. If CAD is used in combination with a human reader, it is advisable to have the human reading done first, so that the human reader is not biased by the CAD abnormality score. Details about recording CXR results, data privacy and security can be found in **Chapter 16**.

7.11.14 Challenges

Challenges related to X-ray equipment – either the initial process to procure it, or breakdowns or overheating in the field – are common. **Box 7.4** summarizes the most common challenges related to CXRs, as reported during national TB prevalence surveys.

Box 7.5 describes the experience of the Eswatini, 2018–2019, TB prevalence survey in terms of CXR technology used, preparation and implementation of CXR in the field, data management, comparison between human reading and CAD score and between field and central reading, and utilization of CXR equipment after the survey.

BOX 7.4
COMMON CHALLENGES RELATED TO CXRS DURING NATIONAL TB PREVALENCE SURVEYS *(6)*

- Initial upfront cost.
- High cost of necessary special equipment (with adequate input power).
- Challenging and delayed procurement in some countries.
- Shortage of trained personnel required for operation and interpretation of CXRs in some countries.
- Breakdowns or overheating of equipment in the field.
- Necessity for in-country servicing of equipment to ensure timely repairs and troubleshooting.
- Necessity for backup machines in case of equipment breakdown.
- Limited accessibility of remote areas and poor road conditions for X-ray trucks.

7.12 Quality assurance

For prevalence surveys, a good-quality posteroanterior view of the chest is required for each participant. To ensure acceptable image quality, QA must be included in the training of medical officers as well as radiographers. Once an X-ray image is available, a basic QA test should be carried out by the medical officer. If the image quality is not acceptable, the X-ray must be repeated. Medical officers can base their judgement on parameters such as rotation, penetration, inclusion of the entire area of interest and accuracy of demographic data. In short, high-quality images can be ensured by employing only qualified individuals for radiography work, pre-survey training of radiographers and medical officers, and on-the-spot QA assessment by the medical officer.

The quality of CXR interpretation can be ensured by pre-survey training of medical officers and employing a two-level (field and central) assessment. An ongoing QA assessment is recommended during and just after each cluster, without waiting until the whole survey is done. This is especially crucial at the start of the survey to ensure adequate reading quality.

If abnormal CXRs are missed, it means there are fewer opportunities to diagnose TB. Ensuring that abnormal CXRs (eligible for sputum examination) are *not* missed has implications for the data analysis because the missed opportunities for sputum collection and potential diagnosis have to be mathematically imputed (see **Chapter 17**).

BOX 7.5
CXRS IN NATIONAL TB PREVALENCE SURVEYS – COUNTRY EXPERIENCE IN ESWATINI, 2018–2019

Sample size: 35 000; number of clusters: 70

Screening methodology: Symptom screening and CXR

All X-rays were taken and read in the field by a medical officer as well as CAD4TB (version 5). X-rays were considered "abnormal" if the medical officer (blinded to the CAD4TB score) identified radiological features suggestive of TB such as opacities, cavitation, fibrosis, pleural effusion, calcification(s), or any unexplained or suspicious shadow. Congenital abnormalities, normal variants and bony abnormalities including fractures were excluded by definition, as were findings such as cardiomegaly and other heart-related abnormalities. Also, images with a CAD4TB score equal to or above the threshold of 40 were considered as abnormal CXRs.

CXR technology: Two types of digital X-ray machines – a OneStopTB truck with an EasyDR stationary X-ray unit (mounted in a container), and two EasyDR portable systems (mobile standalone units) (**Fig. B7.5.1**). Powering of the X-ray systems was done using petrol generators (mostly) and, where available, electricity in community halls (donated for the prevalence survey in some clusters by community leaders).

CAD score threshold: A threshold of 40 was decided upon to minimize missing TB cases while at the same time not resulting in too many sputum-eligible participants. Published data from the Zambia national prevalence survey (2013–2014) served as a reference, as well as reported sensitivity and specificity of the CAD4TB software (version 5) from the manufacturer *(37, 38)*. Also, because determining the potential of CAD was one of the specific objectives of the survey, the threshold set was on the lower side.

Preparation: Previsits to the selected clusters during the preparation phase of the survey were used to evaluate the electricity supply, and the accessibility and location of sites for X-ray examination. A contract with the manufacturer to provide an equipment breakdown service during the survey was in place. No backup machine was available so (as per protocol) all participants were made sputum eligible during X-ray downtime.

SOPs: Standard operating procedures for CXR-related activities at the central and field levels were developed by the X-ray team, which consisted of the chief radiographer, two senior radiographers and two radiologists. Field testing during pilot clusters was conducted by the radiographers (two in each team) and the medical officer, supported by the data and IT team.

Staffing: Each X-ray team consisted of three staff: two radiographers and one medical officer. The radiographers had the following roles and responsibilities:

- ensure that X-ray machines were in good functioning condition, perform preventive maintenance as per training/SOPs and ensure the digital images taken were appropriately stored;
- set up the X-ray unit at the field examination site as per SOPs and ensure it was ready for use;
- explain the X-ray procedure to each participant before conducting their CXR;
- be responsible for taking quality X-ray images and forwarding them to the field and central X-ray readers; and
- be responsible for adhering to Eswatini Radiation Authority safety guidelines and for protecting participants from radiation.

The radiographers took turns in explaining and getting participants ready and taking the images.

The technicians in the X-ray group were responsible for simple maintenance and repair of the X-ray systems. More complex maintenance and repair

Fig. B7.5.1

Example of CXR equipment being used in the national TB prevalence survey of Eswatini, 2018–2019

Photo credit: Eveline Klinkenberg.

BOX 7.5
CXRS IN NATIONAL TB PREVALENCE SURVEYS – COUNTRY EXPERIENCE IN ESWATINI, 2018–2019

was provided by the manufacturer (Delft) through a subcontractor based in South Africa who would travel to Eswatini to support the team with maintenance and repair. A biomedical engineer from the Ministry of Health was also trained and worked with the subcontractor.

Training: Before implementing the survey, the radiographers and IT team were trained by the X-ray manufacturer in technical aspects of how to use the X-ray equipment, CAD4TB software, connectivity and preventive equipment maintenance. Following that, the radiographers were attached to a health facility (clinic or hospital) to get experience before commencing survey activities. The medical officers were trained by an experienced radiologist from South Africa due to limited in-country capacity; training included how to control quality and read the images, score them as normal or abnormal, and ensure recording, scoring and recording were all standardized.

Fieldwork: In the field, X-ray images were interpreted by the field medical officer (blinded to CAD4TB) as either normal, abnormal consistent with TB, or other abnormality. The results were recorded in the digital data management system designed for the survey. The CAD4TB score was calculated automatically after the image was taken and the score was automatically recorded in the data collection system. Once the medical officer entered their findings, the system would combine these with the CAD4TB score and the results of the symptom screening and indicate an automated decision as to whether the participant would be eligible to provide sputum or not.

Over the 6-month fieldwork period, a CXR was taken for 22 960 of the 24 356 (94.2%) eligible participants who reported at the survey site reception and consented to participate in the survey. The median number of images taken per day was 153 (interquartile range 87–218), although the number of images taken per day was largely determined by participant flow, and varied from 11 to 427 per day, with 3 days where just one or two images were taken. A total of 1396 (5.8%) participants did not undergo X-ray for various reasons. The most common reasons were problems with the X-ray equipment (60%), pregnancy (12%) and the participant being unable to stand (22%).

Participants were guided to the X-ray station after completing symptom screening. When it was their turn, they were asked to change into a survey T-shirt to avoid metal or clothing interfering with the X-ray. The total time needed to take one CXR was 3–5 minutes. Each participant received direct feedback from the medical officer about their CXR result. If severe abnormalities were found, participants were given a referral form to the nearby health clinic at the medical officer's clinical discretion.

Data management: Each participant had a barcoded invitation card that was used to register their X-ray as well as to pull up their image for review. Barcodes were scanned to avoid any mis-linking of data. Each CXR image was labelled with the participant's individual survey ID number and the date of the CXR.

All the digital CXR images were stored on the PACS in the field, and immediately transmitted to the linked CAD4TB cloud.

Quality control: To ensure acceptable image quality, QA was included in the training of medical officers as well as radiographers. SOPs for radiographical investigations detailing all QA procedures were developed. Pre-survey training of medical officers, IT officers and radiographers was conducted by a radiologist to ensure a clear and common understanding of required procedures.

All abnormal images, images from Xpert ® MTB/RIF-positive cases and 17% of normal images were read by a radiology team at the central level.

Concordance between human reader and CAD4TB score: There was good concordance between the medical officer reading and CAD4TB scoring: 94% for normal images and 56% of abnormal images (**Table B7.5.1**). A total of 1119 (6%) images were read by the medical officer as normal and scored as abnormal by the CAD4TB. Fortunately, most of these participants were made sputum eligible based on their CAD4TB score as either the human reader classification or CAD score counted towards an abnormal CXR.

Medical officers were trained to over-read images to minimize missing TB cases; hence, some images (**Table B7.5.1**) were identified as abnormal by the medical officer but scored as normal (<40 threshold) by the CAD4TB. These participants were considered sputum eligible.

BOX 7.5
CXRS IN NATIONAL TB PREVALENCE SURVEYS – COUNTRY EXPERIENCE IN ESWATINI, 2018–2019

Table B7.5.1

Field X-ray screening versus CAD4TB (version 5) scoring, TB prevalence survey of Eswatini, 2018–2019

CAD4TB SCORE	FIELD READING			
	NORMAL	ABNORMAL SUGGESTIVE OF TB	ABNORMAL NOT SUGGESTIVE OF TB	TOTAL
<40	19 252	741	359	20 352
≥40	1 119	1 194	213	2 526
Total	20 371	1 935	572	22 878[a]

CAD: computer-aided detection; TB: tuberculosis.

[a] Data were included for those images where both results were available; six images were scored as not interpretable by the medical officer; for 23 images, the reading result was unknown (missing data); for 53 images, the CAD score was missing from the survey database.

Table B7.5.2 shows agreement between central-level reading and field reading, by both the medical officer and CAD4TB scoring. It is clear there was over-reading by medical officers, with 1107 (785+322) images scored as abnormal in the field while they were classified as normal by central radiology reading. There were 32 images considered normal during field reading but re-classified as abnormal suggestive for TB during central reading. It is important to note here that the CAD4TB score was maintained at a low threshold of 40 to minimize missing TB cases.

Table B7.5.2

Agreement between central-level radiology reading and field reading (human and CAD4TB, version 5)

CENTRAL RADIOLOGY READING RESULT	FIELD READING				CAD4TB SCORE		
	NORMAL	ABNORMAL SUGGESTIVE FOR TB	OTHER ABNORMAL	TOTAL	<40	≥40	TOTAL
Normal	3 236	785	322	4 343	3 813	536	4 349
Abnormal suggestive of TB	32	281	14	327	30	299	329
Abnormal not suggestive of TB	245	868	236	1 349	538	811	1 349
Total	3 513	1 934	572	6 019[a]	4 381	1 646	6 027

CAD: computer-aided detection; TB: tuberculosis.

[a] Four images were considered not interpretable in the field, and four images had an unknown field-reading result.

Use of equipment after the survey:

Immediately after completion of field operations, the X-ray equipment procured as part of the survey was handed over to the Ministry of Health. During the COVID-19 pandemic, the mobile truck was used as part of the national pandemic response. Due to the nature of the portable X-rays, which are more suitable for field use, these have not yet been set up in hospitals but have been used in outreach activities.

A post-survey retrospective analysis of any mismatches between radiology and bacteriology results further enhances diagnostic accuracy. Of vital importance in ensuring quality and reliability in reading radiographs is the principle of accepting only images of standard size, posteroanterior view, that are correctly positioned and of acceptable technical quality.

7.13 Management of imaging data

X-ray images are important pictorial documentation. Whether using film-based or filmless technology, storage and management of imaging data are very important. It is ethically imperative to have accurate data management; that is, verifying and entering the correct participant details (name, age, sex, survey ID number) and ensuring the corresponding CXR matches that person. Utilization of individual barcode scanning is recommended to avoid manual entry of demographic data (see **Chapter 16**). Radiographers and medical officers should also be trained on good data management principles (see **Chapters 11** and **16**) *(34)*. The X-ray reference manual developed by the survey team should contain advice on imaging data storage and management.

If DR is used for the survey, adequate backup files should be created and archived while in the field. Daily storage of images in cloud servers is possible, and highly recommended, if digital technology is used, but having a disk backup is always advisable. A contract with the CXR vendor to access the images during and after the field operations needs to be arranged. There have been instances where survey teams could not access images because the licence fee to access them was not paid. Images can also be electronically transmitted from the field to the central level in real time, or daily if internet connectivity is not available at the field site. The X-ray team may require IT support for proper archiving. The workstations and backup data need to be periodically checked for corrupt files and computer viruses.

In some countries, paper registers may have to be maintained and archived in addition to the X-ray data sheets or survey forms.

The survey image collection is helpful for other uses as a large volume of data is available from the general population, spanning from young to old people. For example, CXR data can be used after the survey to estimate a country's active case detection CAD threshold, and images can be used to evaluate the extent of conditions other than TB (e.g. cardiomegaly, lung malignancies) *(25, 26)*.

Box 7.6 describes the critical steps relating to CXR that must be undertaken during preparation and implementation of TB prevalence surveys.

BOX 7.6
CRITICAL STEPS IN THE USE OF CXR IN THE CONTEXT OF NATIONAL TB PREVALENCE SURVEYS

Identify X-ray technology:

- Involve country experts, technical partners, WHO etc.
- Base decisions on available infrastructure (e.g. roads and electricity), regulations on radiation safety, human resource availability and cost.
- Decide whether human reading will be done with or without CAD.

Procure:

- Start procurement as early as possible as it will take a considerable amount of time.
- Possible facilitators include, for example, WHO, UNICEF, UNOPS and the Global Drug Facility.

X-ray team (core group):

- Identify teaching hospital radiology personnel, expert radiologist, chest physician and radiographer.
- Achieve consensus on methodologies (e.g. interpretation and QA).

X-ray manual:

- The manual should be developed by the X-ray team, assisted by a technical partner.
- Include, for example, SOPs, QA, interpretation, methodology, radiation safety, CAD software and maintenance.

Training:

- Training is to be done by the central X-ray team.
- Include hands-on training and field simulation.

Piloting of survey:

- If CAD is to be used, conduct a calibration study.
- Coordinate the X-ray team, survey team, technical partners and experts.
- Identify practical issues and how to tackle them.

Previsit of field site:

- Inspect the survey site for housing X-ray equipment.
- Sketch a map for participant flow in the X-ray area.

Fieldwork:

- Fieldwork is to be carried out by the field X-ray team under supervision of the team leader.
- Take initiative and adapt to local factors and needs.
- Ensure good communication with participants about CXRs, which will inform their consent to participate.
- Follow SOPs for participant referral in case of serious CXR findings (not necessarily TB).

Archiving and data management:

- Employ field archiving.
- Oversight is to be provided from the central level.
- Monitoring (including central reading of CXRs, see also **Chapter 14**):

Monitoring is to be done by the central X-ray team.

- Monitor for QA and inter-reader consistency of interpretation.
- Monitor (and limit excessive) over-reading and under-reading.
- Monitor for CAD performance (if CAD is used).
- Possibly read 100% of images at the central level.

Clinical management and case classification:

- These functions are to be done by the central X-ray team.
- Clinical decisions should be made by a survey medical panel.
- Ensure cases are classified according to the definitions in the protocol.
- Decide on what to do about cases with mismatched radiological and bacteriological results (e.g. referral, follow-up, other).
- Develop a plan about post-survey use of CXR equipment.

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Annex 7.1 Interpretation of chest X-ray at the central level, national TB prevalence survey of Myanmar, 2017–2018

Field readers first categorized chest X-ray (CXR) for tuberculosis (TB) using the categories used in the field (normal, abnormal eligible for sputum or other abnormality). Those categorized as abnormal eligible for sputum were then further categorized as one of the following:

CATEGORY	DESCRIPTION
Active TB suggestive with cavity	CXR images that show abnormalities usually associated with active pulmonary TB, with cavitation (unilateral or bilateral).
Active TB suggestive without cavity	CXR images showing abnormalities usually associated with active pulmonary TB such as apical involvement, parenchymal opacities with or without pleural effusion, parenchymal opacities with mediastinal or hilar lymph node enlargement, isolated lymphadenopathy, miliary parenchymal mottling, and involvement of typical tubercular sites such as apices and upper segments of lower lobes.
Possible TB	CXR images showing abnormalities not typical for TB but for which TB cannot be totally excluded; for example, nodule(s) and bronchopneumonia. These findings would require differential diagnosis and further assessment.
Healed TB	CXR images that show significant abnormalities, but the radiologist is certain that they do not point to any active disease. Examples include pleural thickening, evidence of prior surgery such as lobectomy or pneumonectomy, classical fibrosis, residual or calcified scars and densely calcified nodules without any peripheral satellite lesions.
Other abnormality detected	CXR images where a significant abnormality is detected but the radiologist is certain that the cause is non-tubercular. Examples include emphysema, classic bronchiectasis, classic lobar consolidation with air bronchogram sign (conventionally labelled as bacterial pneumonia), spiculated or stellate masses (which suggest neoplastic nature), cannonball metastases and pulmonary congestion or other vascular abnormalities, bone fracture (any type), scoliosis or kyphosis, extrapulmonary soft tissue masses such as goitre, dextrocardia, abnormal cardiac contour, signs of mitral stenosis, aortic aneurysm and abnormalities of pulmonary vasculature. Abnormal cardiac size (cardiomegaly, or enlargement of any chamber) is also classified in this category, because it bears no relation to pulmonary TB and also because in isolation it is a poor indicator of cardiac disease in the population.

Annex 7.2 Example chest X-ray fact sheet for survey participants

Definition

A chest X-ray is a photo of the chest obtained by using X-rays. A small dose of radiation is used to create this image. It is one of the most common medical tests done.

Reasons for getting a chest X-ray

Chest X-rays are done to look for abnormalities of the heart, lungs, bones or blood vessels in the chest. In a hospital or clinic, your doctor may order a chest X-ray if you have certain symptoms, such as:

- bad or persistent cough
- difficulty in breathing
- coughing up blood
- chest pain
- chest injury
- fever

A chest X-ray is also often taken before any major surgery. Chest X-rays are widely used for health or tuberculosis (TB) screening programmes; for example, for people who are in environments where TB is common, for people in contact with people who have TB, and (in some cases) for new job recruits and visa applicants.

Chest X-ray and children

Children are more susceptible to the effects of X-rays – this is one of the main reasons why children aged below 15 years are excluded from TB prevalence surveys.

Chest X-ray and pregnancy

Chest X-rays are done using a very small dose of radiation. The risk associated with a chest X-ray is very small because the radiation exposure from the new machines used in the survey is very low, and the X-rays are directed at the chest. However, if you are pregnant or have any concerns about the potential effects that the X-ray may have on your health or on that of your unborn baby, please discuss your concerns in detail with the study clinician and make sure all your questions are satisfied. You can continue to participate in the study even if you choose not to have a chest X-ray.

The risk for a baby of performing an X-ray of a pregnant woman is negligible if the X-ray is performed properly. Chest X-ray is a safe examination. Moreover, staff doing the X-ray are careful to restrict the area of exposure to the chest only; they avoid direct exposure to X-rays of the abdomen and reproductive organs. However, in many places and where possible, X-rays are traditionally avoided during pregnancy. If you are pregnant or think you might be pregnant, and you have concerns about safety, please share your concerns with the interviewer, medical officer or X-ray receptionist. If you have had close contact with someone who has had TB in the past 2 to 3 years, or if you have any symptoms, an X-ray is a helpful tool to quickly identify your health problem so that it can be treated.

What if you would not like to undergo chest X-ray for any reason?

You can tell your interviewer or X-ray staff that you do not want to have a chest X-ray examination. You can decline the chest X-ray and do not need to explain the reason. If you decline the X-ray, you can still participate in the survey. What happens before the X-ray is taken?

The X-ray technician will check your identity. You will be asked to remove all jewellery and metal accessories from the waist up. You may be asked to wear a disposable gown or T-shirt if your clothes are not appropriate for the examination. In the past, a lead apron was placed over the hip and waist, but there is some evidence to justify not using them *(1,2)*.

What happens while the X-ray is taken?

Undergoing an X-ray is like being photographed. For a chest X-ray, the *photo* is usually taken from the back. An X-ray technician will position you. You will stand against the X-ray machine with your hands up or placed on your waist. You will then be asked to take a deep breath and hold it while the X-ray is being taken. You will also be asked to stay as still as possible when the X-ray is taken. You may notice that the film cassette feels cool to your skin.

What happens after the X-ray is taken?

After the X-ray, you will be asked to wait a few seconds while it is checked for quality. If the quality is satisfactory, you will be asked to change back into your clothes and wait for further instructions.

How long will the whole procedure take?

The X-ray itself will take only about a second. It might take about 3–5 minutes to prepare and position you, and for you to change your clothes.

Will it hurt?

Having a chest X-ray does not hurt. It is like having your photo taken.

When will I get the result?

A medical officer or a special computer will look at your X-ray for a few minutes after the procedure and decide whether you need a sputum examination. Being asked to give a sputum sample does not mean that you have an illness; it simply means that it is advisable to test further. If the medical officer detects a condition that

needs further check-up or urgent treatment, that person will talk to you and explain what needs to be done and where. Within a few days, your X-ray will also be looked at by a radiologist and by other doctors, if necessary. If you need further follow-up or treatment, your district or local health office will share with you the chest X-ray report and advice provided by the group of specialists. Although all efforts will be made to give you feedback as early as possible, it may sometimes take up to 2 months, especially if the results of a sputum examination are needed to confirm the X-ray findings. If you do not receive any feedback, it means that everything is fine and you do not need to see a doctor.

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Annex 7.3 X-ray equipment checklist

	ITEM	PER TEAM	TOTAL FOR 5 TEAMS	REMARKS
I	**X-ray basic unit**			Contents of assembled unit differ, depending on suppliers
I-1	X-ray tube	1	5	
I-2	X-ray tube spare battery	1	5	Optional
I-3	X-ray tube battery charger	1	5	
I-4	X-ray stand	1	5	
I-5	Detector (flat panel)	1	5	
I-6	Detector stand	1	5	
I-7	X-ray operator laptop	1	5	
I-8	Barcode/QR code reader	1	5	
I-9	Detector battery charger	1	5	
I-10	Detector spare battery	1	5	
I-10	Peripheral connection tools	1 set	5	
I-11	Boxes for transportation	1 set	5	
I-12	Steps for height adjustment of a CXR participant	1	5	
I-13	Image backup storage (temporal)			Virtual or hard disk
I-14	Power generator	1	5	
I-15	Portable changing room or equivalent curtains	2 sets	10	
I-16	Disposable gowns or T-shirts for a participant			Depends on the situation
II	**X-ray screening reading**			
II-1	Laptop computer	1	5	
II-2	X-ray viewer or PC display (high-resolution)	1	5	
II-3	Barcode/QR code reader	1	5	
II-4	Tablet	1	5	
II-5	CAD system	1	5	Optional
II-6	Referral slip/ information sheet			Template if printable on site
III	**Radio safety materials**			
III-1	Radio protection partition with lead glass window	1	5	
III-2	Radio protection partition without lead glass window	(1)	(5)	Optional
III-3	X-ray operator apron	1	5	
III-4	Gonad protection apron	1	5	Optional
III-5	Film badge	2		Depends on number of the staff
III-6	Radiation caution sign	1	5 or 10	
III-7	Tape/rope to indicate restricted area	1 set		Disposable
IV	**General infection control tool**			
IV-1	Alcohol spray and disposable wiper			
IV-2	Disposable gown			
V	**Furniture**			
V-1	Long tables for X-ray controller and X-ray screening	2	10	Rental or leasing option
V-2	Chair	15	75	Including for waiting area

CAD: computer-aided detection; CXR: chest X-ray; PC: personal computer; QR: quick response.

CHAPTER 8

Diagnostic investigations

National tuberculosis (TB) prevalence surveys seek to determine the prevalence of bacteriologically confirmed pulmonary TB in those aged 15 years and older. Quality-assured diagnostic testing is essential to confirm the presence or absence of viable *Mycobacterium tuberculosis (Mtb)* complex bacteria in samples from people who screened positive for TB on a symptoms-based questionnaire or chest X-ray (CXR). Implementation can often be challenging, because national surveys require a large number of samples to be collected and processed. Thus, it is crucial to ensure that national diagnostic capacity and capability are sufficient for the diagnostic needs of the survey, without compromising routine laboratory services.

This chapter describes the diagnostic tests to be used for the two diagnostic algorithms recommended for national TB prevalence surveys, referred to as Option 1 and Option 2, and discusses each of these options in terms of the laboratory workload required. It then explains the diagnostic process in a prevalence survey (applicable to both options), which comprises specimen collection, specimen storage and transport, laboratory procedures for testing of samples, and communication of results. Finally, the chapter discusses broader laboratory management issues that must be carefully considered in a survey, including human resources, training, biosafety, laboratory data management and quality assurance (QA).

8.1 Overview

National TB prevalence surveys measure the burden of bacteriologically confirmed pulmonary TB disease in those aged 15 years and older. The target population is enumerated, and screened for TB signs and symptoms using a questionnaire and CXR; those who meet screening criteria ("screen-positive" individuals) are then tested to confirm the presence or absence of *Mtb* complex bacteria in a respiratory sample. The surveys are designed to provide national, and sometimes subnational, prevalence estimates. To ensure that a representative sample of the population is taken, clusters are selected across the entire country. Hence, the diagnostic services for the survey need to match the distribution of survey clusters; this requires careful and advanced planning.

The diagnostic process starts with screen-positive individuals, who have a much higher likelihood of TB disease (based on reported symptoms or CXR abnormalities) than those who screen negative. Because surveys entail screening of the general population in community settings, individuals with TB disease will be detected earlier in the disease stage (and generally have lower bacillary loads) than is usually the case, where detection relies on people deciding to seek health care. Sputum production in people with TB disease may be poor, affecting the ability to undertake diagnostic tests; this means that sample collection requires careful attention. Furthermore, because the prevalence of TB disease in most settings will be below 1% (i.e. <1000 per 100 000 people), achieving a robust estimate of the population prevalence of bacteriologically confirmed pulmonary TB requires a combination of highly sensitive screening and highly specific diagnostic methods that are recommended by the World Health Organization (WHO) and quality assured.

The recognized microbiological reference standard test for the diagnosis of pulmonary TB disease is liquid culture. However, the logistics and time delays of getting samples to centralized laboratories for culture (and subsequent processing times) is challenging, and the specialized infrastructure required for culture limits its availability. Xpert® MTB/RIF Ultra (Xpert Ultra) – or an equivalent molecular WHO-recommended rapid diagnostic test (mWRD) with the same or better sensitivity – is recommended as the initial test in both of the diagnostic algorithms recommended in this guidance (Option 1 and Option 2) (**Chapter 3**). These tests provide accurate, fast and quality-assured detection of *Mtb* DNA; they can be used in community settings where the survey is being carried out; and they ensure that individuals with TB disease can be promptly detected and linked to care (**Chapter 9**).

From 2017 to 2023, Xpert Ultra was used to test all screen-positive individuals in national TB prevalence surveys implemented in Cambodia, India, Lesotho, Myanmar, South Africa and Timor-Leste. As of 2024, no other mWRD had equivalent or better sensitivity than Xpert Ultra. In surveys implemented between 2015 and 2019, Xpert MTB/RIF was used to test all screen-positive individuals in national TB prevalence surveys implemented in Bangladesh, Eswatini, Kenya, Mozambique, Namibia, Nepal, the Philippines and Viet Nam; however, this test has lower sensitivity than Xpert Ultra, and is no longer available for use because production has ceased.

After receiving samples for testing from the cluster, providing timely results to the field team or health

programmes in the survey area is important. Regular communication between the survey team and the testing laboratories can be challenging, because the survey teams are often moving between clusters, so it is essential to be well prepared through advanced planning. The two diagnostic algorithms recommended in this guidance (explained in more detail in **Chapter 3**) are:

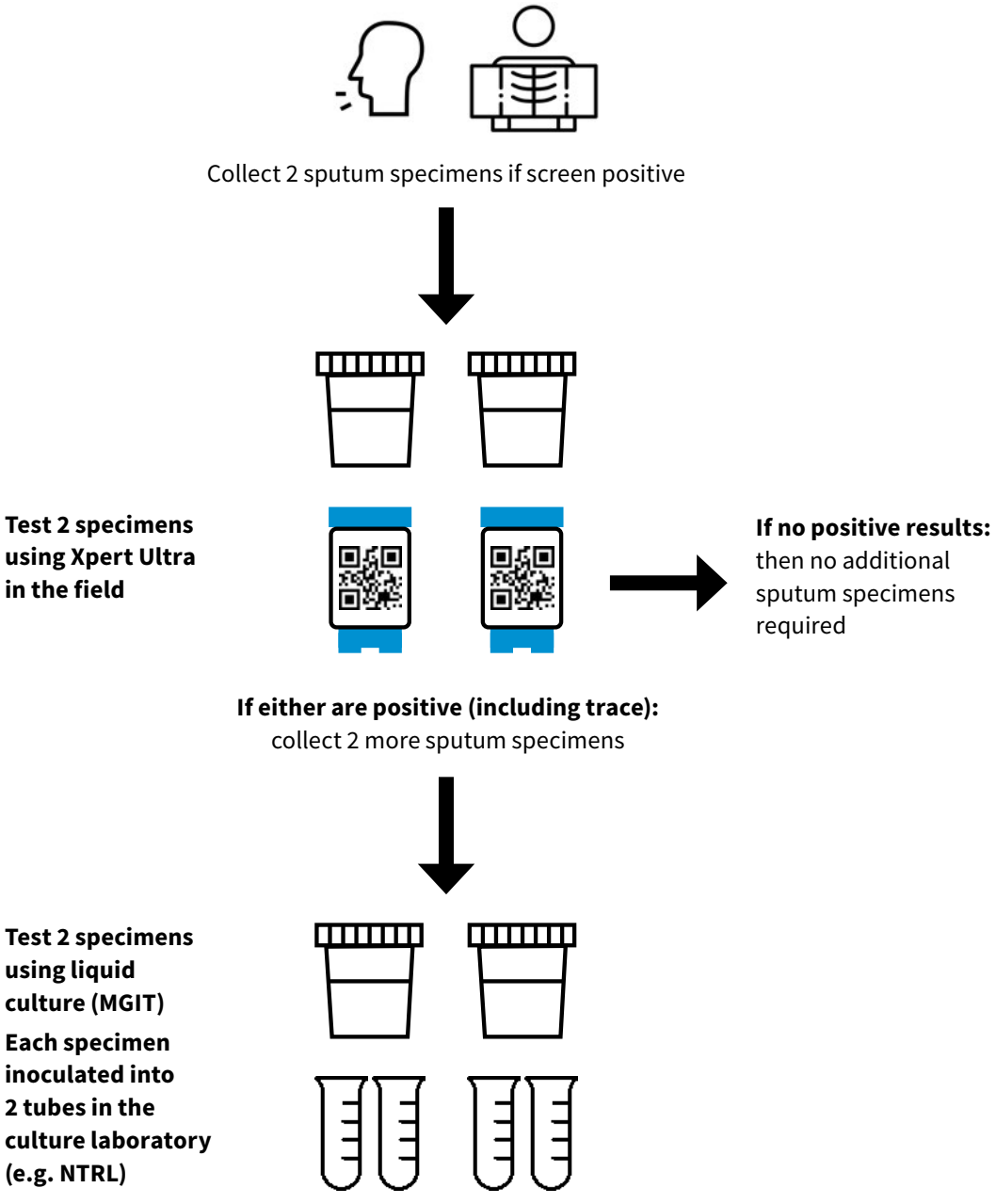
- Option 1 – use of two Xpert Ultra tests followed by liquid culture in two mycobacterial growth indicator tubes (MGIT™) for those with any positive Xpert Ultra test (**Fig. 8.1**); and
- Option 2 – use of two MGITs, with an Xpert Ultra test for clinical care (**Fig. 8.2**).

If culture facilities are of high quality, then Option 2 could be considered; otherwise, Option 1 is the recommended diagnostic algorithm.

Whichever diagnostic algorithm is used, QA of the entire diagnostic process is crucial to ensure that diagnostic test results are reliable and can thus be used to produce reliable estimates of the prevalence of TB disease. The process includes sample collection, storage of

Fig. 8.1

Illustration of diagnostic algorithm "Option 1"[a]

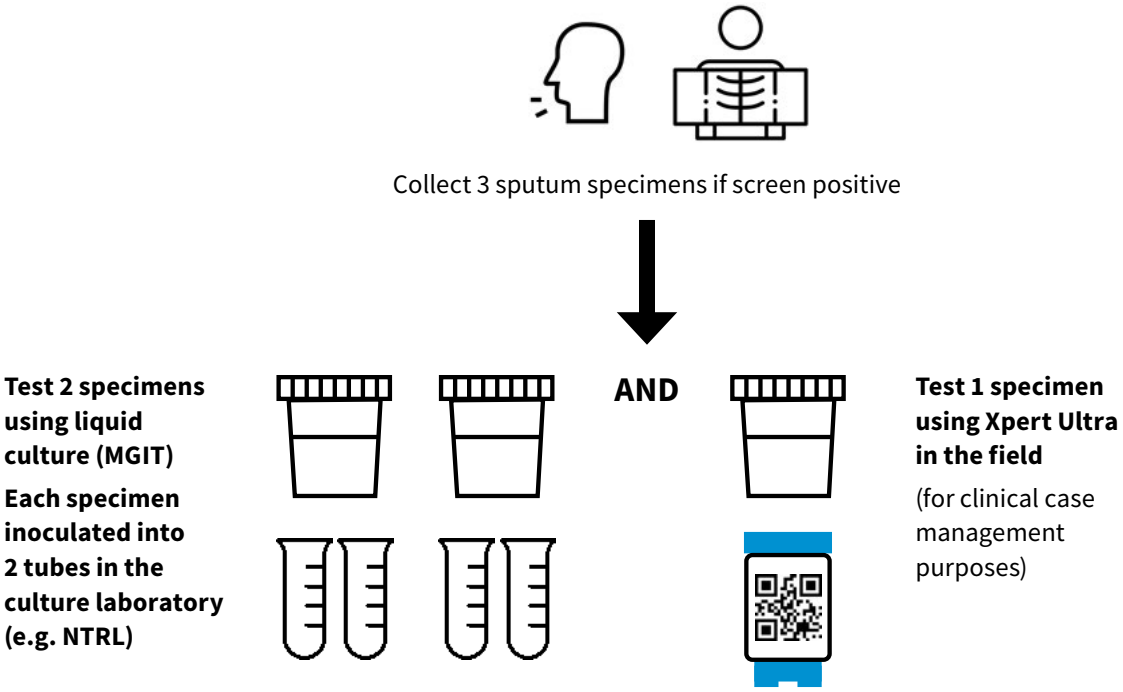


MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for Xpert Ultra testing and, if either specimen is positive, two additional sputum samples are collected for confirmatory testing using liquid culture (MGIT).

Fig. 8.2

Illustration of diagnostic algorithm "Option 2"[a]



MGIT: mycobacteria growth indicator tube; NTRL: national TB reference laboratory; TB: tuberculosis.

[a] Screen-positive participants submit two specimens for liquid culture (MGIT) and one for Xpert Ultra testing. The Xpert Ultra test is used to ensure a rapid result is available to be used for clinical management purposes only (not the estimation of TB prevalence). The priority is to take two specimens for MGIT testing. Xpert Ultra testing can be done on the sediment of an MGIT sample; however, if this is not possible, a third sample should be collected for Xpert Ultra testing, to be done in the field. Further details are provided in this chapter. Clinical management of those with a positive Xpert Ultra result is discussed in **Chapter 9**.

the sample and transport to the testing site,[1] conducting of the test and generation of results; and recording and reporting of data.

8.2 Diagnostic tests to be used

This guidance recommends two primary diagnostic tests for use in national TB prevalence surveys:

- molecular testing using Xpert Ultra (Cepheid®); and
- culture on liquid media (e.g. BACTEC™ MGIT; Becton Dickinson).

Both liquid culture and Xpert Ultra have advantages and disadvantages *(2)*. Hence, combining them provides a practical and effective approach.

Laboratory staff must be familiar with both tests; also, there needs to be in-country experience of using the tests within the national TB programme (NTP). If the technology or skills are not available for either of the tests (e.g. for MGIT culture), a national TB prevalence survey might provide an opportunity to address these shortcomings. However, adequate support and the quality of testing need to be assured. Support for introducing a new test and for supervision during survey implementation should be requested from a WHO supranational TB reference laboratory (SRL) *(3)*.

[1] Unless diagnostic testing is conducted at the field site.

Specific details related to liquid culture and Xpert Ultra are available elsewhere *(4–6)*.

In the future it is possible that other mWRDs, including non-sputum-based assays with equivalent or better performance, could be alternatives to Xpert Ultra *(6)*. Similarly, assays with equivalent or better performance could be used as alternatives to MGIT in the future.

8.2.1 Xpert Ultra

Xpert Ultra is an mWRD that can detect *Mtb* and rifampicin resistance in less than 2 hours. It is now preferred to Xpert MTB/RIF because of its higher sensitivity (including among people with HIV) and the discontinuation of Xpert MTB/RIF production in 2023 *(7)*. Xpert Ultra provides a semiquantitative categorization of the bacillary load when *Mtb* is detected, with results listed as high, medium, low, very low or trace. These categories correlate with the sputum bacillary burden of *Mtb*.

The main advantages of Xpert Ultra are:

- higher accuracy than smear microscopy and solid culture;
- increasing availability and use in routine clinical services;
- prior experience of its use in the context of national TB prevalence surveys, including deployment in mobile vehicles;

- lower infrastructure and biosafety requirements than for culture testing, with minimal training required on biosafety and processing of samples; and
- rapid availability of results, typically within hours.

Xpert Ultra testing can be performed at a temporary survey site, providing an option for mobile testing within a cluster or region. This means that samples can be tested in real time as they arrive at the testing site, without batching. However, there are challenges with using Xpert Ultra in the context of national TB prevalence surveys, as highlighted in **Box 8.1**.

BOX 8.1
CHALLENGES EXPERIENCED WITH XPERT ULTRA TESTING IN NATIONAL TB PREVALENCE SURVEYS

- The sensitivity of a single Xpert Ultra test is lower than for the reference standard of liquid culture, particularly in the context of case-finding in the general population.
- The specificity of the Xpert Ultra test is lower than for the reference standard of liquid culture, particularly in those with a previous history of TB.
- The Xpert Ultra test cannot differentiate between live and dead bacilli.

A general limitation of mWRDs, including Xpert Ultra, is that they detect *Mtb* DNA and cannot distinguish between viable and non-viable bacilli. This leads to a considerable amount of discordance between results from culture and Xpert Ultra in a national TB prevalence survey *(2)*. In clinical care, the discordance between results from culture and Xpert Ultra testing is mostly seen among individuals with a recent history of previous TB *(8)* and is associated with trace results. However, in national prevalence surveys, participants are sampled from the general population, and most individuals with TB disease in the general population have paucibacillary disease (i.e. have few bacilli). A higher number of trace positive results are found in a national survey *(9, 10)*, leading to a higher proportion of discordant results than in clinical settings.

Recent publications provide insights into discordance between results from culture and Xpert Ultra in TB prevalence surveys *(1, 11)*. Under survey conditions, the trace results and other discordant results need to be managed clinically according to local guidelines (**Chapter 9**); **Chapter 4** explains how to classify a participant as a survey TB case (or not), based on laboratory test results.

8.2.2 Liquid media culture

WHO recommends using commercial liquid culture systems for diagnostic testing *(12)*, because TB culture using the recommended MGIT liquid culture media is the most sensitive TB detection test that can distinguish viable from non-viable bacilli *(12)*. TB culture is prone to contamination if sterile techniques are not strictly followed, but compared with solid culture it is up to 20% more sensitive and faster at diagnosing TB *(13–15)*. Culture using solid media is perceived to be less costly; however, depending on the setting, this may not be the case when the method is fully costed *(16)*.

Although culture is currently the only diagnostic test that can distinguish viable from non-viable bacilli, important factors known to affect the performance of culture in isolating *Mtb* from sputum specimens include:

- the quality and quantity of specimens;
- the time from sputum collection to processing *(17, 18)*;
- the system for storage and transporting specimens (under cold-chain conditions);
- the available capacity to perform culture (facilities and equipment);
- the number, skills and motivation of laboratory workers performing the test;
- the decontamination protocol (i.e. the method used to remove contaminating organisms from each specimen); and
- whether the required QA measurements are in place.

Due to the high biosafety risk, culture also requires biosafety cabinets (BSCs) and must be performed in a biocontainment laboratory *(19)*. Most countries have only one biocontainment laboratory that can perform culture (only a few countries have more than one).

The BACTEC MGIT liquid culture system is available at negotiated prices for low- and middle-income countries *(20)*. The MGIT 960 and MGIT 320 instruments can incubate 960 or 320 tubes, respectively. The reading of bacterial growth in the MGITs is fully automated, allowing prompt identification of tubes where growth is present. The incubation time for a culture to be declared negative using the MGIT instrument is 6 weeks (42 days).

Challenges experienced with using liquid culture testing in the context of national TB prevalence surveys are highlighted in **Box 8.2**.

8.2.3 Optional diagnostics

In national TB prevalence surveys, challenges with using culture are exacerbated if a large number of tests are required over a short period of time. The first diagnostic algorithm recommended in this guidance (Option 1) uses Xpert Ultra as the initial test, with testing using liquid culture only required for those individuals with a positive Xpert Ultra result. This minimizes the number of culture tests that are required and should substantially

BOX 8.2
CHALLENGES EXPERIENCED WITH LIQUID CULTURE TESTING IN NATIONAL TB PREVALENCE SURVEYS

- Establishing quality-assured liquid culture testing capacity takes time.
- Contamination and false negative culture results may occur if:
  - the cold chain cannot be maintained during long transportation times between a survey cluster and the laboratory or laboratories used for culture testing; or
  - there is poor planning, and the numbers of experienced staff and available equipment are inadequate to manage cyclical peaks (typical of prevalence surveys) in the volume of specimens to be tested.
- There is a risk of laboratory cross-contamination of cultures.
- Results take time to receive, particularly if there are limited culture facilities and sample referral systems are not robust.
- It is difficult to standardize techniques when multiple laboratories are used.

reduce the challenges associated with culture testing in the context of a survey.

HIV testing is recommended in all national TB prevalence surveys, especially in countries with a high prevalence of HIV, and is described in more detail in **Chapter 10**.

Smear microscopy and solid culture are no longer recommended as the primary tests for national TB prevalence surveys because of their lower sensitivity *(2)*. They can be included in the diagnostic algorithm if a comparison with a previous survey is considered essential and the previous survey used these methods (see **Chapters 3** and **18**). Details about the methods required for these tests are available elsewhere *(21)*.

8.3 Diagnostic algorithm selection and laboratory capacity required

The two diagnostic algorithms recommended for national TB prevalence surveys are described and explained in **Chapter 3**; they are also shown in **Fig. 8.1** and **Fig. 8.2** for ease of reference.

The first diagnostic algorithm, Option 1, requires two Xpert Ultra tests (on two different specimens) to be **performed in the field**[1] for every survey participant who screens positive for TB, followed by MGIT culture testing (on two different specimens) for all those who test positive on one or both Xpert tests (**each specimen should be inoculated into 2 tubes;**[2] **i.e. 4 tubes per Xpert-positive participant**). This approach substantially reduces the number of MGIT cultures required when compared with most previous surveys that relied on culture testing for all screen-positive individuals.

In Option 1, the reduced number of cultures required should allow high-quality culture testing to be achieved. It is essential to avoid "false negative" cultures, which will compromise the reliability of survey results. During the pilot phase of a survey and the early phases of the main survey, culture and Xpert Ultra results should be compared, and laboratory performance monitored, to assess the performance of culture testing. In addition, all the quality indicators for culture that are specified later in this chapter (**Section 8.5.6**) should be closely monitored. Although Option 1 has the major advantage of providing quick and actionable results, if the patient flow is poorly managed it could lead to additional repeat participant visits and complicate the process for the individual and the survey. This is discussed further in **Chapter 13**.

The second algorithm, Option 2, uses MGIT culture as the primary diagnostic test. **It requires two MGITs per screen-positive participant**. As mentioned above, if resources allow, **each specimen should be inoculated into two tubes (i.e. 4 tubes per screen-positive participant)**.[3] An additional Xpert Ultra test is included in the diagnostic algorithm, to ensure the availability of a test result for clinical management purposes; this test result can also be used for secondary analysis, and for QA if the Xpert Ultra test is done on the sediment of one of the specimens processed for culture (see below). If the Xpert Ultra test is done on the sediment of a processed specimen, then only two samples will be required from each screen-positive participant. If this is not possible, then a third specimen will need to be collected for the Xpert Ultra test.

As in Option 1, high-quality culture results are criti-

[1] "In the field" means that Xpert testing should be performed at or very close to the cluster operation site, so that any positive results can immediately be followed up by asking the participant to return to the site to provide further sputum samples for MGIT testing.

[2] Based on unpublished data from the TREATS (Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB) project *(1)*, the additional yield of a second MGIT ranges from 10% to 24% (E. Klinkenberg [independent], P. de Haas [KNCV Tuberculosis Foundation], The Hague, The Netherlands, personal communication, 14 November 2023).

[3] For Option 2, ideally two tubes should be inoculated per sputum specimen, but depending on laboratory resource availability, at a minimum, there should be one tube inoculated per sputum specimen provided that two different samples can be obtained. If only one sputum sample is provided, then two tubes should be inoculated.

Table 8.1

Illustrative assessment of test capacity required for diagnostic algorithm option 1

ITEM	ASSUMPTIONS	SURVEY TOTAL (12 MONTHS)	1-MONTH PERIOD[b]
Enrolment and participation	Cluster size: 500 Total number of clusters: 100 Total number of individuals invited: 50 000 Participation rate: 90%	50 000 x 0.9 = 45 000 participants	500 x 0.9 x 8 = 3600 participants
Screening	Screen-positive rate: ~15%[a]	45 000 x 0.15 = 6750 participants	3600 x 0.15 = 540 participants
Number of sputum samples collected for Xpert Ultra testing	2 sputum specimens for all screen-positives	6750 x 2 = 13 500 samples	540 x 2 = 1080 samples
Number of participants with at least one Xpert Ultra positive test result	5% of screen-positive participants are Xpert Ultra positive	6750 x 0.05 = 338 participants	540 x 0.05 = 27 participants
Number of sputum samples collected for liquid culture testing (MGIT)	2 additional sputum specimens for all who are Xpert Ultra positive	338 x 2 = 676 samples	27 x 2 = 54 samples
Number of MGIT tubes to be incubated	2 tubes per sample	338 x 4 = 1352 tubes	27 x 4 = 108 tubes

[a] Screen-positive rates vary by country and time of year (e.g. winter/wet season). If the percentage of participants who screen positive is higher (e.g. from 15% to 30%), then testing capacity would need to be doubled. Depending on the number of screening days, approximately 100–200 people could be screened a day per cluster.

[b] It is assumed that there are 3 field teams, but only 2 are active in the field at any one time, therefore as many as 8 clusters can be conducted in a 1-month period.

cal, to ensure the reliability of survey results. The major difference in terms of culture testing in Option 2, compared with Option 1, is that a **much higher volume of culture testing** is required. This means ensuring that sufficient staff and resources are available, on a daily basis, to process the cultures while also maintaining quality and minimizing culture contamination.

Option 1 requires the collection of two sputum samples and Option 2 requires the collection of 2–3 sputum samples, ideally at a single visit; the samples should be taken at least an hour apart. When an individual cannot produce a quality spot sputum specimen, an early morning sample could be collected when the person returns to give the next specimen.

When Option 1 is used, individuals with a positive Xpert Ultra result will need to have two additional samples collected for culture testing. If the individual is still at the field site when the Xpert Ultra results are generated, collection should be attempted at that time. If this is not possible (e.g. if results can only be provided the next day), the two additional samples need to be collected the following day, which must be while the survey field team is at the main survey field site.

Option 1 and Option 2 have quite different requirements in terms of laboratory test capacity. The decision about which algorithm to use in a survey needs to be informed by a careful assessment of these requirements.

An example of a scenario that might apply in a prevalence survey using Option 1 is provided in **Table 8.1**. This scenario is for a survey with a sample size of 50 000 people and a participation rate of 90%; it assumes that 15% of people screened will be "screen positive" and thus eligible for sputum testing, and that two field teams will operate simultaneously through survey operations. It is assumed that 5% of screen-positive individuals will have a positive Xpert Ultra test result.

Option 1 requires minimal culture capacity for testing, but requires field teams with more GeneXpert modules available,[1] or increased work shifts per field team.

Using Option 1 with two field teams conducting eight clusters *in a month*, the approximate monthly number of tests would be 1080 Xpert Ultra tests (540 × 2 tests) and 54 MGIT cultures (540 × 0.05 × 2 tests). Two field teams would need two or three GeneXpert four-module instruments per field site and a single drawer of an MGIT 960[2] at the culture facility.

If there are four (rather than two) field teams operating simultaneously, the number of tests will double; however, the culture numbers should still be manageable (**Table 8.2**). Nonetheless, sample logistics would need to be carefully planned to ensure the timely transportation of specimens from all sites. Increasing the number of field sites to four requires doubling the number of GeneXpert instruments needed in the field; however, the single drawer of the MGIT 960 should still suffice in the culture facility.

Option 2 would require a referral laboratory with high-quality MGIT capacity, quality-assured testing and a fully functional sample referral system that ensures samples are transported via cold chain.

In Option 2, with two field teams operating simultaneously, the approximate monthly number of tests would be 1080 MGIT cultures and 540 Xpert Ultra tests for clinical management (**Table 8.2**). The example in

[1] The GeneXpert System uses 2-, 4- or 16-module configurations, and thus can run 2, 4 or 16 tests simultaneously.

[2] This particular MGIT machine has several drawers.

Table 8.2

Illustrative assessment of laboratory capacity needed on average *per month* for diagnostic algorithms Option 1 and Option 2

DIAGNOSTIC ALGORITHM	OPTION 1 2 × XPERT ULTRA + 2 × MGIT IF ANY SAMPLES ARE XPERT ULTRA POSITIVE	OPTION 2 2 × MGIT + 1 × XPERT ULTRA FOR CLINICAL MANAGEMENT	OPTION 1 2 × XPERT ULTRA + 2 × MGIT IF ANY SAMPLES ARE XPERT ULTRA POSITIVE	OPTION 2 2 × MGIT + 1 × XPERT ULTRA FOR CLINICAL MANAGEMENT
Number of active field teams[a]	2	2	4	4
Individuals eligible for testing per month	540	540	1080	1080
Number of baseline samples per month	1080 (Xpert Ultra)	540 (MGIT & Xpert Ultra) + 540 (MGIT)	2160 (Xpert Ultra)	1080 (MGIT & Xpert Ultra) + 1080 (MGIT)
Number of follow-on samples (if initial test positive) per month	27 individuals × 2 sputum samples = 54 (MGIT[b])	NA	54 individuals × 2 sputum samples = 108 (MGIT[a])	NA
Working days per month per site[c] – Field – Laboratory	 20 12	 NA 12	 20 12	 NA 12
Volume of Xpert Ultra tests per working day – Field – Laboratory	 54 (across 2 teams) NA	 NA 45	 108 (across 4 teams) NA	 NA 90
Number of Xpert Ultra 4-module instruments (12–16 tests per day) – Field – Laboratory	 4–6 (i.e. 2–3 per team) NA	 NA 4–5	 8–12 (i.e. 2–3 per team) NA	 NA 8–12
Volume of MGIT tests per working day – Field – Laboratory	 NA ~5	 NA 100[d] ~60 (if working 5 days/week)	 NA 12	 NA 200[d] ~120 (if working 5 days/week)
Number of MGIT 960 instruments[d] – Field – Laboratory	 NA ~0.2 (1 drawer)	 NA ~2–3	 NA ~0.3 (1 drawer)	 NA ~3–4
Number of other laboratory items – BSC – Class II[e] – Refrigerated centrifuge[f]	 ~1 ~1	 ~4 ~2	 ~1 ~1	 ~8 ~4

BSC: biosafety cabinet; MGIT: mycobacterial growth indicator tube; NA: not applicable.

[a] In this example, there are 2 (or 4) active field teams working simultaneously. It is assumed that an extra field team can be used in rotation thus ensuring continuous screening throughout the survey.

[b] Assumes 5% Xpert Ultra positivity rate at an individual level (n=540).

[c] Assumes 5 days per week for field testing and 3 days per week for laboratory-based batch testing.

[d] This includes positive and negative controls.

[e] Assumes one MGIT 960 = 960 samples (including controls) per 6-week cycle (42 days); therefore, it would take approximately 9 processing days (in 3 weeks) to fill an MGIT instrument (expecting 100 samples per day). Another instrument would be needed for the next 9 processing days (3 weeks). At the peak, 1800 samples must be accommodated simultaneously in a 42-day cycle (1200/30 days = 1800/42 days). Capacity would become available 42 days from the first sample incubated. If the protocol requires 2 MGIT tubes per sample then more instruments will be required.

[f] If the maximum number of samples that could be decontaminated per batch is 18–20, three decontamination batches would be required per day. The time to process a batch and the number of technicians would be needed to determine the number of cabinets required. In this example, we assume four batches could be processed per day and four operators will complete this; therefore, four cabinets would be required.

[g] This would be dependent on the number of batches processed per day and the capacity of the centrifuge. For this example, one centrifuge would be required with 24 samples per batch.

Table 8.2 assumes that Xpert Ultra testing is done on the sediment of the first sample processed for culture, and no extra sample collection would be required. It also assumes batched sample transport three times per week, with 100 sputum samples processed for MGIT culture in each batch (i.e. a total of 300 samples processed per week).

If the number of field teams operating simultaneously were doubled, the volumes per week of cultures and Xpert Ultra tests would also double. In such circumstances, it is unlikely that one single culture laboratory could handle the workload; therefore, an additional quality-assured laboratory would be needed, as well as a specifically designed sample referral system adapted to the different field teams and linked laboratories.

Beyond the testing capacity required, other key fac-

Table 8.3

Key factors beyond laboratory testing capacity that need to be considered when choosing between Option 1 and Option 2

DIAGNOSTIC ALGORITHM – OPTION 1	DIAGNOSTIC ALGORITHM – OPTION 2
• Sufficient exclusive Xpert Ultra testing capacity must be available to deal with the maximum daily needs (at least 2 × 4-module instruments) • If mobile testing is used, backup power and security need to be in place, and sufficient consumables must be on board • There must be sufficient space for disposal of biological waste, and a link should be established with a local laboratory for discarding waste and receiving additional consumables • All individuals with a positive Xpert Ultra result will need rapid referral to treatment services • All individuals with a positive Xpert Ultra result will need to provide two additional samples, and they may require an additional site visit • Referral of samples for culture testing needs timely shipment, and the lower number of samples for testing should not lead to delays in shipping • High-quality culture testing is still essential and needs to be verified before the survey begins • Any positive culture results will only be detected only after the field team has left; hence, it is important to record participants' contact details so that individuals can be contacted and referred for management	• Sufficient culture testing capacity must be available to deal with the maximum daily needs without compromising routine culture testing • The number of active field teams should be balanced with culture-testing capacity • High-quality culture testing is essential and needs to be verified before the survey begins • Sample referral systems are critical; they should be timely and ensure that samples are received by the laboratory within 3–5 days • The performance of Xpert Ultra tests on sediments needs to be part of the laboratory workflow, and a system for rapid communication of the Xpert Ultra result should be established • All individuals with a positive Xpert Ultra result will need rapid referral to treatment services • Any positive culture results will only be detected after the field team has left; hence, it is important to record participants' contact details so that individuals can be contacted and referred for management • Culture is a multistep process and the quality of each step should be monitored

tors that need to be considered when choosing between Option 1 and Option 2 are highlighted in **Table 8.3**.

8.4 The screening and diagnostic workflow in a national TB prevalence survey

The screening and diagnostic workflow in a national TB prevalence survey applies to both Option 1 and Option 2. (The primary impact of the choice of algorithm is on the capacity and placement of laboratory testing, not the process and general requirements for testing.)

A successful national TB prevalence survey requires a robust system for ensuring that each of the seven sequential steps in the screening and diagnostic workflow (shown in **Fig. 8.3**) are implemented well, from the screening of an individual to the communication of results. This requires putting in place well-defined procedures and quality monitoring. This section explains the key considerations at each step, with a specific focus on their application in the context of a national TB prevalence survey.

8.4.1 Symptom screening and CXR

In a national TB prevalence survey, participants are only requested to provide sputum samples for bacteriological testing for TB if they have TB symptoms or a CXR abnormality suggestive of TB (**Chapter 3**).

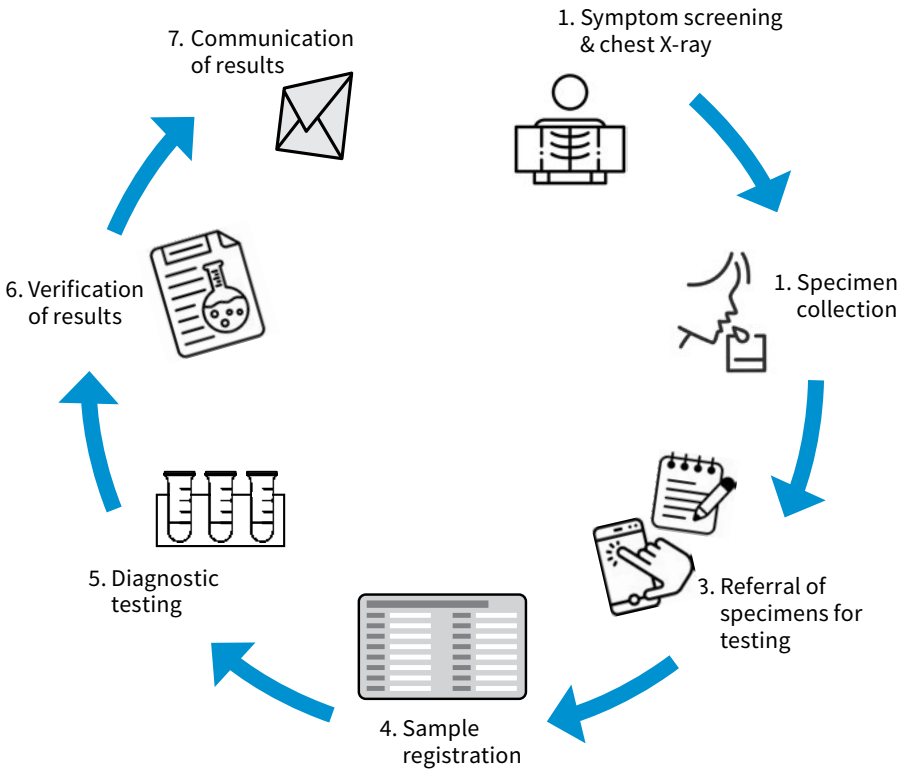
8.4.2 Specimen collection

Achieving high-quality sputum test results requires a specimen of adequate quantity (2–5 mL) and good quality *(22)*. An important consideration is the volume of a specimen, which is a good predictor of yield. Within a national TB prevalence survey, it is usually difficult to obtain mucopurulent sputum samples (i.e. containing both mucus and pus) of high volume from the survey participants. Therefore, the best sputum sample produced should be used, meaning that salivary specimens and those with a low volume (e.g. 0.5 mL) are acceptable in this situation. Clear instructions to survey participants and encouragement, with supervision, to expectorate a good specimen is critical *(23)*. Collection of induced sputum in national TB prevalence surveys is not encouraged because of the logistical and infection control risks under survey conditions; also, such collection does not appear to have additional benefits compared with routine collection methods among ambulatory patients *(24)*.

Sputum containers should be transparent, wide-mouthed, robust, leak-proof and screw-capped *(3, 22)*. Preferably, they should have enough capacity (e.g. 50 mL) to allow both collection of the sputum sample in the field, and decontamination and processing of the sample in the laboratory. The sputum container should be clearly labelled with identifiers, date and barcode labels on the container – not on the lid – and containers

Fig. 8.3

Overview of the screening and diagnostic workflow in a national TB prevalence survey



should be packed correctly before transportation from the field to the laboratory.

Sputum specimens should be collected from all individuals eligible for sputum examination once informed consent has been received. The collection should be done in a designated area in the open air, while ensuring privacy, at the survey site. To avoid infection through aerosol inhalation, survey staff supervising the sputum collection should wear an N95 mask and not stand directly in front of the participant.

Depending on which survey algorithm is used, two to four sputum specimens will be required. Two spot sputum specimens should be collected at least an hour apart *(25)*, rather than a spot specimen and an early morning specimen (unless the individual cannot produce two quality spot sputum specimens). There is no significant difference in diagnostic yield between these two approaches *(25)*, but the former has operational advantages and minimizes the need for the participant to make a return visit. However, an early morning sample should be collected if a person is poorly productive in providing a second spot sample. For Option 1, the individual will need to provide another two spot samples during field operations if either of the two Xpert Ultra tests is positive.

For Option 2, if the routine Xpert Ultra test is not performed on the sputum sediment, an additional sputum sample should be collected (spot or early morning) to ensure that a rapid result is available for prompt clinical management. The additional sample should be referred for testing at the nearest Xpert Ultra testing site. As a rule, all participants should have the required number of specimens submitted per protocol, and every effort should be made to have matched specimens for all eligible participants.

All sputum specimens must be properly labelled, and the outside of the container should be checked for contamination with sputum. If contamination is found, the outside of the container should be cleaned with a disinfectant (e.g. bleach) after the screw cap has been tightly sealed.

8.4.3 Referral of specimens for testing

Referral of specimens for Xpert Ultra testing at the field site

After collection of sputum samples for Xpert Ultra testing, the testing should be done at the field Xpert Ultra testing site, on the same day.

Referral of specimens for laboratory-based testing (offsite Xpert Ultra, if relevant, and TB culture)

- Each sputum container should be placed in a zip-locked plastic leak-proof bag with absorbent material, ideally with a biohazard label.

- The **specimen should be kept cool** (at a temperature of 2–8 °C) in a cooler box (icepack or electrical) until it reaches the laboratory. Temperature probes should be used to monitor the temperature. Specimen bags or containers must not come into direct contact with water from melting ice or ice packs because water may contain contaminants that would affect the quality of the specimens and testing results.
- **Specimens should be transported safely and rapidly to the laboratory where they will be processed**. In some recent surveys, it was possible to use the national postal service for this transport. Whatever service is used, it must have the required International Air Transport Association (IATA) training to handle biological samples, and the courier should be provided with a spill kit. The selection of testing laboratories should consider transportation times, so that the specimens arrive in good condition.
- Specimens processed for Xpert Ultra testing can be refrigerated and should be processed within the time frame specified by the manufacturer. Ideally, the time between submission (collection) and processing of the sputum sample for culture should be 3 days or less, and **within 5 days** when the cold chain (i.e. temperature of 2–8 °C) is maintained. Samples with delays beyond 5 days should still be processed, but might not be included in the analysis owing to the risk of false negative cultures *(17, 18)* (this decision will be made at the data analysis stage). Adequate storage conditions and timely transport of samples are critical to ensure that any *Mtb* in the samples remains viable, and to avoid overgrowth of other bacteria and fungi, so that *Mtb* can be successfully isolated by culture.
- To **ensure that timelines are adhered to**, a designated survey team member should be responsible for arrangements for transporting specimens. The use of courier companies with adequate national coverage can be explored. Routes and timelines need to be clearly defined.
- A **communication link between the courier and the field site coordinator should be established**. A transportation log that records dates of specimen collection and receipt should accompany the samples, to allow tracking of specimens. Specimens reaching the laboratory after excessive delays or not under cold chain conditions should still be processed. Laboratory staff should keep a note in the laboratory register to allow separate data analysis to be done on such samples, if necessary.

Because the time between specimen collection and sample processing for culture is critical, the rollout of the survey has to be carefully scheduled. **Importantly, the 3-day time frame for accepting samples for culture corresponds to 5 days from specimen collection to culture inoculation**.

8.4.4 Sample registration

After registration of specimens in the laboratory (at the field site or offsite), specimens should be visually inspected for leakage. If specimens are properly packed, any leakage will stay inside the specimen bag and will not contaminate other samples. If a specimen does contaminate other samples, all affected specimens should be discarded to avoid cross-contamination and false positive results. The field team should be notified to take corrective action and prevent further leaks in the future; and to then collect replacement specimens from the same individual or individuals if the survey team is still in the cluster. When specimens are processed in a laboratory, they should only be removed from a specimen bag inside a BSC.

If a specimen has leaked but only within its bag, and enough sputum remains for processing, the outside of the container should be carefully disinfected using a tissue drenched in disinfectant. The cap of the tube should be tightly closed and clearly relabelled. If a specimen has leaked and there is insufficient sputum for processing, the specimen container must remain unopened in its bag and be discarded directly into a biohazard waste bag for autoclaving or incineration.

Preferably, specimen containers sent for culture testing should be disinfected when they arrive at the laboratory and before processing. The container should be relabelled if the label becomes unclear.

8.4.5 Diagnostic procedures and laboratory processes

Xpert Ultra testing

Xpert Ultra testing process

In contrast to other nucleic acid amplification tests, in the Xpert Ultra assay there is full automation of the DNA extraction, polymerase chain reaction (PCR) amplification and interpretation of results, and these occur in a closed system (i.e. the Xpert Ultra cartridge). The only manual step required is for sample preparation, which should be performed according to the manufacturer's instructions. Therefore, it is important that the preparation of each sample is done separately, meaning that only one sample and one Xpert Ultra cartridge is opened at a time, to minimize the risk of cross-contamination and clerical errors. The same quality requirements apply to Xpert Ultra tests performed directly on sputum or sputum sediments.

Field-site testing

Field-site testing means testing within a mobile vehicle or using an instrument temporarily placed at the survey field operations site (e.g. in a community hall). Such an approach has been successful in surveys in several countries – including Eswatini *(26)*, India *(27)*, Mozambique *(28)*, Myanmar *(29)*, Viet Nam *(30)* and Zambia *(31)* – although dust affecting the GeneXpert instruments

can be an issue. Each field team should have their own Xpert Ultra instruments and cartridges, and these must be carefully packed for transporting between field sites. Several factors need to be considered to ensure that performance and quality are not compromised if field-site testing is conducted. Requirements include:

- a stable power supply and backup power;
- a temperature between 15 °C and 30 °C day and night; if this is not possible, the instrument should be kept in an air-conditioned environment (e.g. a capacitated mobile van);
- close monitoring of error rates, with weekly charting of trends;
- availability of a ventilated hood or open space for processing samples; once the sample has been treated with SR Buffer,[1] any *Mtb* is inactivated and the sample is safe to handle;
- provision for appropriate management of waste (e.g. an arrangement with a nearby laboratory for medical waste disposal); such waste can accumulate quickly;
- calibration if the instrument is moved from site to site; this should be discussed with the manufacturer, and a budget should be allocated as required;
- running of quality-control (QC) samples for each cluster, and for each new batch of reagents;
- recommended storage conditions for consumables;
- a means of uploading information to the laboratory information system (LIS); the mobile unit can connect to the LIS at the testing sites, but where internet connectivity is limited, LIS-captured information can be uploaded at a later stage once connectivity is established;
- pre-selected secure sites to ensure that the equipment and consumables are kept safe;
- a budget for transport fuel; and
- completion of a field assessment, assessment of staff proficiency and a pilot(s) before starting survey testing.

QC: Xpert Ultra

To ensure QC for Xpert Ultra testing:

- the laboratory doing the testing must be part of an external QA programme;
- the error rate should be monitored and must not exceed 3% during routine operations *(32)*; and
- a service and maintenance contract for the equipment should be in place.

[1] SR Buffer, from GeneDireX®, is designed to reduce the need for serum in culture medium used for cell proliferation.

Pooling of specimens for Xpert Ultra testing

Pooling specimens from the same or different patients to reduce the cost of supplies and equipment and staff capacity for Xpert Ultra testing **is not recommended** in national TB prevalence surveys. A recent review found limited evidence (two published and four other studies) of surveys that pooled sputum *(33)*. However, this approach adds operational complexity, which is challenging in a national TB prevalence survey because teams are regularly moving across the country, thus hindering the re-collection of samples if a batch of pooled sputum specimens is positive by Xpert Ultra testing.

Liquid media culture and identification

Creating batches of samples for culture processing

A batch is a set of samples that are processed at the same time by (ideally) the same laboratory technician. It is important to record each sputum sample, the batch number for each process done and the name of the laboratory technician performing the work to monitor individual staff proficiency. The size of a batch depends on the size of the equipment available and the number of samples one experienced technician can handle. For example, the size of a batch for culture could be 18–20 samples (including the positive and negative controls). A timer **must** be used to ensure that digestion or decontamination (see below) does not exceed the required time. Larger batches may lead to over-decontamination due to prolonged exposure to sodium hydroxide (NaOH) and could result in false negative cultures.

Decontamination protocol

Decontamination is the most critical step when culturing *Mtb*. This step is done to liquefy the sputum specimen and eliminate bacteria other than mycobacteria in the specimen. The *N*-acetyl-L-cysteine (NALC)–NaOH method is the gold standard for sputum decontamination and is the recommended method for liquid culture systems *(21)*. NALC is a mucolytic agent that, at concentrations of 0.5–2.0%, can liquefy mucus within minutes. Because NALC rapidly loses its activity, the NALC–NaOH solution must be freshly prepared each day. The NaOH is a decontaminating agent with liquifying activity, and is typically used at 1% final concentration. Prolonged (>20 minutes) exposure of specimens to NaOH results in the killing of mycobacteria, thus leading to false negative culture results *(21)*.

It is crucial to find the correct balance between eliminating contaminants and ensuring the survival of *Mtb* in any given setting. Some adjustment in the final NaOH concentration may be necessary, with a maximum NaOH final concentration of 1.5% *(21)*. Using a timer is imperative for accurate timing and preventing overexposure to the decontaminant. Culture contamination rates and positivity rates are useful performance indicators and should be monitored to help optimize the

decontamination protocol. Before the survey is initiated, a pilot study should be performed to confirm that recovery of *Mtb* is successful and to select the optimal NaOH concentration given the lower bacillary load compared to specimens tested from routine testing. A pilot is usually initiated for the survey to test other aspects of operation, and sample collection and testing should also be included. Such a pilot should be initiated 2 months before the start of the survey to allow for final culture results to be available and analysed, and for culture optimization steps to be implemented.

To reduce the risk of cross-contamination, the following precautions should be adopted:

- ensure that reagent containers do not come into contact with the edge of the specimen container;
- open only one MGIT at a time;
- keep the MGIT cap closed until ready to add to the medium; and
- open the MGIT for the shortest possible time.

If possible (depending on available space and capacity), dedicated MGIT instruments or drawers should be used for the prevalence survey samples.

Tubes that flag positive or negative should be removed from the MGIT instrument daily and examined in the routine workflow. The presence of turbidity in the positive flagged tube is indicative of contamination. The presence of *Mtb* in a positive tube should always be confirmed by Ziehl–Neelsen stain (cords should be visible) and by immunochromatographic assay. A high contamination rate will need to be investigated. The survey laboratory coordinator should inform the field coordinator of any contaminated results in case specimen collection technique needs to be improved.

QC: TB culture

A positive control (well-characterized, known positive, drug-susceptible *Mtb* isolate; e.g. H37Rv) and a negative control (decontamination solution, water or other bacteria; e.g. *Escherichia coli*) should be included with each batch – details for this are provided elsewhere *(5)*. The use of a low-positive control has been proposed; however, there is currently no accepted definition, standardized methodology or evidence for its utility. The best way to monitor the efficiency of culture is through performance indicators *(5)*.

The mycobacterial contamination rate is calculated as the total number of contaminated tubes divided by the total number of media inoculated; ideally, this should be calculated for each batch. Contamination rates should fall within acceptable limits (8–10% in liquid media) *(17)*. Monthly monitoring of trends can help to ensure prompt identification of variations that warrant further investigation. If the contamination rate is higher than expected, a careful review of in-laboratory procedures (including sterile technique) is needed, and it may be necessary to retrain staff. The time and temperature logs of a sample shipment should also be reviewed, and problems addressed.

In extreme situations, a pause in the survey may be needed if the laboratory contamination rate is a persistent problem affecting consecutive clusters.

It is useful to monitor the agreement between Xpert Ultra and culture test results on a monthly basis. At least 90% agreement is expected between Xpert Ultra semi-quantitative high or medium results and culture among participants with no previous or current history of TB treatment history.[1] In addition, when reviewing culture results, consistency within a case series should be taken into consideration. In situations where multiple positive cultures occur within the same batch, this needs to be investigated to exclude potential cross-contamination (e.g. consecutive positives).

Contaminated cultures

Contaminated cultures can be divided into three groups: cultures completely contaminated with bacteria other than mycobacteria such that no mycobacteria can be isolated; cultures overgrown with non-tuberculous mycobacteria (NTM) so that *Mtb* cannot be excluded; and cultures overgrown with bacteria and mycobacteria. Contaminated specimens in the first of these groups can sometimes be detected after a few days, in which case there may be time to collect further sputum specimens from the same survey participant for reprocessing; however, this is not always feasible.

Repeating the process of decontamination is cumbersome and requires proper supervision. The percentage of *Mtb* that will finally be recovered is expected to be small. In a prevalence survey, it is essential to decide whether to repeat the decontamination process or to deduct contaminated samples from the denominator. If it is agreed to proceed with repeating the decontamination, any cultures designated as "contaminated with the presence of acid-fast bacilli (AFB)" should be decontaminated again, and a proper system needs to be in place for storing leftover decontaminated sputum samples. Samples that are contaminated with AFB can still be processed for rapid antigen testing or an mWRD test to provide a final identification. For cultures overgrown with bacteria or NTM, repeating the decontamination is of limited value. A molecular test (e.g. Xpert Ultra) could be used to determine whether the AFB are *Mtb*.

[1] Based on results from the national TB prevalence survey in South Africa (2017–2019) (F. Ismail, Centre for Tuberculosis, National Institute for Communicable Diseases, Johannesburg, South Africa, personal communication, 24 January 2024). Specifically, among survey participants with no history of TB treatment, 42 of 46 (91%) Xpert Ultra-positive specimens (high or medium) grew in MGIT culture. By comparison, among those with a history of TB treatment, 16 of 28 (57%) Xpert Ultra-positive specimens (high or medium) grew in MGIT culture.

Culture identification using an immunochromatographic assay

In a national TB prevalence survey, NTM will be isolated more frequently than in clinical practice, so it is vital to use a good identification test to differentiate between *Mtb* complex bacteria and NTM. The choice of the appropriate identification assay mainly depends on the assays used in routine practice and on the skills of the laboratory staff.

WHO recommends commercially available immunochromatographic assays using a monoclonal antibody to detect *MPT64* as the method of choice for the identification of *Mtb*. These rapid antigen tests have a high specificity and sensitivity, and are more cost-effective than biochemical testing *(16, 34)*. These tests can be done directly from the positive MGIT and do not require any expensive equipment. Recent reports *(35, 36)* show that such tests are ideal for identifying *Mtb* complex bacteria from a culture in a low-income setting. However, *Mtb* complex strains could be missed due to mutation in the *MPT64* gene *(37)*, and weak positive bands or higher frequencies of NTM should have further confirmatory testing using a molecular test.

QC: immunochromatographic assay

QC of *Mtb* identification relies on internal controls incorporated in the immunochromatographic assays. Re-checking the culture with a molecular test is helpful where unexpected numbers of AFB are determined to be NTM, based on the immunochromatographic test alone, or where there is discordance between Xpert Ultra and culture results.

Drug susceptibility testing

Results from drug susceptibility testing (DST) should be used to ensure that people with bacteriologically confirmed TB who are identified through the survey are appropriately managed.[1] Every person diagnosed with TB should have at least a result for rifampicin resistance obtained by Xpert Ultra testing (or by another method in the case of an Xpert Ultra trace result). If rifampicin resistance is detected, then the sample should undergo testing for fluoroquinolone resistance. Additional drug-resistance testing should be performed based on the local policies and algorithms, in line with WHO policies and guidance. Further details of diagnostic testing for drug resistance are available elsewhere *(38)*.

8.4.6 Verification of results

All *Mtb*-positive results must be verified by a senior staff member or a microbiologist and, once confirmed, should be communicated to the laboratory focal point and survey coordinator. Results of an mWRD will be available within 48 hours, and from culture in 3–6 weeks. The verification process involves reviewing all the results in the specific batch (both for Xpert Ultra and culture). Patterns of multiple positive results in a batch are a helpful indicator; consecutive positives could indicate cross-contamination that needs to be investigated. The correlation between Xpert Ultra and culture results should also be analysed. Although discordance is well known and expected, an investigation should be done to check that all processes have been followed correctly and no laboratory or data management errors have occurred, and that the discordance is due to the limitations of each diagnostic tool.

Approach to discordant results

- Conduct traceability to ensure that no laboratory errors have occurred before, during or after the analysis; for example:
  - specimen mix-up – the name or barcode on the laboratory request form should match the specimen received;
  - mislabelling – labelling of samples during the analytical process should be correct;
  - decontamination errors – the date of sample processing and the operator should be reviewed, to identify patterns where decontamination may have been too harsh, leading to false negative cultures; or
  - transcription errors – these can occur if recording of results is not interfaced with the instrument.
- Determine whether the patient has a previous history of TB. Xpert Ultra test results could be positive owing to detection of DNA of non-viable bacilli.
- Review the semiquantification of the Xpert Ultra results (i.e. high, medium, low, very low or trace) to assess the degree of discordance between samples (i.e. between the two Xpert Ultra tests, and between Xpert Ultra and culture):
  - Potentially consistent results – a participant with a trace or very low Xpert Ultra result could have a negative culture result (in the case of two Xpert Ultra tests, one very low and one low result could be acceptable).
  - Inconsistent results – high and trace or negative Xpert Ultra results from the same participant, or a high Xpert Ultra result and a culture-negative result, is unusual and could suggest a possible processing or data management error.
  - Semiquantification results – if culture samples are missing or culture results are not available, the semiquantification results are needed to determine whether a participant meets the case definition (see **Chapter 4**).
- Consider repeating testing on stored sediments, if available.

[1] Results cannot be used to produce population estimates of the percentage of people with TB who have drug-resistant TB *(38)*.

It is important to note that differences in specimen quality of the two samples processed could also lead to discordant results.

8.4.7 Communication of results

Reporting of Xpert Ultra and culture test results should follow the local reporting rules, as per the national guidelines. The survey team should include a dedicated person to whom all results are reported, and urgent communication should be established (e.g. by mobile phone) for any TB-positive or drug-resistant result. The designated team member will then share the results with the relevant people at the NTP, to ensure that the participant is receiving care, and will be treated or managed according to national guidelines. Positive results should also be forwarded to the case management team for further discussion about the participant's inclusion as a survey TB case (as per the case definitions provided in **Chapter 4**).

8.5 Other laboratory considerations when implementing a national TB prevalence survey

8.5.1 Laboratory team structure

A strong diagnostic team is essential for the success of a survey, and clear structures and communication lines should be established before the survey begins. A survey coordinator should serve as the link between the laboratory (or laboratories) and the field survey team.

An overall laboratory lead should be selected to serve as the single final decision-maker on diagnostic matters. Ideally, this person should be the head of the national TB reference laboratory (either a clinical microbiologist or the laboratory manager). If multiple laboratories are used in a country, the head or manager (or equivalent) of each of these laboratories should be designated as the contact person responsible for liaising with the person with overall responsibility for survey-related laboratory work. If multiple laboratories are used in a survey, they must all perform their tasks according to the same quality standards. The laboratory head or manager (or equivalent focal point) should oversee the day-to-day operations. That person needs to ensure that the available staff and infrastructure are deployed so that all laboratory survey activities can be completed with the necessary quality without compromising routine services.

The minimum laboratory staffing requirements recommended for a survey are:

- a laboratory survey coordinator, to oversee all laboratory-related survey work;
- a QA manager;
- a laboratory manager in each of the laboratories used in the survey;
- an overall laboratory focal point in each of the laboratories used in the survey (this could be the same person as the laboratory manager);
- a sufficient number of laboratory technicians and technologists in each laboratory used in the survey, according to the anticipated testing workload (i.e. the volume of samples expected);
- a laboratory clerk in each of the laboratories used in the survey; and
- administrative staff to support procurement.

8.5.2 Laboratory work – roles and responsibilities

The roles and responsibilities of the staff involved in laboratory work are summarized in **Table 8.4**.

8.5.3 Training

All staff working with *Mtb* need to have adequate knowledge about the precautions needed to mitigate TB-related risks. The clinical field staff should be trained on sample collection, forms to be filled out, sample packaging, the diagnostic algorithm and expected turnaround times for results. To ensure the reliability of results, laboratory staff should have enough background knowledge to understand each step of the specific laboratory test procedure that is being performed. Depending on the setting and skills available, it is always useful to have staff capable of performing both Xpert Ultra assays and MGIT culture, to ensure that all the procedures can be covered in case of staff shortages.

All laboratory staff participating in a survey should undergo training or refresher training on the laboratory procedures required in the survey before the survey starts. Staff competency should be evaluated before and after training, and staff performance should be monitored throughout the survey for each of the testing methods being used. This will include observation of practical procedures undertaken by each staff member, and regular monitoring of quality indicators, particularly for culture (e.g. the culture contamination rate per specimen processed by each individual technician). It cannot be assumed that experienced technicians will automatically have good laboratory techniques and perform tests according to the standard operating procedures (SOPs). Staff should have a successful competency assessment before they begin to process samples, so that the quality of laboratory results is not compromised. All staff working in a containment laboratory must have proper training on biosafety procedures, on the correct use of personal protective equipment (PPE) and on equipment maintenance (especially of BSCs). Documentation of all training must be filed as part of staff records.

Similarly, the laboratory supervisor who will routinely monitor the laboratories to ensure that the SOPs are being followed, and who will be responsible for QA, should be appropriately trained. Retraining should be

Table 8.4

Staff roles and responsibilities for laboratory work in a national TB prevalence survey

ROLE	RESPONSIBILITIES
Clinical staff	Collecting sputum samples, and labelling and packaging of samples. Staff could be specifically allocated these tasks. Alternatively, these tasks could be integrated into the responsibilities of the survey staff who obtain informed consent from participants and administer questionnaires.
Laboratory clerk	Receiving samples from the survey site and registering them in an LIS or other survey-specific system; cross-checking samples against the sample log sheet received from the survey site; promptly notifying the laboratory survey coordinator if any sample is missing or rejected; and documenting the temperature of specimen containers received by the laboratory to ensure that the cold chain was maintained.
Technical staff (field and laboratory)	Laboratory processing of all samples received according to the SOPs. This involves laboratory staff at both the reference laboratory and any other decentralized laboratory. It also involves any field staff who perform testing at mobile units. For field testing, at least two staff should be included per mobile unit to provide TB and HIV testing and to ensure backup if one person is unavailable.
Laboratory survey coordinator	Liaising between the laboratory and field site survey team in cases where samples are not received or rejected (this will enable a repeat sample to be collected from the participant if the team is still present within the specific site/cluster); ensuring the entry of laboratory results into a database and the cleaning of laboratory data; communicating all positive results to the laboratory lead; and assisting with the compilation of cluster reports.
Laboratory manager	Training of survey staff on appropriate specimen collection and transportation procedures; ensuring the required consumables (i.e. sputum containers, laboratory request forms and specimen bags) are sent to the survey sites; managing the consumables required for laboratory processes so that there are no shortages or stock-outs that would negatively impact the laboratory workflow; and ensuring all samples are processed according to the SOPs with the appropriate QA measures in place, including monitoring of specific indicators (10% check of negative results, and checking of all positive results, should be performed by the laboratory manager).
Laboratory focal point	Overseeing the entire laboratory process and ensuring that laboratory results are accurate; ensuring timely communication of all positive results to the survey case management team; compiling and disseminating cluster reports; and collating all laboratory data.

HIV: human immunodeficiency virus; LIS: laboratory information system; QA: quality assurance; SOP: standard operating procedure; TB: tuberculosis.

provided whenever required. Oversight and additional training could be provided by a WHO SRL linked to the country.

8.5.4 Biosafety

To determine safety requirements, it is important to know and understand the risks for infection based on the specific organism, its mode of transmission and the laboratory tests to be performed. The two laboratory tests recommended in this guidance for national TB prevalence surveys (liquid culture and Xpert Ultra) have different risk levels, as explained in the WHO laboratory biosafety handbook *(39)*. Xpert Ultra testing is low risk whereas liquid culture is high risk. Minimizing aerosol production, along with the correct use of appropriate PPE and equipment (BSCs), is an effective way to ensure the safety of staff.

A laboratory with appropriate, well-maintained biosafety facilities, and regularly maintained and certified equipment (especially BSCs and centrifuges with safety buckets), must be in place before any work can commence. Furthermore, all laboratory staff need access to appropriate PPE, including fit-tested N95 respirators, gloves (different sizes) and gowns. Providing appropriate PPE and equipment is not sufficient; staff also need to be trained on their use because improper use could result in a safety breach. WHO guidelines on biosafety, which describe regulations for a TB facility, are available *(39)*.

A safety manual that describes all safety, emergency (e.g. how to handle spillage of live culture or sputum) and waste management regulations needs to be in place at the testing site. This manual should be part of the learning materials during training.

Sputum specimens are classified as biological materials, whereas live cultures are classified as infectious materials. To provide more protection to laboratory staff, a specific ventilated station should be set up in the field for processing samples to be tested by Xpert Ultra; a Class II BSC is required for processing samples for culture.

Cultures of *Mtb* may only be manipulated in a Class

II BSC within a certified containment facility that has appropriate physical separation between functionally clean and dirty areas, and a proper airflow ventilation system.

8.5.5 Waste management

All biological and infectious waste should be collected in biohazard-labelled bags and placed in biohazard boxes, buckets or sharps containers. All infectious materials from TB-containment laboratories and mycobacterial cultures should be autoclaved before being removed from the laboratory. Containment laboratories should have onsite autoclaving facilities. Biohazard boxes, buckets and sharps containers must be sealed and labelled before being moved to a lockable storage area to await collection from a designated waste disposal contractor.

Specific information on waste management that is applicable to TB laboratories can also be found in the WHO laboratory biosafety manual *(39)*. The same information and principles apply to laboratory sites in the field.

If mobile Xpert Ultra testing is done, provision should be made for appropriate waste disposal at the field site. This includes collection and removal of the infectious waste from the field site, which could be transported to the nearest laboratory or health care facility. Prior engagement with the respective authorities will be required. Biohazard containers should be available for disposing of the PPE, cartridges and consumables used during the testing process.

8.5.6 QA

Systems for QA, internal QC and external quality assessment must be in place before any work is started. These systems help to measure human and assay error; they also allow assessment of whether laboratory results are trustworthy. All laboratory processes should be in line with achieving the requirements of the ISO 15189 standard. Ideally, all laboratories should have ISO 15189 accreditation status. Those that are not yet accredited should follow the Stepwise Laboratory Improvement Process Towards Accreditation (SLIPTA) *(40)*.

Laboratory staff need to be well trained in good laboratory practices and QA, to ensure that work is of high quality. Logbooks must be in place to record the daily temperatures of refrigerators, freezers, rooms and incubators, and service and maintenance records should be kept for all equipment used. Dates of reagent preparation and the expiry dates of supplies and assays need to be checked monthly and lot numbers need to be recorded.

Quality indicators that can be used are described in the WHO practical manual on TB laboratory strengthening *(5)*. Minimum requirements and indicators are listed in **Box 8.3** and **Box 8.4**. A supervisory visit by a WHO SRL team should be conducted before the survey starts and at regular intervals during the survey.

BOX 8.3
MINIMUM PRE-IMPLEMENTATION REQUIREMENTS

- Ideally, all laboratories should have ISO 15189 accreditation status to perform the required tests. Those not yet accredited should follow SLIPTA and a pre-assessment visit should be made by a WHO SRL.[1]
- Required biosafety precautions must be in place. This includes availability of Class II BSCs and necessary PPE, as well as training for staff on the appropriate use of PPE and laboratory equipment.
- SOPs for all processes should be available. The SOP for culture should specify that the final concentration of NaOH should not exceed 1.5%, and exposure to NaOH should not exceed 20 minutes.

BOX 8.4
MINIMUM QUALITY INDICATORS TO BE MONITORED

- Time between collection and processing of the sputum sample for culture should be 3 days or less, and not more than 5 days when kept in the cold chain (at a temperature of 2–8 °C).
- The Xpert Ultra error rate should not exceed 3% during routine operations *(5)*.
- The culture contamination rate should be a maximum of 8–10% for liquid media *(5)*.
- The level of agreement between Xpert Ultra semiquantitative high or medium results and liquid culture should be 90% or more among participants who have no previous history of TB treatment and are not currently on TB treatment.

8.5.7 Laboratory supplies

In a prevalence survey, large quantities of laboratory supplies are consumed every day, owing to the large number of specimens processed. Therefore, stock control of laboratory supplies needs to be well organized to ensure uninterrupted continuation of the work.

[1] A presurvey assessment will produce major and minor findings. Corrective actions should be performed to address at least the major findings before the survey starts. However, if there are serious concerns about the laboratory, an alternative laboratory should be used.

A proper stock supply system should be in place, with one person responsible for it. The minimum number of consumables that need to be in stock for a certain period should be recorded. The number of supplies to be procured depends on factors such as the expiry date; availability in the country; average daily use; time between ordering and receiving consumables from abroad; and availability of storage space, including a cold room. To minimize the possibility of stock-outs, the stock available should be enough to cover the lead time between ordering new stock and stock arriving at the testing site. In addition, close liaison with the manufacturer or distributor will ensure that the estimated future needs are met on time.

Stock management for field testing done in a mobile vehicle requires additional considerations. A schedule should be developed that clearly defines where and when new stock should be collected, and where and when biological waste should be disposed of at the laboratory nearest to a cluster. A route map showing the distribution map, timelines and volumes should be developed at the outset. Additionally, the storage conditions of the supplies, both at the regional re-supply laboratories and in the vehicle, must comply with the manufacturer's recommendations.

8.5.8 Laboratory data management

Efficient management of laboratory data allows for the production of good-quality data for key variables, and permits meaningful description and data analysis (also see **Chapter 17**). A central digital database should be used to capture all information collected on the field and laboratory case report forms. Data entry should be initiated as soon as the survey begins. The data should be extracted on a regular basis; also, for QC, a subset of data should be checked against the test reports to promptly detect any anomalies within the processes. Captured data should be checked for completeness.

The survey participant should be assigned a unique personal identification number (PIN), and it is recommended that this PIN is used to label sample containers. If the laboratory uses a laboratory information and data management system (LIMS) that generates a unique laboratory number (i.e. sample ID), the PIN should be captured in the LIMS to link the sample to the participant. The use of barcoded labels is recommended because barcodes are easy to capture and thus minimize transcription errors. A unique PIN is critical for the accurate merging of field and laboratory data. The LIMS could also be interfaced with the GeneXpert and MGIT systems to directly transmit test results, thereby minimizing error.

If laboratory reports can be produced within the LIMS, they could be directly imported into the central digital database used for the survey, to merge laboratory information with field data. The use of a central digital database facilitates the tracking of survey progress and the provision of meaningful metrics in real time. A real-time dashboard connecting the survey and testing data will be ideal for monitoring survey progress.

There should be regular matching of field and laboratory data, including data cleaning and verification, to:

- allow for early identification and correction of systematic errors;
- ensure that other errors can be promptly identified and corrected;
- minimize the amount of data checking and correction needed at the end of the survey; and
- enable timely analysis of the reasons for discordant results and prompt correction action.

8.5.9 Archiving and storage of sediments and isolates

Storage of survey sediments and isolates is recommended. Both sample types (i.e. sediment and cultured isolates) should be stored at an ultra-low temperature (−80 °C) as soon as the laboratory process is completed. The sediment can be stored without additional storage solution (raw), whereas the isolate should be stored using an appropriate storage medium. The sediment should have achieved neutral pH after processing, but this should be checked (and corrected if necessary) before storage.

Stored material is useful when there is unexpected discordance between Xpert Ultra and culture results (e.g. the sediment could be used to repeat the Xpert Ultra or culture test). Any testing related to discordant results should be described in the survey protocol. If additional work is planned (e.g. molecular typing or sequencing), this should also be described in the protocol and the informed consent form. The stored isolates can also be used to assess the level of resistance to anti-TB drugs.

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CHAPTER 9

Clinical management: TB and other conditions

A fundamental principle of research studies is that feedback about all tests and investigations undertaken during the survey is communicated to participants. This is an ethical imperative *(1)* and is in line with the principles of good clinical practices *(2)*.

In the case of a prevalence survey, some participants will be newly diagnosed with tuberculosis (TB) or drug-resistant TB (DR-TB), and appropriate clinical management needs to be ensured for these individuals. Participants diagnosed with TB should be linked to care, and those with DR-TB need to be linked to programmatic management of drug-resistant TB (PMDT) services. In addition, chest X-ray (CXR) may detect conditions or abnormalities other than TB, such as cardiac pathology or cancer-like lesions, and bacteriological tests might identify other pathogens, such as non-tuberculous mycobacteria (NTM), which also need to be appropriately managed. Similarly, all newly identified HIV-positive participants should be linked to appropriate HIV care. For those who already know their HIV status, it should be ascertained whether they are linked to care; if they are not, appropriate referral should be made.

Although all survey test results (even normal or negative) should be communicated to survey participants, in most cases, participants are informed at the start of the survey that they will be traced through their local TB coordinator (or equivalent person), within a limited period, only if laboratory results on their sputum samples are positive.

Appropriate and timely clinical management is a crucial parameter of survey quality, and it deserves careful preparation and monitoring throughout the survey, for the benefit of both the individual and the community.

This chapter describes how to inform participants about survey laboratory results and who is responsible for doing this, how to manage participants newly diagnosed with TB and participants already on TB treatment who still have positive laboratory results, how to manage conditions other than TB (e.g. severe clinical conditions, abnormal CXR with negative or invalid laboratory results, or other diseases), and how to refer participants to the health system for proper care if needed.

9.1 Responsibility for clinical management of participants

Survey participants might present with clinical conditions requiring health care, which may be due to TB or other diseases. Although the scope of the survey is to assess survey participants' symptoms and CXRs to identify those who may have TB, timely clinical management of all conditions deserving medical attention is critical, and must be clearly addressed during survey preparation and implementation. In addition, informing participants about laboratory test results (e.g. Xpert® MTB/RIF Ultra [Xpert Ultra], culture and HIV tests), especially where results are positive, and referring those in need of care to the health system is important and needs careful preparation.

Who is responsible for the clinical management of survey participants?

In all cases, clinical management of survey participants in need is the responsibility of the entire survey staff. However, different scenarios may arise. For example, it is important to delineate between clinical management that needs to be taken immediately in the field and that which may be required at a later stage.

Conditions that need **immediate action** during field operations include:

- severe clinical conditions or abnormalities identified on CXR that require immediate care, not necessarily related to TB (e.g. pneumonia, pneumothorax, massive pleural effusion, cancer-like lesions);
- HIV-positive test in the field; and
- Xpert Ultra-positive result on sputum processed in the field.

These situations need to be addressed by the survey team and, in particular, by the field **medical officer**.

Other conditions may require action **at a later stage**, such as when laboratory test results from the reference or central laboratory are available. For example:

- a positive culture for *Mycobacterium tuberculosis (Mtb)*;
- a positive Xpert Ultra test result;[1] or
- central CXR reading that identifies a participant with abnormalities suggestive of TB who did not submit

[1] If the diagnostic Option 2 is selected (see **Chapter 3**), Xpert Ultra testing may be conducted at a central laboratory rather than in the field.

sputum samples during the survey, or with negative or inconclusive laboratory test results, or with other conditions that may need medical care, such as cancer-like lesions or other abnormalities.

In these situations, decisions about clinical management should be taken by the **survey medical panel** at the central level.

Survey medical panel

The medical panel usually comprises the survey coordinator, one or two radiologists, one or two respiratory physicians, a laboratory expert, a survey data manager and an administrative assistant. The panel's primary role is to take decisions about the clinical management of survey participants (i.e. case management function). It should meet regularly (e.g. weekly) and discuss, at a minimum, **all participants with TB as indicated by their laboratory results** (e.g. positive Xpert Ultra test or culture positive for *Mtb*), reviewing their CXR images, HIV status, treatment history and other available information. **The medical panel should also discuss participants with an abnormal CXR (or with high computer-aided detection [CAD] scores), even if laboratory tests were not positive**, or if culture results indicated NTM.

Aside from medical officers, other survey team members and the medical panel who are responsible for **identifying** those in need of care and **linking them to the TB programme and local health authorities** do not have to provide care or treatment of any disease beyond appropriate first aid and referral. However, mechanisms should be put in place to ensure that participants in need are linked to care and that enrolment on TB care or other interventions is documented. An example of the role of the survey medical panel during Nepal's national prevalence survey (2018–2019) is outlined in **Box 9.1**.

Clinical management versus survey TB case definition

Although all participants with a positive Xpert Ultra test or positive culture for *Mtb* will require review by the medical panel, not all of them, or those referred to care, will necessarily be counted as survey TB cases for the estimation of prevalence. Clinical definitions of presumptive or confirmed TB differ from prevalence survey TB case definitions, which are based on bacteriological

BOX 9.1
THE NATIONAL TB PREVALENCE SURVEY OF NEPAL: WHAT DID THE SURVEY MEDICAL PANEL DO? *(3)*

The TB prevalence survey of Nepal (2018–2019) was the first-ever nationally representative TB survey conducted to estimate the prevalence of bacteriologically confirmed pulmonary TB among those aged 15 years and older in Nepal.

The central clinical (or medical) panel comprised a radiologist, a microbiologist and a TB specialist, supported by the data manager and secretary. The panel reviewed the records of participants with positive laboratory results and recommended TB treatment according to national guidelines.

Based on a list of participants' records to be reviewed by the medical panel (known as a case book), developed by the data management unit, the panel conducted weekly meetings to decide how to clinically manage these participants. First discussed were all the participants with positive laboratory results; that is, all participants with a positive Xpert MTB/RIF result, followed by those who were Xpert MTB/RIF negative but Löwenstein–Jensen (LJ) culture positive or smear positive. Second, the panel discussed those with negative laboratory results but a CXR image consistent with active TB. The panel also discussed participants requiring clinical follow-up for conditions other than TB, identified during subsequent central X-ray readings.

The case book contained participant information such as age, sex, reported symptoms and TB treatment history. Based on available laboratory results, the panel advised either re-screening, follow-up, or consultation at a health facility or a specialist. At the end of each meeting, a written list of survey participants with TB, presumptive TB or other disease(s), including CXR results, was sent to the respective health facilities with a recommendation to start treatment or other disease management. Staff of the National Tuberculosis Control Center were responsible for transferring the information to the respective TB staff in health facilities. If the participant was deemed to be in an emergency condition or rifampicin resistance was detected, an immediate phone call was made to the participant and TB focal person of the health facility.

In addition to identifying 225 participants with TB for prevalence estimation, the survey medical panel decided to refer an additional 49 participants for initiation of TB treatment based on the participants' clinical history, CXR findings, reported symptoms and all available bacteriological test results (i.e. smear, Xpert test and culture). It was verified that 248 of these participants were initiated on TB treatment as suggested by the panel; unfortunately, the remaining 26 (10%) could not be contacted.

confirmation. **Thus, some participants may start TB treatment based on laboratory results and national guidelines for TB diagnosis, but they do not necessarily meet the prevalence survey TB case definition as stated in the protocol** (see **Chapter 4**). In this scenario, they will be counted as TB cases by the national TB programme (NTP), but not necessarily by the prevalence survey team.

This chapter describes the clinical management of survey participants in need of medical care, provides examples of who should make clinical management decisions and proposes modalities for participant referral for medical care. For clinical management of newly identified HIV infection or referral to care for participants who already know their HIV status, please refer to **Chapter 10**.

9.2 Clinical management and follow-up of participants with confirmed or presumed TB

A prevalence survey will typically identify about 100–200 people with pulmonary TB disease. The management and follow-up of participants depends on the timing of positive laboratory results (according to the diagnostic algorithm used in the survey; see **Chapter 3**) and whether the participant is already enrolled on TB treatment at the time of the survey (i.e. participants with known TB).

9.2.1 Participants newly diagnosed with TB at the time of the survey

Survey participants newly diagnosed with TB (i.e. based on a positive Xpert Ultra test or culture, or both) must be **immediately referred to the NTP for registration, and possibly enrolment on TB treatment** pending review by the reviewing medical officer. Newly diagnosed participants should be referred to the NTP as soon as possible (i.e. within 24 hours) after positive laboratory tests are available, to ensure rapid enrolment on treatment and, therefore, limit the spread of the infection in the community.

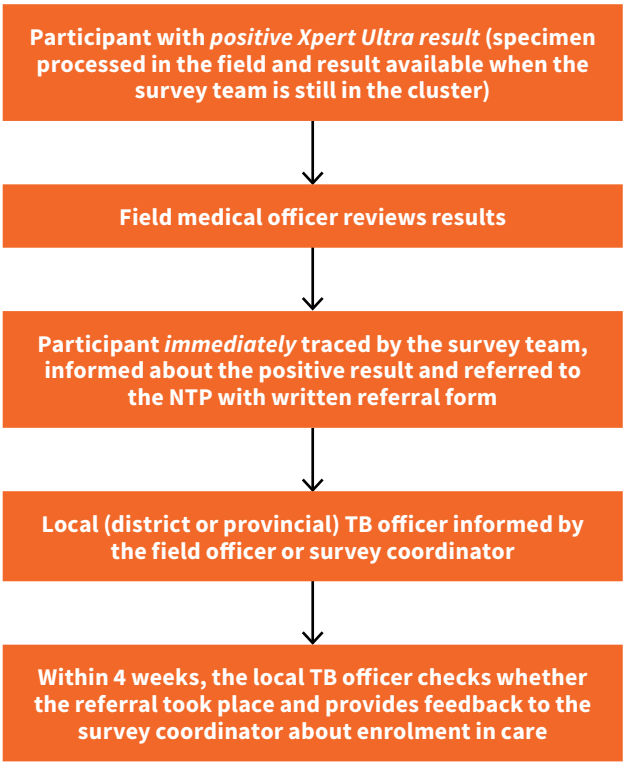
A **written referral form is recommended** to document the positive Xpert Ultra or culture results (or both) and the medical officer's or medical panel's decision; to allow appropriate transmission of feedback to the local TB coordinator; and for file archiving.

Establishing good lines of communication between the survey coordinator, the medical panel and the NTP (with direct involvement of local health officers or equivalent) is extremely important to ensure smooth linkage of participants to the health system. Facilities that participants should be referred to must be predetermined during survey preparation (e.g. during the pre-survey visit to a cluster).

Fig. 9.1a and **Fig. 9.1b** illustrate different scenarios and modalities of referral and providing feedback about positive laboratory results to participants (e.g. whether

Fig. 9.1a

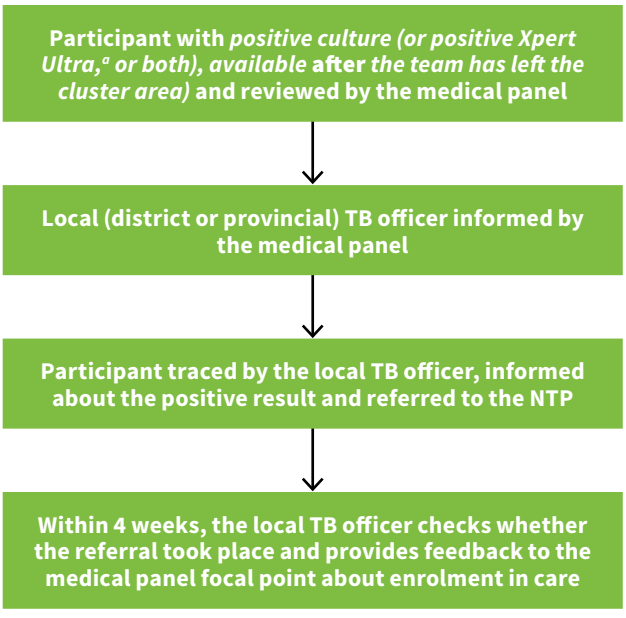
Example of informing the participant about positive laboratory results during field operations



NTP: national TB programme; TB: tuberculosis.

Fig. 9.1b

Example of informing the participant about positive laboratory results after field operations



NTP: national TB programme; TB: tuberculosis.

[a] If diagnostic algorithm Option 1 is undertaken, a participant will only have a culture result if the field Xpert test was positive. In Option 2, an Xpert Ultra test may be done in the field but only for clinical management purposes, and the Ultra test does not have to be positive for a culture to be undertaken (see **Chapter 3**).

the participant is directly informed by the field medical officer, or the local TB or health officer is informed by the medical panel).

Recommended actions

For participants with a positive Xpert Ultra result who are not on TB treatment at the time of the survey

A written referral form including the Xpert Ultra result and rifampicin resistance pattern (i.e. sensitive, resistant or indeterminate) is recommended. The referral form and decision about enrolment on TB treatment should follow national guidelines but with the following considerations:

- Is a single positive Xpert Ultra result sufficient to start TB treatment?
- Are Xpert Ultra "trace call" results considered sufficient to start TB treatment?
- Is a history of TB treatment taken into consideration before starting TB treatment, if a positive Xpert Ultra result is the only positive laboratory test available?

Therefore, the receiving clinician should make treatment decisions based on a complete clinical history, TB treatment history, physical examination and additional investigations as needed.

If rifampicin resistance is detected, a specific referral to PMDT is recommended, so that rifampicin resistance can be confirmed and second-line TB treatment drugs started.

If Xpert testing is implemented in the field and the result is available while the survey team is still at the field site, the **field team medical officer** is responsible for writing the referral form and giving it directly to the survey participant for immediate management and linkage to the health system. A copy of the referral form should also be provided to the local TB health officer, so they can verify whether the referral was successful (e.g. a referral book can be printed using carbon copy paper: one for the participant to take to the clinic, one for the local TB or health officer, and one for the survey team). The participant's referral should be registered in the survey register and database immediately.

If the Xpert result is available only after the survey team has left the cluster site, the **medical panel** is required to complete the referral form and dispatch it to the NTP through the survey coordinator or medical panel focal point. The participant's referral should be registered in the survey register and database immediately.

For participants with a positive culture for Mtb *who are not on TB treatment at the time of the survey*

A written referral form from the medical panel, including the culture result, is recommended. This step will happen after the cluster activities have been completed depending on the duration required for culture to grow (weeks). The **medical panel** therefore has the responsibility to review the culture result, review all available information, discuss how to manage the individual and complete the referral form to be sent to the local TB officer. This step should take place as soon as possible after the culture result is available.

When the survey incorporates diagnostic algorithm Option 1 (see **Chapter 3**), the participant must have had at least one Xpert Ultra-positive result during the survey. They should therefore have already received a referral form, and should already be on TB treatment when the culture result becomes available. A written **notice about the positive culture result should be dispatched to the local TB officer, paired with a request to follow up to ensure that the participant is actually enrolled on treatment**. If drug susceptibility testing (DST) results are available, they should be attached to the referral form.[1] A specific referral to PMDT for all participants with DR-TB is recommended.

If diagnostic algorithm Option 2 (see **Chapter 3**) was chosen, the initial Xpert Ultra results might be negative (or invalid or not done); in this case, the positive culture becomes the first confirmatory test for TB diagnosis and therefore the medical panel should provide a timely written referral form (that form should go to the TB officer, who should then track down the participant with a positive culture result).

All participants newly identified with TB during the survey must be immediately notified, as per national guidelines. Standard operating procedures (SOPs) should be developed and should describe in detail who is responsible for notifying a person with TB (i.e. survey coordinator, medical panel, NTP officer or other).

9.2.2 Participants already on TB treatment at the time of the survey

Survey participants who are already on TB treatment may still have positive laboratory tests during the survey (e.g. Xpert Ultra or culture, or both). These participants should still be informed about positive laboratory tests, as they provide additional confirmation that the earlier TB diagnosis was correct and add important information about the participant's response to treatment (i.e. persistence of positive culture during treatment might indicate poor response to treatment or treatment failure).

If multidrug-resistant TB (MDR-TB) and rifampicin-resistant TB (RR-TB) is identified during the survey, it is imperative to verify that the participant is receiving the correct treatment regimen (i.e. second-line treatment)

[1] DST is usually not a specific survey activity, but because positive culture tests are expected to be limited in number, countries might decide to perform DST in specific cases. Positive sputum culture in individuals already on TB treatment requires attention to make sure that ongoing treatment is correct, and DST is therefore advisable in these cases.

and, if they are not, to take corrective action. Because it is beyond the survey team's responsibility to verify the appropriateness of treatment or the participant's response to treatment, it is crucial that, once laboratory test results are available, the participant is referred to care with a clear indication of the laboratory test result(s), so that the treating clinician can take appropriate action.

Recommended actions

For participants with a positive Xpert Ultra (including trace) result who are already on TB treatment at the time of the survey

Written feedback using a standardized referral form, including the Xpert Ultra result and rifampicin resistance pattern (i.e. sensitive, resistant, indeterminate), should be provided to the participant and the local TB officer. Specific linkage to PMDT is recommended for all participants with RR-TB. A printout of the Xpert result should be attached.

If Xpert testing is implemented in the field and the result is available while the team is still at the field site, the **field team medical officer** should complete the referral form and give it directly to the survey participant. A copy of the referral form can also be provided to the local TB health officer, so they can verify whether the referral was successful. The participant's referral should be registered in the survey register and database immediately.

If the Xpert result is available only after the team has left the cluster site, the **medical panel** is required to complete the referral form and dispatch it to the local TB health officer through the survey coordinator. The local TB health officer is then required to trace the participant and provide the referral form. The participant's referral should be registered in the survey register and database immediately.

For participants with a positive culture for Mtb *who are already on TB treatment at the time of the survey*

Positive culture in participants already on TB treatment might indicate poor treatment response or treatment failure *(4)*. A referral form from the medical panel for treatment re-evaluation and treatment adherence counselling is advisable. **If DST results are available, they should be attached to the referral form. A specific referral to PMDT for all DR-TB is recommended**.

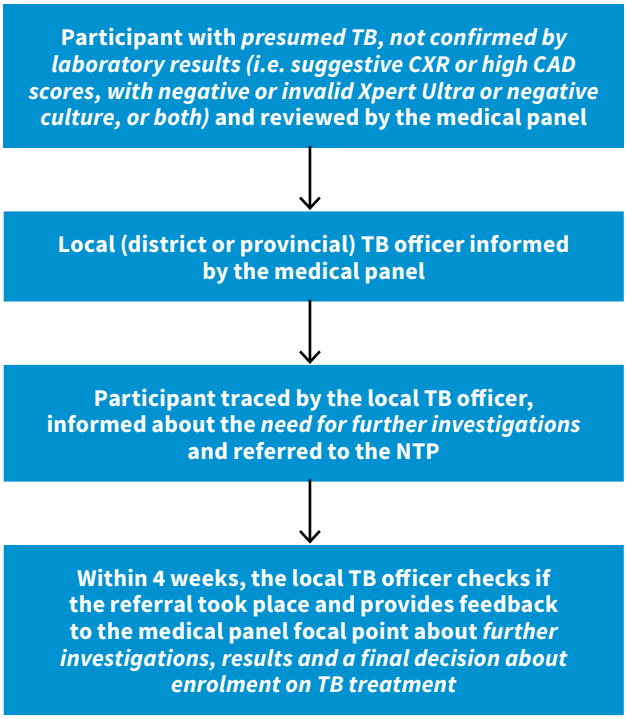
Although the written note from the medical officer or medical panel about positive laboratory tests might not be considered urgent for a participant who is already on TB treatment, **it is advisable to send it as soon as the test result is available** because it might indicate the need for treatment revision or compliance reinforcement.

9.2.3 Presumptive TB, not confirmed by laboratory tests

The medical panel should also discuss participants for whom a definitive TB diagnosis cannot be made based on laboratory results; for example, if laboratory tests were negative for TB or not done, but the participant's CXR was highly suggestive of TB (e.g. cavities, pleural effusion or a high CAD score). These participants should be referred to the NTP for further investigations, as part of national TB treatment guidelines (**Fig. 9.2**). Such individuals are known to have a higher risk of TB disease progression, thus necessitating follow-up and potentially preventive treatment *(5)*.

Fig. 9.2

Example of referring a participant with presumed TB *after* field operations



9.3 Management and follow-up of participants with other conditions

In TB prevalence surveys that follow the recommended screening strategy (see **Chapter 3**), systematic CXRs will reveal abnormalities other than TB in some participants. Such abnormalities may include the presence of a pneumothorax, a mass lesion, cancer-like lesions, cardiac insufficiency or other pathology. The types of abnormalities expected and the nature of action to be taken (e.g. immediate referral or consultation with central radiologists) should be clearly described in SOPs. Processes (and their timeliness) must be systematically evaluated during the survey to ensure that these SOPs are correctly followed.

The symptom-screening interview may identify people with respiratory symptoms, such as a severe chronic cough or difficulty breathing, or people who have other conditions such as asthma or chronic obstructive pulmonary disease. Such participants should be referred by the medical officer to health facilities for further examination as per appropriate national guidelines and survey SOPs. Immediate assessment by the medical officer from the field team and transportation of the participant to the nearest health facility may be required.

With the development of remote communication technologies, online consultation with expert physicians has become feasible. When the survey field team has difficulty judging the immediate clinical management of participants, use of a remote tool such as online video consultation could be considered.

Non-tuberculous mycobacteria

The sputum culture test might identify mycobacteria other than TB (known as NTM), which represent over 190 species and subspecies, some of which can produce disease in humans of all ages and can affect both pulmonary and extrapulmonary sites. The significance of NTM isolated from sputum samples must be carefully interpreted in the context of the number of positive cultures and the specific species isolated. NTM can be isolated from respiratory specimens owing to environmental contamination, and some individuals who have NTM isolated from their respiratory tract do not show evidence of progressive disease. Therefore, specific clinical, radiological and microbiological criteria are required to formulate a diagnosis of NTM pulmonary disease (NTM-PD) *(6)*. Clinical management of individuals with NTM-PD varies based on clinical presentation, radiology and the type of NTM isolated. Given the challenges with diagnosing true NTM disease, expert consultation is highly recommended. Survey participants diagnosed with NTM infection or NTM-PD should be referred for management according to national guidelines.

COVID-19 prevention and management in the field

During the coronavirus disease (COVID-19) pandemic, many outreach activities at the global level were interrupted or delayed. This included ongoing TB prevalence surveys (and the planning of such surveys) where public gatherings posed risks for participants and survey staff. Although it is hard to predict the magnitude and severity of future waves of COVID-19 and future pandemics, it is important during survey preparation and implementation to take action to prevent and manage the possible spread of SARS-CoV-2 (or other future respiratory viruses) during field operations and in the laboratory. Regardless, universal infection control measures are still critical for all aspects of a survey, such as crowd control, spacing of stations at the field site, hand hygiene, cough etiquette and wearing of masks, specimen collection, and handling and processing of sputum specimens.

9.4 Referral mechanism

Referring a participant to medical care can be decided by the medical officer in the field or by the medical panel at the central level. A standardized referral form can be used, and a copy provided to the local TB coordinator, or equivalent, for follow-up.

It is **important to verify the identity of the participant** before informing them of a TB (or another) diagnosis and referring them to medical care. The participant's details (e.g. first name, last name, age, sex) and unique survey ID number in the survey database (and paper forms if used) and on CXR images and laboratory test results should be verified before discussing the case in the medical panel meeting and dispatching the referral form. Therefore, the role of the data manager as part of the medical panel is critical.

The referral form itself should include all available information about the specific participant including first name, last name, age, address, phone number,[1] symptoms reported, TB treatment history, HIV status (including HIV test result if conducted), CXR result (detailed final reading), Xpert Ultra results, culture result (if available) and reason for referral. The decision about how to manage a participant's medical conditions identified during the survey must be a facility decision, in line with national TB and HIV clinical management guidelines. Clinical management is therefore usually not "prescribed" by the field medical officer or medical panel but left to the receiving clinician.

The referral letter for participants diagnosed with pulmonary TB may include a note suggesting TB-preventive therapy for family members, in accordance with national guidelines. A clear plan for case referral and management of people with RR-TB identified by Xpert Ultra, or DST for culture-confirmed cases, should be prepared in advance, in line with national guidelines.

When instructions about referral will be given later from the central level, the exact flow of information to individual participants should be clearly defined in SOPs. Particular attention should be paid to maintaining confidentiality and to reaching the participant within a precise time frame (e.g. no later than 2 weeks after the laboratory result is available).

Although participants with positive test results and those who need medical care are traced and referred to the health system, all study participants who underwent bacteriological examination should be given contact information in case they want to know their

[1] During field operations, it is important to obtain the correct address and phone number of all participants so they can be contacted if TB or other disease is suspected and diagnosed.

results. Systematically sending negative results back to participants (e.g. via text messaging) should also be considered.

Referral procedures must be part of the survey's SOPs and approved by a research ethics committee before starting the survey (see also **Chapters 2** and **11**). A follow-up mechanism to verify whether referral to care was successful is recommended after a defined period of time (e.g. 4 weeks). In Eswatini (2018–2019), for example, one survey officer was tasked with actively following up whether all referred participants reached their referral destination and were linked to appropriate care, as recorded in the survey's register (**Fig. 9.3**). Processes (and their timeliness) must be systematically evaluated during the survey to ensure that procedures are correctly followed.

For survey participants enrolled on TB treatment after referral, collection of data about treatment outcome would be useful for comprehensive assessment of the clinical management process. However, these data will only be available many months (e.g. 6–9 months) after field operations are implemented, and it might be challenging to link these data with NTP data about treatment outcomes after such a long period of time.

Fig. 9.3

Example of a register for referrals during field operations, Eswatini, 2018–2019

SURVEY ID	NAME OF PARTICIPANT	TYPE OF REFERRAL	DATE OF REFERRAL	NAME OF FACILITY REFERRED TO	NAME OF REFERRAL CONTACT	CONTACT DETAILS OF REFERRAL CONTACT	RECEIVED FEEDBACK FROM HEALTH FACILITY

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CHAPTER 10

HIV and comorbidities

The World Health Organization (WHO) has identified five comorbidities that account for a substantial proportion of new cases of tuberculosis (TB) globally: undernutrition, HIV, diabetes mellitus (DM), alcohol use disorders and tobacco use.

This chapter starts with an overview of the rationale for including data collection and testing for TB-related comorbidities in a national TB prevalence survey. Considerable attention is then given to HIV testing, which is recommended in all national TB prevalence surveys. Three strategies for HIV testing are described, and a detailed country illustration of the strategy recommended for countries with a generalized HIV epidemic is provided. The remainder of the chapter discusses diabetes mellitus; undernutrition; alcohol, smoking and other substance use disorders; and examples of other conditions for which data collection might be relevant, in some contexts.

Annex 10.1 provides a generic set of questions to be asked about HIV in the context of a national TB prevalence survey.

10.1 Overview

The incidence and prevalence of TB are affected by various health-related risk factors. These include HIV, DM, undernutrition, tobacco smoking, disorders due to the use of alcohol or drugs, and silicosis. Globally in 2023, an estimated 0.96 million incident cases of TB were attributable to undernutrition, 0.75 million to alcohol use disorders, 0.70 million to smoking, 0.61 million to HIV infection and 0.38 million to DM *(1)*. When these risk factors are concurrent in a person with TB disease, they are referred to as comorbidities. All comorbidities are associated with poorer TB treatment outcomes and adverse socioeconomic impacts. Integrated approaches for identifying and managing people with TB and these comorbidities within the health care system are important, informed by evidence about the joint burden of TB and comorbidities *(2)*.

National TB prevalence surveys provide an opportunity to collect representative data about TB-related comorbidities *(3, 4)*. At the same time, the additional costs and logistical challenges of adding additional data collection to a TB prevalence survey should not be underestimated.

Across the world, people living with HIV suffer disproportionately from TB; in some regions and countries, HIV is a key driver of the TB epidemic. National TB prevalence surveys are ideally suited for obtaining additional information about HIV status and the uptake of HIV treatment, and for providing access to HIV testing for participants.

For the other comorbidities, asking additional, standardized questions in a national TB prevalence survey could provide valuable data about their prevalence (both in the general population and among those with TB or presumptive TB). For example, standardized questions about tobacco smoking, alcohol use and DM status (diagnosed or not) could be asked. If this is done, then for the purposes of estimating prevalence in the general population, it is not necessary to ask all survey participants these questions; data would only need to be collected from a sample of survey participants. In some settings, data collection for other measures such as height and weight, and additional screening for DM, could be useful.

Decisions about data collection on comorbidities as part of a national TB prevalence survey should be taken by the survey steering committee, after careful assessment of benefits, costs, risks and whether there are alternative and better options for data collection (compared with a national TB prevalence survey). **Additional studies should only be added to a national TB prevalence survey if they will not compromise the quality of the prevalence survey itself, particularly in terms of non-participation.**

The committee should carefully assess the capacity and capability of survey staff, time constraints during field operations, the total duration of the survey operation, the implications for data management and additional costs. In all cases, the rationale for and objectives of including the condition should be clearly identified, because it will affect the survey design. **For all comorbidities, it is essential that the survey team can provide clinically relevant results to participants and facilitate referral for appropriate care or treatment.** Provision of results is much easier if rapid diagnostic screening tests are available in the field; such tests will minimize the costs and time involved in tracing individuals.

10.2 HIV

Surveillance of the prevalence of HIV among people with TB is one of the essential activities included in the WHO End TB Strategy *(5)*. WHO guidance on TB and comorbidities recommend that all countries should

BOX 10.1
STANDARDS FOR SURVEILLANCE OF HIV AMONG TB PATIENTS

The following are adapted from WHO policy on collaborative TB/HIV activities: guidelines for national programmes and other stakeholders (9):

- Surveillance of HIV should be conducted among people with TB, and surveillance of TB disease should be conducted among people living with HIV in all countries, irrespective of national adult HIV and TB prevalence rates, to inform programme planning and implementation.
- Countries with unknown HIV prevalence rates among people with TB should conduct a seroprevalence survey (either periodic or sentinel) to assess the situation.
- In countries with a generalized epidemic state,[1] HIV testing services for all people with presumed or diagnosed TB should form the basis of surveillance. Where such testing services are not yet in place, periodic surveys or sentinel surveys are suitable alternatives.
- In countries with a concentrated epidemic state,[2] where groups at high risk of HIV infection are localized in certain administrative areas, HIV services for all people with presumed or diagnosed TB in those administrative areas should form the basis of surveillance. Where such HIV services are not yet in place, periodic (special) or sentinel surveys every 2–3 years are suitable alternatives.
- In countries with a low-level epidemic state,[3] periodic (special) or sentinel surveys are recommended every 2–3 years.
- HIV testing should be an integral part of TB prevalence surveys and surveillance of anti-TB drug resistance.

[1] Generalized epidemic state: HIV prevalence is consistently >1% in pregnant women.

[2] Concentrated epidemic state: HIV prevalence is consistently >5% in at least one defined subpopulation and is <1% in pregnant women in urban areas.

[3] Low-level epidemic state: HIV prevalence has not consistently exceeded 5% in any defined subpopulation.

undertake surveillance of HIV in people with TB, and that this can be done through routine data collection or periodic surveys *(6, 7)* (see **Box 10.1**). WHO guidance distinguishes between different categories of HIV epidemic (generalized, concentrated, low level) and recommends that HIV testing should be an integral part of national TB prevalence surveys.

With further integration and collaboration between TB and HIV programmes at the national level, some prevalence surveys have started to include direct HIV testing in the field. It was initially thought that this would reduce survey participation rates, but this was not found to be the case when surveys were well coordinated. In many of the national surveys implemented in African countries, the proportion of participants who already knew their HIV status was quite high, indicating a high level of acceptance of testing in general *(8)*. However, only nine of the 17 African countries that conducted a national TB prevalence survey between 2007 and 2019 included HIV testing in the field, and none of the countries in Asia collected data about HIV.

Although offering HIV testing services to TB prevalence survey participants is especially relevant for countries with generalized HIV epidemics, it also provides much needed missing data in settings with more localized or focused HIV epidemics. Even in settings that have a high HIV prevalence and highly accessible HIV testing, a national TB prevalence survey provides an opportunity to further expand HIV testing and offer enhanced access to HIV prevention and treatment services. No country has yet reached the Joint United Nations Programme on HIV/AIDS (UNAIDS) 95:95:95 targets[1] *(9)* for all subpopulation groups; also, in many countries the groups that are not being reached with HIV testing overlap with the groups most at risk for TB (e.g. men, people who use drugs or with disorders related to alcohol use, and people living in poverty), which means that offering HIV testing services is especially important.

As discussed in **Chapters 9** and **11**, clinical data or test results gathered from participants must be fed back to them, for ethical reasons; this is particularly important for HIV testing. Surveys should follow nationally recommended guidelines related to HIV testing, in terms of whom to test, the testing strategy and the five Cs (consent, confidentiality, counselling, correct test results, and connection or linkage to prevention, care and treatment). Unlinked anonymous testing for HIV is NOT recommended (nor is it acceptable) because results cannot be traced back to individuals who need HIV care and treatment. For HIV testing to be offered,

[1] The 95:95:95 targets refer to 95% of people living with HIV knowing their HIV status, 95% of people who know that they are living with HIV being on life-saving antiretroviral therapy (ART), and 95% of people who are on treatment being virally suppressed.

HIV care and provision of antiretroviral therapy (ART) need to be in place, so that individuals newly diagnosed with HIV during the survey can immediately receive treatment and services based on national guidelines.

10.2.1 Strategies for HIV testing in the context of a national TB prevalence survey

In the context of a national TB prevalence survey, HIV testing could be offered using one of three strategies. These are described below.

Strategy 1: HIV screening and testing offered to all survey participants

In settings with a generalized HIV epidemic, it is recommended that HIV screening and testing should be offered for all participants in a national TB prevalence survey. Surveys that have done this include Lesotho, 2019 *(10)*; Mozambique, 2018–2019 *(11)*; Namibia, 2018 *(12)*; and Zambia, 2013–2014 *(13, 14)* (see **Table 10.1** for examples of countries choices of strategy and experiences).

This approach can provide a simple and streamlined activity in which all participants attend an HIV screening station where they can be asked questions about prior knowledge of HIV status; participants living with HIV can then be asked further about use of ART. Any participants who do not report being HIV-positive can be offered HIV testing using a rapid diagnostic testing algorithm, according to the country's pre-defined HIV testing policy (see **Box 10.2** for an example of questions and numbers from the TREATS [Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB] study).

The advantages of this strategy are that it provides additional information about knowledge of HIV status and access to ART in a random population sample, it permits analysis of the contribution of diagnosed and undiagnosed HIV for individuals with symptoms or chest X-ray (CXR) suggestive of TB and those with confirmed TB, and it provides a useful service to participants by providing easy access to HIV testing and referrals to care for any participant found to be HIV-positive.

The disadvantages of this strategy are that it incurs additional costs in providing rapid HIV diagnostic tests to all participants (except those reporting a positive HIV status and those declining) and the need to have trained HIV counsellors or other health staff authorized to conduct HIV testing available at the field sites. HIV rapid tests generally take up to 20 minutes for a result to be available, and this may delay progress through the prevalence survey activities. Innovation in the siting of the HIV testing station and considering whether other procedures (e.g. sputum collection) or questionnaire activities could be done while waiting can mitigate this delay (see **Box 10.2** on the TREATS experience).

Another option that has not yet been tried could be for participants to do HIV screening using oral HIV self-tests. Such tests are recommended by WHO, and a national TB prevalence survey would provide an ideal setting for their supported use, with group counselling on the correct way to use the tests, participants doing self-screening, and the completed tests being returned to survey staff for checking and further testing if indicated.

Strategy 2: HIV testing offered to all participants who screen positive based on symptoms or CXR abnormalities suggestive of TB (or both)

The minimum recommended standard is to offer HIV testing to all participants with symptoms or CXR findings suggestive of TB; such participants are asked to provide sputum samples for further evaluation for TB. This strategy aligns with the WHO recommendation for HIV testing in all individuals with presumed or diagnosed TB *(7)*. The advantage of this strategy is that the number of participants needing HIV testing is reduced (to about 15–20% of participants). This strategy may disadvantage screen-negative participants who would welcome the opportunity to be tested for HIV, although opt-in testing could be offered for all participants as an additional service.

This strategy provides no information on the prevalence of HIV and ART use in the general population, and limits analysis of the relative contribution of HIV for people with and without TB symptoms and CXR abnormalities. However, it does allow estimation of the prevalence of HIV in the equivalent of people with presumed TB and allows for estimation of the level of TB/HIV comorbidity. Several countries have adopted this model of HIV testing in surveys, including Rwanda, 2012,[1] United Republic of Tanzania, 2012, Uganda, 2013–2014 and Eswatini, 2018–2019.

This strategy is appropriate for settings with a concentrated HIV epidemic. As with Strategy 1, a series of questions about HIV testing, status and access to ART would be asked. Individuals not known to be living with HIV would be provided with a rapid diagnostic test at the field site, following the nationally recommended testing algorithm. Additional staffing needs may be the same as those for Strategy 1.

Strategy 3: HIV testing offered to all participants found to have TB

WHO policy states that all people diagnosed with TB should be offered HIV testing *(6, 7)*. If individuals are diagnosed as part of a national TB prevalence survey, it is incumbent on the survey to provide HIV testing for those participants. Any participant identified with TB must be followed up to ensure that they know their test results and can access treatment. Rapid testing for TB is part of both of the diagnostic algorithms recommended

[1] In Rwanda, offering HIV testing to all people presumed to have TB was the policy that was adopted in 2012 – the policy was innovative at that time.

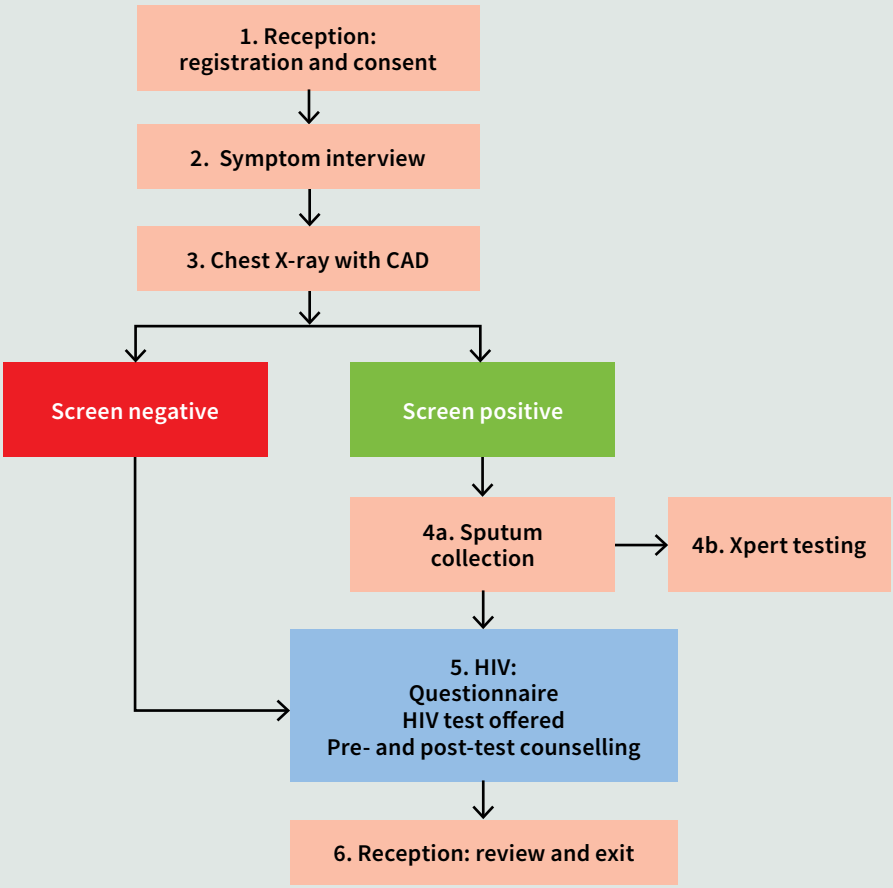
BOX 10.2
HIV TESTING IN THE TREATS TB PREVALENCE SURVEY

The TREATS study conducted a TB prevalence survey in 21 communities spread across two countries, South Africa and Zambia, in 2019–2020. The overall sample size of the prevalence survey was similar to many national surveys, recruiting almost 50 000 participants. Owing to both countries having generalized HIV epidemics, and to the special interest in HIV within the TREATS study, it was decided to offer onsite HIV testing to all survey participants as part of the TB prevalence survey.

All participants were invited to attend an HIV station and the flow of participants is shown in **Fig. B10.2.1**; a minimum set of questions asked at the HIV testing station is listed below.[1] The outcomes of the self-reported knowledge of HIV status and testing are shown in **Fig. B10.2.2**.

Fig. B10.2.1

Flow diagram of field flow including HIV testing (station 5) in the TREATS TB prevalence survey, 2019–2020



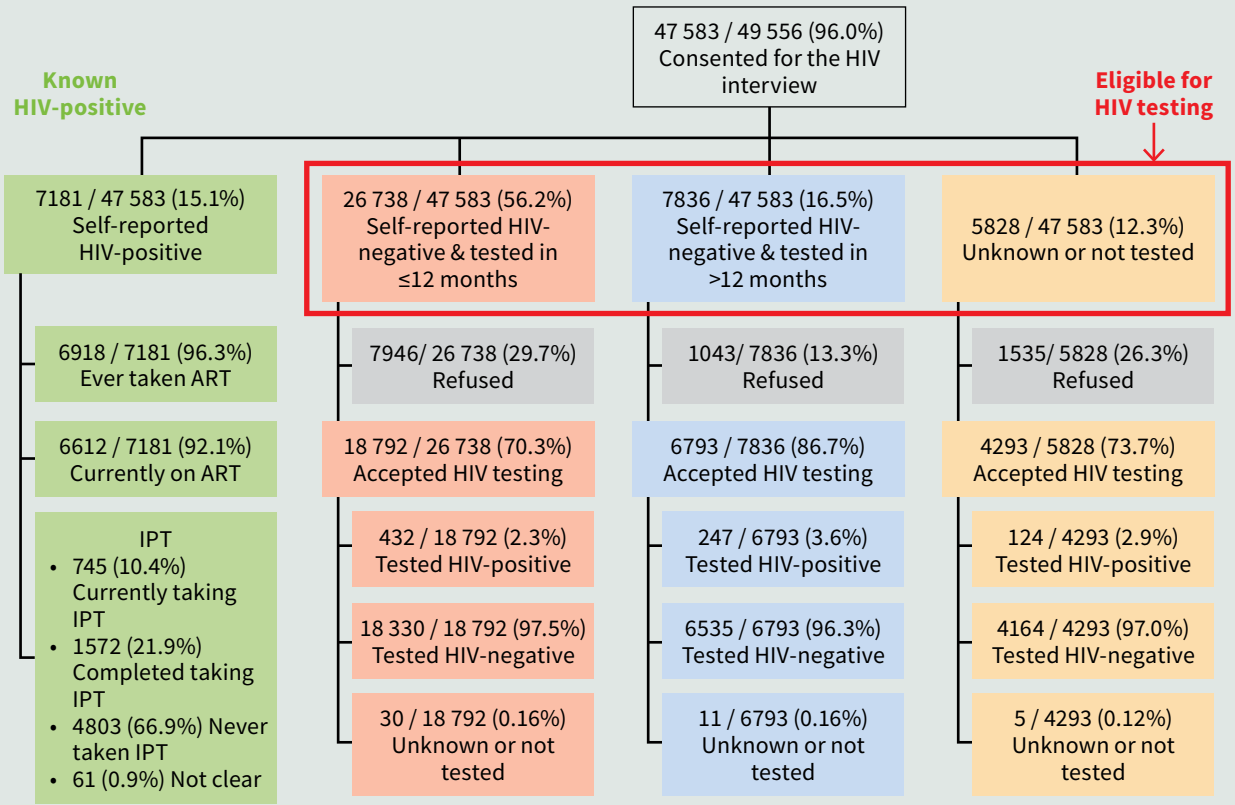
CAD, computer-aided detection; HIV: human immunodeficiency virus; TB: tuberculosis; TREATS: Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB.

[1] A full set of generic questions is shown in **Annex 10.1**.

BOX 10.2
HIV TESTING IN THE TREATS TB PREVALENCE SURVEY

Fig. B10.2.2

Outcomes of self-reported knowledge of HIV status and testing in the TREATS TB prevalence survey, 2019–2020



ART: antiretroviral therapy; HIV: human immunodeficiency virus; IPT, isoniazid preventive therapy; TB: tuberculosis; TREATS: Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB.

Minimum set of questions to be asked at HIV testing station

1. Have you ever been tested for HIV?
   - ☐ Yes = 1 (go to question 2)
   - ☐ No = 2 (end of section – check eligibility for HIV testing)
   - ☐ Don't know = 3 (end of section – check eligibility for HIV testing)
   - ☐ No answer = 99 (end of section – check eligibility for HIV testing)
2. Have you been tested for HIV in the past 12 months?
   - ☐ Yes = 1
   - ☐ No = 2
   - ☐ Don't know = 98
   - ☐ No answer = 99
3. If you feel comfortable, would you mind telling me what the result of your last HIV test was?
   - ☐ HIV-negative = 1
   - ☐ HIV-positive = 2
   - ☐ HIV-indeterminate = 3
   - ☐ Not comfortable or don't know = 98
   - ☐ No answer = 99

Note the following questions are to be asked to all those who report being HIV-positive.

4. Have you ever taken antiretroviral therapy (ART)?
   - ☐ Yes = 1
   - ☐ No = 2
   - ☐ No answer = 99

BOX 10.2
HIV TESTING IN THE TREATS TB PREVALENCE SURVEY

5. Are you currently taking ART (or have you taken ART in the past 1 month)?
   - ☐ Yes = 1
   - ☐ No = 2
   - ☐ No answer = 99
6. In the past 12 months, have you ever stopped taking your ART?
   - ☐ Yes = 1 (specify the duration of treatment interruption – in weeks or months)
   - ☐ No = 2
   - ☐ No answer = 99
7. Have you ever taken or are you currently taking isoniazid preventive treatment to prevent TB?
   - ☐ Yes, current = 1
   - ☐ Yes, completed = 2 (specify the duration in months)
   - ☐ No = 3
   - ☐ Don't know = 98
   - ☐ No answer = 99

If the person has an unknown or negative HIV status the person is eligible for HIV testing, and testing should be offered. If eligible, offer the test. If not eligible, the test is not offered, and the participant moves to the next station.

8. Test offered?
   - ☐ Yes = 1
   - ☐ No = 2
9. If offered, test accepted?
   - ☐ Yes = 1
   - ☐ No = 2
10. If test not offered, why not?
    - ☐ a. No test kits available
    - ☐ b. Other reason, specify

What were the results of the HIV testing?

11. Result test assay 1
    - ☐ Reactive = 1
    - ☐ Non-reactive = 2
    - ☐ Invalid = 3
12. Result test assay 2
    - ☐ Reactive = 1
    - ☐ Non-reactive = 2
    - ☐ Invalid = 3
13. Result test assay 3
    - ☐ Reactive = 1
    - ☐ Non-reactive = 2
    - ☐ Invalid = 3
14. Final HIV test result
    - ☐ Positive = 1
    - ☐ Negative = 2
    - ☐ Inconclusive or unknown = 3

What challenges were encountered in the TREATS prevalence survey?

Challenge: Biggest bottleneck onsite was the HIV counselling and testing (HCT) station, owing to the time taken to do HIV counselling and testing.

Lesson: The sites in South Africa started with two HCT stations but were increased to three or four HCT stations, depending on the community.

Do differently: Start with four HCT stations but hire additional lay counsellors who can work at other stations in the survey (e.g. reception or sputum collection) so that during peak times they can assist with HCT.

BOX 10.2
HIV TESTING IN THE TREATS TB PREVALENCE SURVEY

How did the HIV testing affect the overall results?

In the TREATS TB prevalence survey, the prevalence of TB in people living with HIV was higher than in HIV-negative individuals, with an adjusted odds ratio of 2.29 (95% confidence interval [CI]: 1.54–3.41) in sites in Zambia and 1.61 (95% CI: 1.13–2.30) in sites in South Africa *(29)*. This is despite the survey taking place in communities with good access to HIV testing and ART, and with a high reported uptake of ART among participants who knew their HIV-positive status. The absolute prevalence of TB in people living with HIV was 104 per 100 000 population in sites in Zambia and 194 per 100 000 population in sites in South Africa.

Despite reported increases in the uptake of TB preventive treatment (TPT) among people living with HIV, this survey found that most participants who reported being HIV-positive had not received TPT. Thus, the survey provided an additional opportunity to prevent TB in these communities.

These findings show the need to increase efforts to identify TB in people living with HIV. The TREATS study measured the impact on TB of the PopART universal test and treat intervention for HIV. This intervention included active door-to-door screening for TB and HIV for the entire community every year for 4 years. The screening was done using a symptom screen followed by Xpert® testing for people living with HIV. The study concluded that this level of screening is not sufficient to reduce the risk of TB, especially in people living with HIV, and that additional screening using CXR or WHO-recommended molecular testing for TB will be required for the burden of TB to be reduced at community level *(29)*.

in this guidance (**Chapter 3**); thus, it should be possible for this follow-up to occur on the same or the following day, facilitating rapid identification and referral. In this situation, HIV testing should be conducted as part of the same process.

In the past, countries have relied on participants with confirmed TB being referred to routine services and have assumed that HIV testing will be offered there. **However, in most of these surveys, information on the HIV status of these participants was not available to the survey team and therefore it could not be assured that the testing was done, and the dual burden of TB and HIV could not be assessed.**

10.2.2 Important factors for any HIV testing strategy

The following points should be considered when deciding how to offer HIV testing in the context of a national TB prevalence survey:

- Offering **HIV testing during field operations has not been shown to compromise the primary survey objectives** by lowering the survey participation rate owing to stigma or other barriers. HIV testing should be clearly explained to participants as part of sensitization information, along with the rationale and benefits. Engagement with the community and careful planning of appropriate language and communication strategies can help with this process.
- HIV testing should be offered as **opt-out testing** (i.e. it is offered to all eligible survey participants, but they can opt-out of testing); however, a strategy of opt-in testing could be considered to expand testing reach.
- The additional time required for HIV testing and follow-up should be considered, and adequately trained staff should be deployed to prevent long waiting times.
- Confidentiality and privacy need to be considered when offering HIV testing during survey operations, and appropriate space should be organized for this (see the "5 Cs" in **Box 10.3**).
- Care must be taken not to inadvertently disclose an individual's status; for example, by a person's rapid progress through the HIV testing area (possibly indicating known HIV-positive status) or by having a person who may have received unexpected news of a positive HIV test having to pass other waiting participants. Arranging the HIV testing stations so that the exit is separate from the waiting area can overcome these challenges.

In earlier guidance *(30)*, reference was made to the option of performing unlinked anonymous HIV testing. **This is no longer acceptable because results cannot be traced back to individuals in need of HIV care.** It is also **not acceptable** to place an additional burden on participants to access their test results, such as participants needing to travel to the health facility to receive results, which is likely to result in many participants not accessing their results and thus lead to some individuals who need HIV care not accessing it. If possible, rapid

Table 10.1

HIV testing strategies used in national TB prevalence surveys in African countries, 2012–2019

COUNTRY	EXPERIENCE
Strategy 1: HIV screening and testing offered to all survey participants	
Zambia, 2013–2014 *(13–15)*	Zambia provided onsite HTS to all participants using an opt-out model. Separate consent was obtained, and testing was done by nurses. Of 46 099 participants, 44 761 (97.1%) underwent counselling and 30 604 (68.4%) consented to be tested. Participants could be tested and not get their results; however, 99.1% of those tested wanted to receive their results, which were provided following testing. A total of 2068 (6.8%) individuals tested HIV-positive.
Namibia, 2018 *(12)*	Namibia provided onsite HTS for all participants. The initial plan was to use an opt-out model, but concern was raised that this might be affecting the overall participation rate, so some clusters moved to an opt-in model. Of 29 495 participants, 21 795 (73.9%) stated that they had previously tested for HIV with 3132 disclosing that they were HIV-positive. A total of 11 256 (38.2%) people were tested onsite as part of the survey, with 259 new HIV-positive participants identified.
Mozambique, 2018–2019 *(11)*	Mozambique provided HTS to all participants. Over 99% of participants presented to the HIV testing station. A total of 2162 people were known to be HIV-positive; of the 30 043 offered testing, 16 869 (56%) accepted. An additional 804 people were identified as HIV-positive. The uptake of HIV testing varied substantially among regions and between urban and rural areas.
Lesotho, 2019 *(10)*	Lesotho provided onsite HTS for all participants following the Ministry of Health's HIV testing algorithm. An NGO provided testing in the first 10 clusters, but data collection fell short of survey requirements, so these data were not reported. HIV testing resumed directly under the auspices of the survey team and were reported. Of the 21 719 survey participants, HTS was offered to 17 048, and 3915 (23%) tested HIV-positive.
Strategy 2: HIV testing offered to all participants with screening symptoms or CXR abnormalities suggestive of TB (or both)	
Rwanda, 2012 *(16, 17)*	Rwanda offered onsite HTS for participants who screened positive on either symptoms or CXR. Among 4747 eligible participants, 4445 (94%) were tested and 218 tested HIV-positive, of whom 181 already knew their status. Therefore, an additional 37 participants with HIV were newly identified.
United Republic of Tanzania, 2012 *(18, 19)*	The United Republic of Tanzania offered onsite HTS for participants who screened positive on either symptoms or CXR. Of 6271 eligible participants, 4405 (70.2%) had a final HIV status whereas 1866 (29.8%) did not test.
Uganda, 2014–2015 *(20)*	Uganda offered onsite HTS for participants who screened positive for symptoms or CXR. Among 5142 eligible participants, 4386 (85.3%) were tested and 9.6% tested HIV-positive. In those individuals who were found to have TB, 26.9% were HIV-positive.
Eswatini, 2019	Eswatini offered onsite HTS to those participants who were eligible to provide a sputum sample. Of the 6542 people who were eligible, 5576 (85%) completed the HIV interview. A total of 1579 people reported being HIV-positive and HIV testing was offered to 3997 participants, of whom 2528 (63%) accepted. An additional 73 participants were found to be HIV-positive. Overall, among the sputum eligible participants, 63% had a known HIV status at the end of the survey.
Strategy 3: HIV testing offered to all participants found to have TB	
Zimbabwe, 2012 *(21, 22)*	In Zimbabwe, participants diagnosed with TB in the survey were referred to the health facility for PITC and it was requested that results be linked to prevalence data. Only 66.4% of results were available. The team reported the lack of HIV testing as a major limitation of the survey.
Kenya, 2015–2016 *(23, 24)*	In Kenya, participants diagnosed with TB were referred for PITC at the health facility. Of 305 participants, results were available for 245 (80.3%), of whom 41 (16.7%) were found to be HIV-positive.
Other	
Malawi, 2013–2014 *(25)*	Malawi opted to ask participants about their HIV testing history and knowledge of HIV status only. A total of 62.7% of participants reported ever having tested for HIV and 9.3% reported being HIV-positive. Testing was higher in women than in men (70.1% vs 52.4%) and was also higher in urban areas than in rural areas.
South Africa, 2018–2019 *(26, 27)*	In South Africa, all participants were asked to provide a dried blood spot for HIV testing and were provided with a barcoded form to take to a local HIV testing site to access testing. No results were provided to participants, and it was not possible to know how many participants accessed HTS or their results. The ethics of this approach have been questioned *(28)*.

CXR: chest X-ray; HIV: human immunodeficiency virus; HTS: HIV testing services; NGO: nongovernmental organization; PITC: provider-initiated testing and counselling; TB: tuberculosis.

BOX 10.3
WHO'S "5 CS" FOR HIV TESTING SERVICES *(34)*

- **Consent.** People receiving HTS must give informed consent to be tested and counselled (verbal consent is sufficient; written consent is not required). They should be informed of the process for HIV testing and counselling, and of their right to decline testing. It should not be assumed that people who request or report self-testing for HIV are providing or have implicitly provided consent. It is important that all people who self-test are informed that mandatory or coercive testing is never warranted. Provider-assisted referral and social network-based approaches – which offer HTS to their clients' sexual partners, drug injecting partners and social contacts – are voluntary and implemented only with the consent of clients and contacts.
- **Confidentiality.** HTS must be confidential, meaning that what the HTS provider and the client discuss will not be disclosed to anyone else without the expressed consent of the person being tested. Although confidentiality should be respected, it should not be allowed to reinforce secrecy, stigma or shame. Counsellors should discuss, among other issues, whom the person may wish to inform and how they would like this to be done. Shared confidentiality with a partner or family members (i.e. trusted others) and health care providers is often highly beneficial.
- **Counselling.** Concise information before the test and counselling after the test can be provided in a group setting if appropriate, but all individuals should have the opportunity to ask questions in a private setting if they request it. All HTS must be accompanied by appropriate counselling after the test, based on the HIV test result. Quality assurance (QA) mechanisms and supportive supervision and mentoring systems should be in place to ensure the provision of high-quality counselling. Various channels and tools can be used to deliver messages, information and counselling, including peer providers and innovative digital approaches such as videos, social media and other mobile phone applications or services.
- **Correct.** Providers of HTS should strive to provide high-quality testing services, and QA mechanisms should ensure that people receive a correct diagnosis. QA may include both internal and external measures, and should include support from the national reference laboratory. All individuals who receive a positive HIV diagnosis should be retested to verify their diagnosis before initiation of ART or engagement in HIV care.
- **Connection.** Linkage to prevention, care and treatment services should include the provision of effective and appropriate follow-up as indicated, including long-term prevention and treatment support. Providing HTS where there is no access or poor linkage to care, including ART, has limited benefit for PLHIV. Linkage is the responsibility of providers and testers delivering HTS.

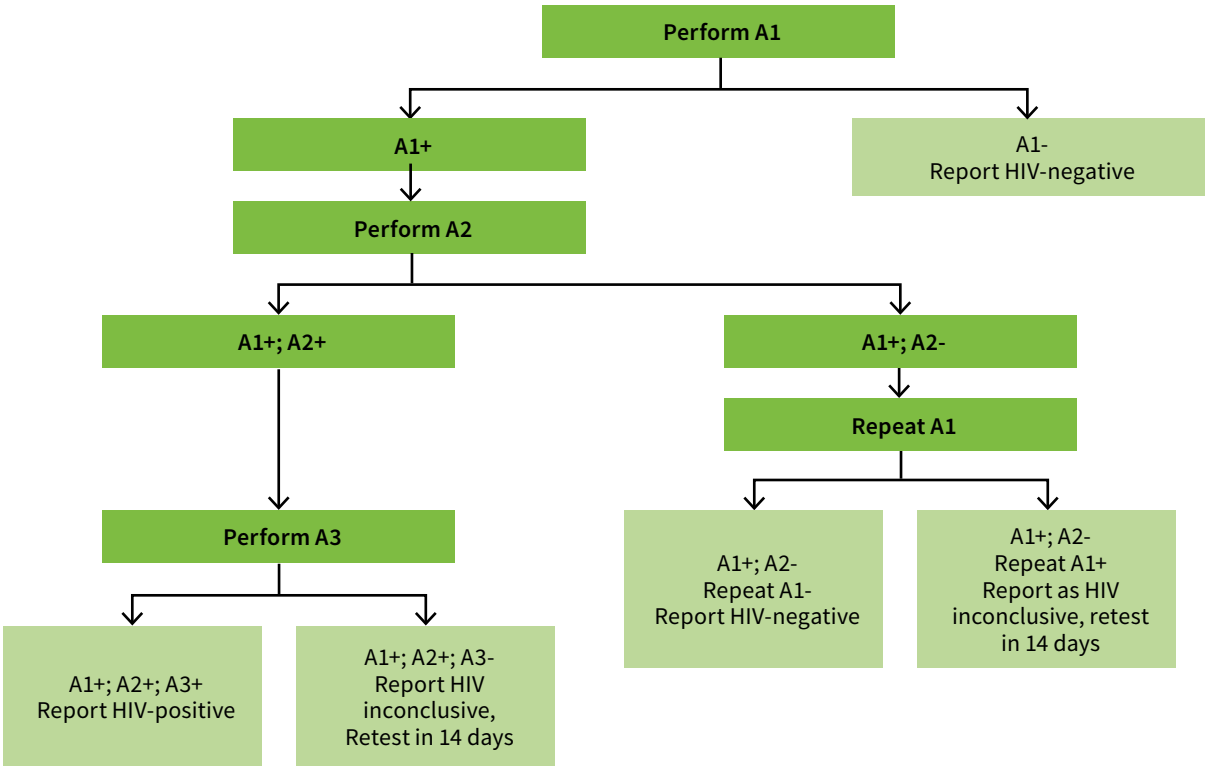
diagnostic HIV tests should be used to provide real-time results. If this is impossible and laboratory testing is needed, then it is the responsibility of the survey team to deliver the results to participants. Whatever the final strategy for HIV testing, all procedures must be part of the survey's standard operating procedures. The strategy should be clearly described and justified in the survey protocol and approved by the national research ethics committee (see also **Chapters 2** and **11**) before starting the survey.

Most people testing for HIV will be negative and will therefore require only one test. However, no single test can be used to provide a definitive positive HIV diagnosis. Therefore, WHO recommends all countries to use three consecutive reactive tests to provide an HIV-positive diagnosis *(31)*.

Fig. 10.1 summarizes the WHO standard testing strategy for HIV-1 diagnosis among people aged 18 months and older. This testing strategy refers to three assays – Assay 1 (A1), Assay 2 (A2) and Assay 3 (A3) – which should be three different HIV assays that share minimal common false reactivity, and each of which may be a rapid diagnostic test or an enzyme immunoassay. The testing strategy does not stipulate the specific products to be used in each step; rather, it provides guidance on the characteristics of the test used at each step. Countries should populate the testing strategy with different products for each step, using products that are WHO prequalified *(32)*. WHO's HIV testing algorithm tool kit also provides guidance to help countries optimize product selection and ensure that the products selected work well together *(33)*. This process should already have been established by the HIV programme in-country; therefore, close engagement with the national HIV

Fig. 10.1

WHO-recommended HIV testing algorithm among people aged 18 months and older *(31)*



+, positive; -, negative.

A1: Assay 1 (first test); A2: Assay 2 (second test); A3: Assay 3 (third test); HIV: human immunodeficiency virus; WHO: World Health Organization. Assay (test) are HIV rapid diagnostic tests (RDTs) or enzyme immunoassays (EIAs).

programme or equivalent will be essential to ensure alignment with national HIV testing policy and algorithms.

In all circumstances, HIV testing services (HTS) should be provided in accordance with WHO's essential five Cs: **consent**, **confidentiality**, **counselling**, **correct** test results and **connection** or linkage to prevention, care and treatment, as defined and explained in **Box 10.3**.

As for any result identified as part of a survey or research study, it is important to provide the participant with both the result and access to treatment. HIV testing within a national TB prevalence survey should be planned in conjunction with the national HIV programme or team, with agreement reached about the testing and about appropriate referrals and follow-up.

Any self-reporting HIV-positive individuals should be asked about current use of ART. Any participants who report not accessing ART or having stopped taking ART should be encouraged to re-engage in care; such participants need careful referral back into the programme to recommence ART. Any participant newly diagnosed with HIV needs post-test counselling, which should include the value of ART for their own health, and the ability of ART to prevent transmission to their partners. Rapid referral to access ART is important so that further counselling and baseline HIV investigations can be done and ART can be rapidly initiated. Close coordination with HIV colleagues should ensure that this is a streamlined service. In rural areas or where ART services are far from the site of the TB prevalence survey, it may be necessary to transport individuals to the closest ART services to facilitate this process.

10.3 Diabetes mellitus

The prevalence of DM is increasing globally, especially in countries that are transitioning from being low income to middle or high income. People with DM have an increased risk of developing TB disease; they also have poorer TB outcomes *(35, 36)*. Screening for TB in those with DM, and vice versa, has been recommended since 2011 *(37)*.[1] Understanding the joint burden of TB and DM will be important in many countries, to facilitate planning of integrated services. For this reason, some countries may choose to broaden the scope of a national TB prevalence survey to include a secondary objective to measure the comorbidity of DM and TB. As

[1] An updated version of the WHO operational handbook on tuberculosis. Module 6: tuberculosis and comorbidities *(7)* will be published in 2024 which will include guidance and recommendations to address TB and diabetes.

with all additions to a national TB prevalence survey, the objective of additional questions or testing should be carefully considered and documented. This will make it easier to decide which participants should be screened and how.

At a minimum, countries could consider asking a question about known diagnosis of DM and access to treatment. This would provide useful data about the prevalence of diagnosed DM and how this compares with the prevalence of DM in people diagnosed with TB. Additional questions or testing could be considered in individuals with symptoms or CXR findings suggestive of TB. To date, nine countries have included questions on self-reported DM in a national TB prevalence survey: Eswatini, 2018–2019; Ghana, 2013–2014; Indonesia, 2013–2014; Mongolia, 2014–2015; Namibia, 2018; the Philippines, 2016; South Africa, 2018–2019; the United Republic of Tanzania, 2012 and Viet Nam, 2017–2018 *(38)*. Among these countries, 2.8% of those without TB had self-reported DM, whereas this increased to 6.4% among those with symptomatic TB.

A subnational TB prevalence survey undertaken as part of a research study (ZAMSTAR) in a population of about 64 000 survey participants used fingerprick random blood glucose measurements *(39)*. This study found that 1.5% of participants in Zambia and 2.8% of participants in South Africa had a random blood sugar (RBS) greater than or equal to 11 mmol/L. There was an increased chance of having prevalent TB in individuals with raised RBS, with an adjusted odds ratio of 2.49 (95% CI: 1.29–4.79) for those with an RBS of more than 11 mmol/L in South Africa and of 4.31 (95% CI: 2.07–8.97) in those with an RBS of 9–11 mmol/L in Zambia (there were few participants with TB and an RBS >11 mmol/L in Zambia) *(40)*. The addition of this test was popular among participants and was felt to increase uptake of the survey because individuals were keen to know whether they had DM. Where fingerprick sampling is being included for HIV, this is a relatively small addition and can be done in the field site, with immediate results provided to the participant. However, this test does not diagnose DM; hence, individuals with raised RBS need to be referred for additional testing and management. Also, people with active TB, especially in association with HIV, may have "reactive hyperglycaemia" owing to their disease and this may affect TB and HIV treatment. Thus, it is important for any survey considering inclusion of DM to collaborate with departments at the ministry of health responsible for DM, as well as any relevant patient and clinician groups in the country, to ensure that messaging and testing follow national guidance.

10.4 Undernutrition

An estimated 0.96 million new episodes of TB were attributable to undernutrition in 2023 *(1)*. Thus, it is vital to recognize the importance of undernutrition and enable MoHs to advocate for increased attention to nutrition and nutritional support interventions.

Nutritional status may be assessed by simple anthropometric measurements. The most commonly used measure is the height and weight of participants, which can be used to calculate a body mass index (BMI). This can be supplemented by measurements of body circumference (e.g. arm, waist and calf) or skinfold thickness. Such measurements have been part of demographic and health surveys (DHS) in children for many years; thus, strategies have been developed for their use in large-scale surveys. A manual on best practices for children, which could be adapted for adults, has been developed for DHS, which may be of value in planning any inclusion of such measurements in TB prevalence surveys *(41)*. A manual on specific measurements for adults is available from the Food and Nutrition Technical Assistance (FANTA) project *(42)*; the manual provides information on the equipment and processes involved in the measurement and also interpretation of the result.

At a minimum, surveys should consider anthropometry for participants found to have TB and could consider it for those with symptoms or CXR suggestive of TB, or for all participants. Surveys that have included anthropometric measurements have chosen to use BMI and abdominal circumference (ZAMSTAR); height and weight (Cambodia [2023–2024], Mongolia [2014–2015] *(43)*, Myanmar [2017–2018] *(44)* [see **Box 10.4**], Namibia [2018] *(12)*, Nigeria [2012] *(45)* and the United Republic of Tanzania [2012] *(18, 19)*); and mid-upper arm circumference (MUAC) (Mozambique [2018–2019] *(11)*).

BOX 10.4
DATA ON COMORBIDITIES COLLECTED AS PART OF THE NATIONAL TB PREVALENCE SURVEY OF MYANMAR, 2017–2018 *(44)*

Blood pressure, height and weight were measured among all survey participants; in addition, an interview was undertaken that included questions about self-reported diabetes, smoking, alcohol use and other risk factors. Among participants, 42% of men and 6% of women were current smokers, 39% of men and 0.5% of women reported current alcohol consumption, and the median BMI was 21.9, with an interquartile range of 19.1–23.8. A total of 2.8% of participants reported having diabetes; this was higher in the capital city of Yangon (4.9%) than in rural areas (2.0%). Hypertension was measured in 16% of participants. The data suggested that smoking and lower BMI were associated with a higher risk of TB disease.

10.5 Alcohol, smoking and other substance use disorders

TB is associated with drug, alcohol and tobacco use; hence, it is important to understand the patterns of use of these substances and their associations with TB, which can be obtained in a systematic way in a national TB prevalence survey.

A recent meta-analysis of national TB prevalence surveys identified people with self-reported diabetes (from 9 surveys) and current smoking (from 16 surveys) as being more likely to have prevalent TB, independent of age and gender *(38)*. The magnitude of the risk was about 1.5-fold higher for both current smoking and self-reported diabetes (for symptomatic TB); estimates for alcohol use (from 8 surveys) were less precise. This type of information can be used to assist with planning, especially for services to provide care and cessation advice for people suffering from these disorders; such services are underdeveloped in many countries. WHO has developed a tool kit called ASSIST (Alcohol, Smoking and Substance Involvement Screening Test), which contains a manual for screening, a manual for primary care and a self-help tool kit *(46)*. ASSIST is an eight-item screening questionnaire, and there are detailed instructions for how it should be administered, scored and used to assign risk levels.

As with other clinically important information, it is vital to be able to provide participants with their scores, and with recommendations for how and where they can receive help and counselling, and engage with substance cessation programmes. Such activities should involve engagement of departments in the ministry of health responsible for such programmes or with nongovernmental organizations (NGOs) and other stakeholders. In some countries, certain substance use is illegal; the survey team will need to consider carefully how to manage these sensitive data and how to reassure participants that the answers to these questions will not be linked to them individually and not be used in a way that would endanger them. Ethics guidance may be required.

10.6 Other conditions

Some countries may wish to include measurement of other conditions within a national TB prevalence survey. This may include other infectious diseases such as coronavirus disease (COVID-19), viral hepatitis or any other pathogen. It may also include other NCDs (e.g. screening for hypertension).

Country teams will need to clearly articulate the objectives and rationale for inclusion of data collection and testing for these additional conditions as part of a national TB prevalence survey, and to decide on the relative merits of testing all participants or a subset (e.g. a randomly sampled group, those with symptoms or CXR changes suggestive of TB, or those identified as having TB disease). The rationale, advantages and disadvantages of including other conditions are similar to those laid out for the comorbidities above, and will depend on the secondary objectives of the survey. For many conditions, the sample size needed to provide a population estimate of the prevalence of the condition will be much smaller than that required for TB; hence, it may be more efficient to consider subgroup screening.

As with the inclusion of comorbidity screening described above, collaborative planning with the relevant department at the ministry of health will be necessary to ensure that plans are aligned to national policies, and that follow-up for further testing or management can be assured. With all additional procedures, it is important to consider the impact of the procedure on the integrity of the survey (by reducing the acceptability for participants), the additional costs and added complexity in terms of logistics. On the plus side, well-planned surveys that offer screening for other conditions may actually be more appealing to the population, as long as the messaging is conducted correctly.

Combined surveys may also be more cost-effective because the infrastructure needed for a national TB prevalence survey can be used to provide other important information. Consideration of including data collection related to TB in other large national surveys could be considered, especially now that CXR units are smaller and more portable, and sputum testing can be conducted in field settings.

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Annex 10.1 **Generic set of questions to be asked at the HIV testing station**

1. Have you ever been tested for HIV?
   - ☐ Yes = 1 (go to question 2)
   - ☐ No = 2 (end of section – check eligibility for HIV testing)
   - ☐ Don't know = 3 (end of section – check eligibility for HIV testing)
   - ☐ No answer = 99 (end of section – check eligibility for HIV testing)
2. Have you been tested for HIV in the past 12 months?
   - ☐ Yes = 1
   - ☐ No = 2
   - ☐ Don't know = 98
   - ☐ No answer = 99
3. When was the last time you were tested for HIV? If you don't know the exact date, give a best guess. Please give the month and year.

   ☐☐ MM ☐☐☐☐ YYYY

   - ☐ No answer = 99
4. The last time you were tested for HIV, where were you tested?

   ☐ Government hospital or clinic (includes antenatal clinic, TB clinic) = 1
   - ☐ Private/church/mission hospital or clinic = 2
   - ☐ Stand-alone HIV testing centre = 3
   - ☐ Mobile testing site (e.g. caravan, tent) = 4
   - ☐ Workplace = 5
   - ☐ Home = 6
   - ☐ Other = 7, specify
   - ☐ Don't know = 98
   - ☐ No answer = 99
5. The last time you were tested for HIV, do you know what type of test was used?
   - ☐ Fingerprick blood sample
   - ☐ Oral self-test
   - ☐ Oral self-test followed by fingerprick test
   - ☐ Other, specify
   - ☐ Don't know = 98
   - ☐ No answer = 99
6. If you feel comfortable, would you mind telling me what the result of your last HIV test was?
   - ☐ HIV-negative = 1
   - ☐ HIV-positive = 2
   - ☐ HIV-indeterminate = 3
   - ☐ Not comfortable/Don't know = 98
   - ☐ No answer = 99
7. Have you disclosed your HIV status to anyone, except to me for the purpose of this study?
   - ☐ Yes = 1 (go to question 8 – to whom disclosed)
   - ☐ No = 2 (end of section – check eligibility for testing)
   - ☐ No answer = 99 (end of section – check eligibility for testing)
8. To whom did you disclose your HIV status? (check all that apply)
   - ☐ Husband/wife
   - ☐ Sexual partner other than married partner
   - ☐ Family member
   - ☐ Friend/neighbour/colleague
   - ☐ Religious leader/someone from church/mosque
   - ☐ Health care worker
   - ☐ Community HIV care providers (CHiPs)
   - ☐ Other
   - ☐ No answer

The following questions are to be asked to all those who report being HIV-positive.

9. When was your first positive HIV test result?

   ☐☐ MM ☐☐☐☐ YYYY
10. Have you ever registered for any HIV-related medical care?
    - ☐ Yes = 1 (go to question 11)
    - ☐ No = 2 (go to question 12)
    - ☐ No answer = 99
11. If yes, when did you last attend the clinic for HIV care?

    ☐☐ MM ☐☐☐☐ YYYY

12. Which clinic did you attend?

.....

13. Have you ever taken antiretroviral therapy (ART)?

- ☐ Yes = 1 (go to question 14)
- ☐ No = 2
- ☐ No answer = 99

14. When did you first start taking ART?

MM YYYY

15. Are you currently taking ART (or have you taken ART in the past 1 month)?

- ☐ Yes = 1
- ☐ No = 2
- ☐ No answer = 99

16. In the past 7 days, did you miss taking any of your ART pills?

- ☐ Yes = 1
- ☐ No = 2
- ☐ No answer = 99

17. In the past 12 months, have you ever stopped taking your ART?

- ☐ Yes = 1 (specify the duration of treatment interruption – in weeks or months)
- ☐ No = 2
- ☐ No answer = 99

18. Have you ever taken or are you currently taking isoniazid preventive treatment to prevent TB?

- ☐ Yes, current = 1
- ☐ Yes, completed = 2 (specify the duration in months)
- ☐ No = 3
- ☐ Don't know = 98
- ☐ No answer = 99

If the person has an unknown or negative HIV status the person is eligible for HIV testing, and testing should be offered. If eligible, offer the test. If not eligible, the test is not offered, and the participant moves to the next station.

19. Test offered?

- ☐ Yes = 1
- ☐ No = 2

20. If offered, test accepted?

- ☐ Yes = 1
- ☐ No = 2

21. If test not offered, why not?

- ☐ No test kits available
- ☐ Other reason, specify
- ☐ What were the results of the HIV testing?

22. Result test assay 1

- ☐ Reactive = 1
- ☐ Non-reactive = 2
- ☐ Invalid = 3

23. Result test assay 2

- ☐ Reactive = 1
- ☐ Non-reactive = 2
- ☐ Invalid = 3

24. Result test assay 3

- ☐ Reactive = 1
- ☐ Non-reactive = 2
- ☐ Invalid = 3

25. Final HIV test result

- ☐ Positive = 1
- ☐ Negative = 2
- ☐ Inconclusive or unknown = 3

CHAPTER 11

Ethical considerations

National tuberculosis (TB) prevalence surveys should be conducted ethically and with a patient-centered approach. That is, even though a survey is primarily focused on estimating the burden of bacteriologically confirmed pulmonary TB at a national level, surveys should be ethically designed and conducted with an individual's rights and welfare in mind.

This chapter briefly describes the ethical values that govern public health, research and surveillance. It also provides an overview of the purpose and functioning of research ethics committees (REC), the principles of good clinical practice (GCP) and good data management practice (GDMP), and errors. Finally, this chapter describes ethical issues pertinent to national TB prevalence surveys, including the use of artificial intelligence.

11.1 Ethical values

The general conduct of research involving human subjects is guided by internationally recognized principles of bioethics, including the Nuremberg Code, 1949 *(1)* and the World Medical Association's Declaration of Helsinki, 1964 *(2)*. The first principle of the Nuremberg Code was the centrality of the voluntary participation of subjects with their informed consent. The Declaration of Helsinki built on the Nuremberg Code, adding a distinction between therapeutic and nontherapeutic research, a call for institutional review mechanisms, and a provision for family members to provide permission for participation if the subject could not give consent. The Declaration of Helsinki, revised in 2013, reflects the deepening appreciation of the many elements included in fully informed consent. It emphasizes the critical importance of ethical review by a committee that is independent of the researcher.

The Council for International Organizations of Medical Sciences (CIOMS) has produced publications on the ethical guidance for biomedical research involving human subjects and clinical research in resource-limited settings *(3, 4)*. The CIOMS guidelines outline the importance of scientific validity and social values as necessary conditions for ethical research. Given increased concern about the exploitation of research populations in less-developed countries by investigators from wealthy countries, the CIOMS guidelines focus on the steps necessary to prevent exploitation and to ensure culturally sensitive informed consent. Further, the guidelines underscore the obligation of investigators to protect the confidentiality of the information they obtain from research participants, and emphasize issues of justice; for example, what is owed to participants after the research and the relevance of the specific research to the host community.

Following the World Health Assembly's adoption of the World Health Organization's (WHO's) End TB Strategy in 2014 *(5)*, the WHO Global Programme for Tuberculosis & Lung Health (WHO/GTB) developed guidance to ensure the ethical implementation of the strategy *(6)*. That publication built on the original guidance on the ethics of TB prevention, care and control, published in 2010 *(7)*.[1]

The guidance documents from CIOMS and WHO follow the central ethical principles that have been generally agreed for research with human subjects, and that equally apply for planning and carrying out national TB prevalence surveys:

- **First, do no harm (beneficence):** This refers to the ethical obligation to maximize benefits and minimize harms to individuals participating in the survey. A survey that is scientifically unsound is unethical because it will expose subjects to risk or inconvenience and achieve no benefit in knowledge.
- **Respect people:** This generally denotes to treating people with dignity and as beings that are intrinsically valuable and hence, as ends in themselves. The notion of respect for persons is often tied to notions of autonomy.
- **Autonomy:** This principle allows people to be able to choose from a reasonable range of choices in light of one's values and beliefs. Informed consent is one process of promoting autonomy, though not the only way.
- **Treat populations and individuals fairly:** This principle requires the equitable distribution of the burdens and the benefits of participation in research and surveys.

11.2 Review by an REC

11.2.1 Background

Many countries and jurisdictions have laws and regulations based on the aforementioned ethical principles, recognized in internationally agreed guidelines. These laws and regulations usually require that all research

[1] Due to be updated in 2025.

with human subjects is subject to prior review by an REC.

Surveillance is a core function of public health. There has been an ongoing debate about whether surveillance activities should be governed by the same ethical standards as research. Although some activities can unambiguously be identified as research and others as surveillance, there is a grey zone of activities that cannot easily be classified *(8)*.

11.2.2 Purpose and objectives of ethics review

The purpose of an ethics review is to ensure the rights, safety and welfare of human subjects in research or a survey. The review includes an examination of particular details of the study design and context, to balance what may be conflicting ethical principles and to determine the best solution in the particular setting. Not all ethical principles weigh equally, and not all principles weigh the same in different contexts. For example, a health survey in an outbreak situation may be assessed as ethically acceptable even if a usual ethical expectation (e.g. privacy) cannot be fully ensured in this context, provided the potential benefits clearly outweigh the risks and the investigators give assurances of minimizing risks. It may even be unethical to reject such a study if its rejection would deny a community the benefits the study offers. The challenge of ethical review is to make assessments that consider potential risks and benefits, and to weigh them in relation to each individual study.

Ethics review requires that different members of a committee consider differing initial opinions on the ethically best approach to a research study. Ideally, the committee's discussion should result in a solution that all members agree will safeguard the rights, safety and well-being of all study subjects or surveyed individuals. Those conducting the study then have particular responsibilities to safeguard the well-being of more vulnerable populations, including those who lack decision-making capacity or are less aware of the meaning of research *(4)*.

Membership of ethics committees should be multidisciplinary. Independence from the investigators is maintained by precluding any survey member with a direct interest in a proposal from participating in its assessment. The community to be studied should be represented in the ethical review process. This is consistent with respect for the culture, dignity and self-reliance of the community, and aims to achieve full understanding of the study among community members. Lack of formal education should not disqualify community members from joining in constructive discussion on issues relating to the study and the application of its findings.

WHO has developed a toolkit to help countries to evaluate their capacity to provide appropriate ethical oversight of health-related research involving human subjects *(9)*. The toolkit helps countries to identify strengths and limitations in their laws, and in the organizational structures, policies and practices of the bodies responsible for oversight of research ethics. It also provides indicators that can be used to assess an REC's structure and composition, resources, procedures, transparency, accountability and performance. Finally, the toolkit provides indicators to assess whether research institutions fulfil their responsibility to ensure that any health-related research under their purview adheres to the ethical principles in WHO guidance, as well as any national laws and policies consistent with those principles. Guidance has also been developed to help research institutions to offer an appropriate environment for their researchers to conduct their activities according to the highest standards in research ethics and regulation *(10)*. The national TB programme (NTP) and survey implementers should provide this oversight throughout the survey, along with those who conduct regular monitoring (**Chapter 14**).

11.2.3 Some key issues that an REC will address

Privacy

Investigators must protect the privacy of data; for example, by omitting information that might lead to the identification of individual subjects or restricting access to the data. In epidemiological surveys, numbers are usually aggregated to obscure individual identities. TB is a notifiable disease in many countries, meaning that a diagnosis of TB must be reported to public health officials. Where this is the case, RECs and participants should be told about the potential consequences of participating in a national TB prevalence survey.

Information obtained about survey participants can generally be divided into:

- *unlinked information* – that is, information that cannot be linked to the person to whom it refers and the investigator cannot know the identity of the person; and
- *linked information* – that is, information that is linked to the person by means of personal identification (usually the name and date of birth).

In prevalence surveys, information is usually linked to survey participants. Names and contact details of participants in TB prevalence surveys should only be used for the follow-up of people diagnosed with TB (or other serious diagnoses). Information that identifies participants should be discarded from data used for statistical analysis. However, for the clinical management of participants newly diagnosed with TB (or with other serious conditions), it is also important to use as many identifiers as possible (**Chapter 9**). This will minimize the risk of data management error, which in turn could prevent a well person from being treated for TB, or a person with TB not being treated at all.

When personal identifiers remain in the records used

for a survey, investigators should explain to RECs why this is necessary, how privacy will be protected and who will have access to the data. Where investigators link different sets of data regarding individuals (with the consent of the individual participants), they normally preserve privacy through anonymization by aggregating individual data into tables or diagrams.

Balancing personal and social perspectives

When performing reviews, RECs will consider both individual and social (community) perspectives. An individual's freely given and informed consent may not be sufficient on its own to render a survey ethical if the individual's community finds the survey objectionable.

Assuring scientific soundness

An ethical review should protect human subjects from risks of harm or wrong, and facilitate beneficial studies. Scientific and ethical review should be considered in parallel: a study that is scientifically unsound is unethical because it will expose subjects to risk or inconvenience and achieve no benefit in knowledge. Normally, therefore, RECs consider both scientific and ethical aspects of a study. An REC may refer technical aspects of the scientific review to a scientifically qualified person or a scientific review board (this step sometimes also precedes the ethics review); however, the REC will reach its own decision on the basis of qualified advice and scientific soundness. If a review committee is satisfied that a proposal is scientifically sound, it will then consider whether the expected benefits justify any risk to the participants, and whether the proposal is satisfactory with regard to informed consent and other ethical requirements.

Externally sponsored studies

Most national TB prevalence surveys are initiated and conducted by national researchers; hence, they need local ethical approval. Externally sponsored studies are those undertaken in a host country but initiated, financed and sometimes wholly or partly carried out by an external international or national agency, with the collaboration or agreement of the authorities of the host country. Such surveys imply two ethical obligations: the initiating agency should submit the protocol for ethical review, in which the ethical standards should be no less exacting than they would be for a survey carried out in the initiating country; and the REC in the host country should satisfy itself that the proposed survey meets its own ethical requirements. It is in the interest of the host country to require that proposals initiated and financed externally are submitted for ethical approval in the initiating country, and for endorsement by a responsible authority of the same country (e.g. a health administration, a research council, or an academy of medicine or science). Investigators must comply with the ethical rules of the funding country and the host country. Therefore, they must be prepared to submit proposals to RECs in each country. Alternatively, there may be agreement to submit to a single or joint REC. In addition, if an international agency sponsors a survey, its own ethical review requirements must be satisfied.

11.2.4 Information to be provided by investigators to the REC

Typically, the investigator will have to submit a detailed protocol and application form (if such exists) comprising:

- a justification for undertaking the survey;
- a clear statement of the objectives, having regard to the present state of knowledge;
- a precise description of all proposed procedures and interventions;
- a plan indicating the number of individuals to be involved;
- the criteria determining recruitment of individuals;
- participant information sheets and forms to obtain informed consent (see **Chapter 6**);
- evidence that the investigator is properly qualified and experienced, or (when necessary) works under a competent supervisor, and that the investigator has access to adequate facilities for the safe and efficient conduct of the survey;
- a description of the proposed means of protecting data privacy during the processing and publication of survey results;
- a reference to any other ethical considerations that may be involved, indicating how international ethical standards will be respected;
- a plan for clinical management and referral procedures that includes free treatment for all forms of diagnosed TB (including drug-susceptible and drug-resistant forms), even if these are not available within the national programme in the country where the study is conducted;
- plans for clinical management and referral procedures for conditions other than TB diagnosed during the survey (see **Chapter 9**);
- a plan for disseminating results, including for the community being surveyed; and
- a plan to protect researchers from any risks of contracting TB during the conduct of the survey.

WHO has developed guidance on how to develop a research proposal that meets the requirements of an REC *(11)*.

11.2.5 Informed consent

Purpose

Informed consent is a process that is based on the ethical principles of autonomy and respect for the

individual. The purpose of informed consent is to tell individuals about the procedures involved in the survey, and the potential risks and benefits involved; the aim is to allow individuals to decide freely whether or not to participate in the survey. For participants to be truly informed, they must understand the implications of the survey.

Information

Each potential survey participant must be adequately informed of the following in an acceptable format (verbal or written) and language:

- the purpose, methods and procedures of the survey;
- why and how the potential participants were selected;
- possible risks or discomforts involved and the anticipated benefits;
- what treatment or referral options are available if the participant is diagnosed with TB or with one or more other conditions;
- the individual's right to abstain from participation in the survey or to withdraw consent to participate at any time without reprisal;
- the sources of funding of the survey, any possible conflicts of interest and the institutional affiliations of the researcher;
- a description of how anonymity, privacy and confidentiality will be protected;
- the extent to which results will be made available to the participant and community; and
- the requirement to notify authorities (where applicable).

Participants should also be given an opportunity to ask questions about the survey.

Consent

Ascertaining whether the individual really understands the implications of consent is difficult. Allowing individuals to ask questions will help to clarify the process and could increase the response rate. After ensuring that the subject has understood the information, the investigator should then obtain the individual's freely given informed consent. Assent is an agreement by an individual not competent to give legally provided informed consent. In the context of a prevalence survey, this would be someone between 15–17 years of age. If consent cannot be obtained in writing, then non-written consent must be formally documented and witnessed. For more information about informed consent see **Chapter 6** and the WHO website *(11)*.

11.3 Good clinical practice and good data management practice

Within the context of national TB prevalence surveys, the application of principles related to GCP and GDMP are required to protect the rights, safety and well-being of survey participants, and to ensure the integrity of the survey data to support evidence-informed national policies. In collaboration with WHO/GTB, the WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR) developed guidance to describe and explain how to apply these principles, as outlined in **Box 11.1** *(12)*. All stakeholders involved in implementing a survey – especially the principal investigator, survey coordinator, central level coordinators and field team leaders – should formally learn these principles before conducting a survey.[1] They should ensure that all survey team members adhere to the principles, or possibly undergo the training themselves.

11.4 Errors

Errors are most often detected during supervisory onsite visits or in analysis of data, through monitoring and routine quality control checks; it can be categorized as low, medium or high grade, depending on the intention and its effect on the survey overall *(12)*:

- **Low-grade** errors are random and unintentional; they are often due to inattention or negligence. Such errors can be fixed by immediate action then correction and additional training. They are easy to detect and fix, and will have little impact on the survey overall.
- **Medium-grade** errors are intentional; examples are enrolling participants who do not meet inclusion or exclusion criteria, or not collecting sputum samples from people who screen positive. The impact of such errors on the survey will depend on the parameter and the extent.
- **High-grade** errors involve wilful deception, such as falsified test results, fictitious data, abuse of participant rights or misappropriation of funds. This type of error can be difficult to detect, usually cannot be fixed and is likely to have a strong negative impact on the survey; in extreme cases, it can lead to data having to be discarded or the cancellation of the entire survey.

Most low-grade errors in TB prevalence surveys are caused by unintentional data-entry errors. Carelessness and fatigue can play a part in the creation of such errors; hence, ensuring high team morale, and comfortable working and living environments for the team are as important as ensuring a high-quality data

[1] An example of an online GCP/GDMP training course can be found here: https://globalhealthtrainingcentre.tghn.org/ich-good-clinical-practice/

management system (DMS) and systematic monitoring. Barcoding and digital data collection have helped to minimize manual data-entry errors.

Medium-grade errors can lead to protocol deviations, usually owing to misunderstanding of the procedures or data-entry errors. Most instances can be prevented through training, setting the DMS to automatically identify mistakes and conducting frequent supervisory visits, especially during the early phase of field operations. If a major protocol deviation persists, then data from those particular clusters may need to be excluded from the final analysis.

High-grade errors are rare, and can be classified as misconduct. This is defined as "the generation of false data with the intent to deceive" *(13).* Misconduct can be committed by anyone, whether acting alone or in a group, and the reasons for doing so can vary. Such misconduct can be avoided by putting in place good governance, transparent financial management, frequent engagement with donors and monitoring by external parties.

The survey protocol should include details of the process for reporting, investigating and escalating suspected cases of misconduct.

11.5 Specific ethical issues that arise in national TB prevalence surveys

Stigmatization

When collecting risk-factor data in national TB prevalence surveys, it is crucial to maintain the privacy of all data. A particular concern is the need to avoid community stigmatization of participants identified as having TB or other diseases, in particular HIV. During follow-up visits by survey team members in households of identified TB cases, it is important to ensure that the individual and household members are not stigmatized. The potential for stigma is affected by the geographical, ethnic and cultural context, and the risk of being stigmatized will affect the risk–benefit ratio of the survey. Survey teams should work with communities to determine the potential for stigma, and develop ways to reduce it. A common poor practice is interviewing participants in an open space; this displays a lack of privacy, and may also reduce the reliability of answers provided by the participants. Another issue relates to the greater use of mobile phones as a camera. Although sharing of information via mobile phones has increased communication efficiencies, the survey team should be aware of the privacy issues related to the sharing of photos and videos with images of participants, personal identifiers and data.

Identification of drug-resistant TB

Surveillance of drug resistance in TB raises a particular ethical dilemma in situations where there is limited capacity to properly treat patients identified

BOX 11.1
THE PRINCIPLES OF GCP AND GDMP AS THEY RELATE TO NATIONAL TB PREVALENCE SURVEYS *(12)*

- Surveys should adhere to the central ethical principles of beneficence, respect, autonomy and fairness.
- Surveys should be scientifically sound, and methods should be described in a clear, detailed protocol, as prescribed in the technical guidance documents applicable to the survey.
- The medical care given to, and the medical decisions made for, survey participants should always be the responsibility of qualified medical officer(s), or trained health care provider(s), and should be in accordance with relevant guidelines from the national TB programme (NTP) and WHO.
- Each individual involved in the design, planning, implementation, analysis and reporting of the survey should be qualified by education, training and experience to perform their respective task(s).
- Throughout the survey period, community education and engagement should be performed in a culturally sensitive and appropriate manner.
- Every survey participant should give their informed consent and assent voluntarily before participating in the survey.
- All survey-related information should be recorded, handled and stored in a way that allows accurate reporting, interpretation, verification and reconstruction. This applies to all records on paper or electronic media.
- Quality assurance systems should be implemented throughout the design, implementation, recording, reporting and archiving of the survey, to assure the quality of all aspects of the survey.
- Current best practice methods should be applied when analysing the data.
- The survey results must be reported, published and disseminated.

with drug-resistant strains. Therefore, before a survey or surveillance programme is implemented, provisions must be in place to facilitate the communication of results to participants and to ensure that all people with drug-resistant TB (DR-TB) have access to appropriate treatment and care, in line with the most recent WHO guidelines *(14–16)*.

HIV testing services, comorbidities and incidental conditions

All HIV testing services within a national TB prevalence survey should adhere to the human rights-based principles known as the "5 Cs": consent, confidentiality, counselling, correct test results and connection (i.e. linkage to prevention, care and treatment services). **Box 10.3** in **Chapter 10** has more details on the "5 Cs" *(17)*. Clinically relevant results must be conveyed to participants by the survey team, and there should be robust referral pathways for further diagnosis, treatment and care. The same principle applies to new diagnoses of conditions other than TB diagnoses or serious comorbidities in survey participants (see **Chapters 9** and **10**).

Researchers should ensure that study participants receive free medical care and compensation for any injuries contracted as a result of their participation *(4)*. The extent to which there is an obligation to provide care for non-related ("incidental") conditions that occur during the survey is a matter of debate; however, as a minimum, the survey team should refer the affected participants for appropriate follow-up and care.

Testing with Xpert® MTB/RIF Ultra (Xpert Ultra)

The reference standard for the diagnosis of TB is liquid culture; however, it can take several weeks before culture-positive results are available and up to 6 weeks before results can be classified as culture negative. In contrast, Xpert assays can provide results within a few hours; hence, many countries use Xpert as an initial diagnostic test for TB. The diagnostic algorithms in this guidance (see **Chapter 3**), which include both liquid culture and Xpert Ultra, are designed to ensure that all participants who screen positive have at least one Xpert result for clinical management (see **Chapter 9**). All relevant results must be conveyed to participants, and mechanisms should be in place for appropriate referral and management where necessary.

Potential use of stored biological samples and related data for other research

Issues can arise if isolates of sputum samples are to be stored and used for future research projects. To make use of such biological samples and the related data, investigators should obtain informed consent from participants in the survey. The consent should specify

> *"…the conditions and duration of storage; who will have access to the samples; the foreseeable uses of the samples, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies; and the intended goal of such use, whether only for research, basic or applied, or also for commercial purposes…" (4).*

A specific informed consent form template for storage and future use of unused samples can be downloaded from the WHO research ethics review committee website *(18)*.

Data management

Every effort should be made to minimize (and, ideally, to eliminate) errors in the survey's database. Although it is rare, a worst-case scenario is the misclassification of people with and without TB; that is, incorrectly diagnosing a survey participant with TB when they are not infected, or not diagnosing someone with TB when they are infected. Errors due to issues with data management can happen at any step along the participant pathway of the survey, but they usually stem from the incorrect identification of participants or the assignment of the wrong identifiers and barcode in the field (e.g. at reception, during interview, chest X-ray or field laboratory stations) or the central laboratory. Manual data entry of identifiers or laboratory results – typically undertaken when the barcode scanner fails or the process is deemed too cumbersome – is highly prone to data error. Ensuring high data quality and the maintenance of integrity requires regular monitoring of activities, the development and practice of a clear data management plan and (as previously mentioned) ensuring that all staff are trained in the principles related to GCP and GDMP, and adhere to those principles.

11.6 Artificial Intelligence and national TB prevalence surveys

Artificial intelligence (AI) is the ability of algorithms encoded in technology to learn from data so that they can perform automated tasks without a person needing to explicitly program every step in the process *(19)*. This fast-evolving technology could be used in screening and diagnostic tools, as part of future TB prevalence surveys. Currently, CAD software that screens digital CXRs for TB is the only tool used in prevalence surveys that benefits from the use of AI, with CAD products using software algorithms that are typically trained and developed by AI. In 2021, WHO issued a recommendation on the use of CAD for screening (and triage) for TB disease *(20)*.

In 2021, WHO published comprehensive guidance on the ethics and governance of AI for health *(19)*. The guidance outlined potential benefits and risks of the use of AI in health care, and provided six principles for consideration in the policies and practices of governments, developers and providers that are using AI. The principles, which are extensively outlined elsewhere *(19)*, are:

- protecting human autonomy;
- promoting human well-being, human safety and the public interest;
- ensuring transparency, explainability and intelligibility;
- fostering responsibility and accountability;
- ensuring inclusiveness and equity; and
- promoting AI that is responsive and sustainable.

Given the large datasets generated from national TB prevalence surveys, there is potential for the future application of generative AI; that is, a category of AI techniques in which algorithms are trained on data sets and can be used to generate new content. One type of generative AI, large multimodal models (LMMs), which can accept one or more type of data input and generate diverse outputs, may have survey applications; for example, they could be used in areas from screening and risk factor assessment for TB through to participant interviews, drafting of medical referrals, data analysis and reporting of survey results. However, this rapidly developing field requires consideration of the overall governance and framework for the use of LMMs (and AI in general) in health care, to ensure ethical oversight and integrity *(21)*.

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CHAPTER 12

Survey organization and training

Implementing a tuberculosis (TB) prevalence survey is a large undertaking and should not be underestimated. Organization is key to a successful survey, which comprises numerous activities both in the field and at the central level. These activities need to be carried out in a coordinated manner, following standardized procedures, by a large group of people with diverse skillsets. Therefore, it is important to have clear agreement on the tasks that need to be performed by each team member, with well-defined roles and responsibilities, and to ensure that careful supervision is undertaken to monitor implementation of these tasks to as high a standard as possible.

This chapter describes the organization and roles of the main roles and groups within the survey team. It then provides a description of the qualifications and tasks for each of the main roles, followed by a training outline and modules that should be developed. Finally the role of those who provide technical assistance is described.

12.1 Lines of supervision

Strong lines of supervision are needed throughout the survey to ensure that activities are implemented in a standardized manner as outlined in the standard operating procedures (SOPs). Careful consideration is needed of the qualifications and experience of key personnel and the coordination structure of the survey, with defined roles and responsibilities for all survey staff and clear lines of supervision. An example of a supervision structure is depicted in **Fig. 12.1**. Most surveys to date have used this general structure but it can be adapted to the availability of human resources. The steering committee has overall responsibility for the survey, the survey coordinator has day-to-day responsibility for overseeing all survey activities (at both the field and central levels) and the field team leaders have responsibility for the implementation of field activities by their team. The core survey team is made up of the principal investigator, the survey coordinator, the central-level coordinators and the field team leaders, and should all meet regularly.

12.1.1 Steering committee and principal investigator

The steering committee is ultimately responsible for designing the study, maintaining the quality of the study's conduct, ensuring that the objectives set are reached, writing the final study report and disseminating the key findings. Therefore, the committee monitors the full process of survey design, implementation and analyses, intervening where necessary. The committee comprises representatives of stakeholders such as the national TB programme (NTP), the public health service and local research institutions. Given the diverse constitution of the committee, it is critical to appoint a principal investigator; in some instances, there may be a co-principal investigator as well. The principal investigator is the liaison for communication outside the steering committee.

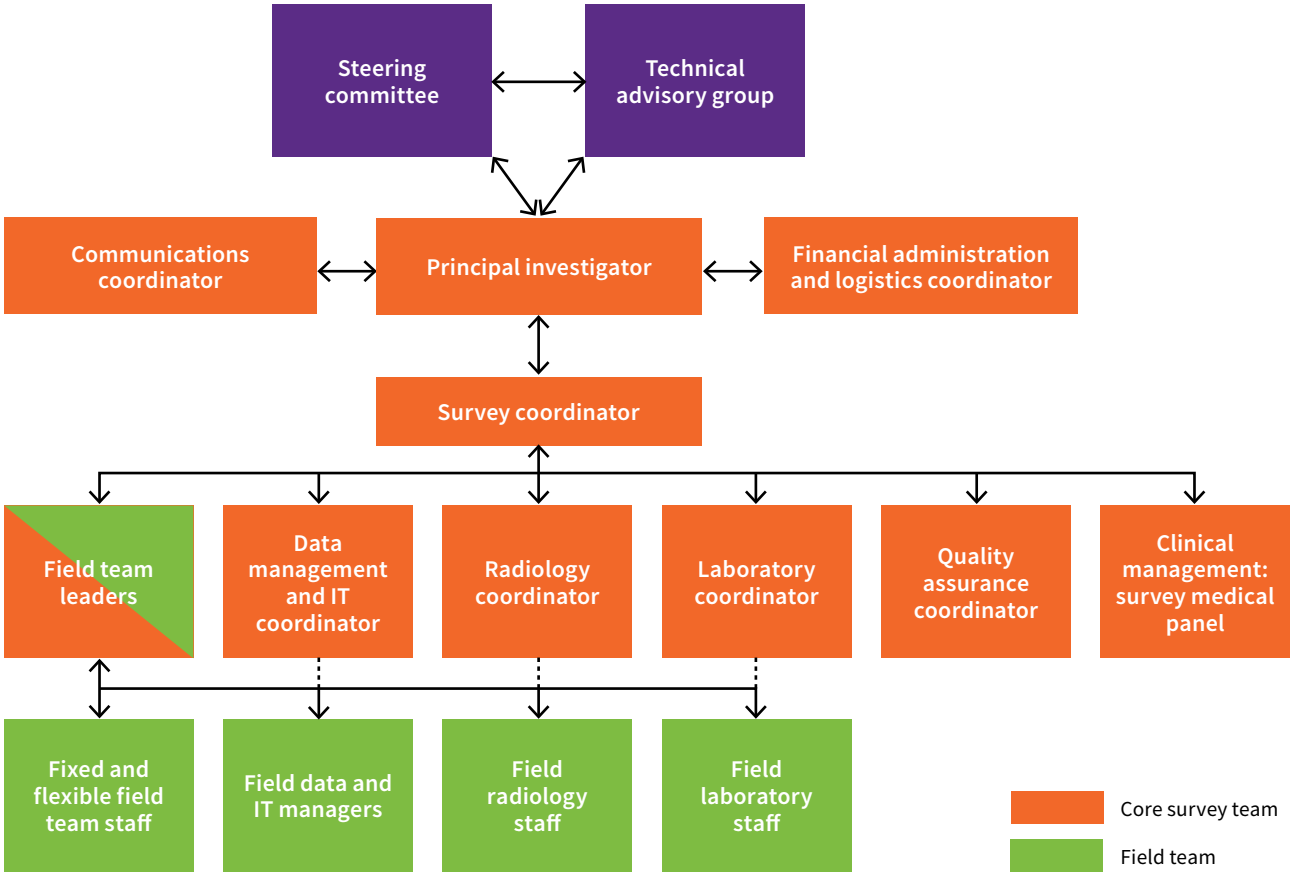
The committee can choose to outsource all or part of its responsibilities to a research institute (e.g. a public or a contracted research institution). However, the act of outsourcing does not mean that the committee has outsourced its responsibilities. Thus, it should be made clear (by formal contract) what is expected from the research institute with respect to deliverables, human resources and financial arrangements. Care should be taken when specific parts of a survey are outsourced or managed by different partners, to ensure that roles and responsibilities are clear and all tasks are completed as a joint effort, to ensure a consistent and integrated approach to implementation. The chosen outsourcing organization should implement appropriate quality assurance (QA) and quality control (QC) measures in the survey, to ensure that high-quality data are generated.

Examples of outsourcing can be found in several surveys:

- **Namibia** contracted survey laboratory testing to the partner that conducted the same tasks for their routine surveillance activities. Namibia did not have the capacity to perform all the survey's laboratory work, so some specimens were tested in South Africa.
- **Mozambique** contracted a local software developer to design and build their data management system (DMS). That organization also provided a lot of hands-on support during the survey. Eswatini, which started its survey just after Mozambique, contracted the same software developer. The developer adapted the Mozambique system to the Eswatini country context, and built the capacity of the in-country team needed to run the survey and adapt the system.
- **Lesotho** did not have an available radiologist in-country; hence, all digital chest X-rays (CXRs) were re-read remotely by a radiologist in South Africa.

Fig. 12.1

Example organogram for a national TB prevalence survey



IT: information technology.

Eswatini also did not have full capacity to read digital CXRs, so a proportion of them were sent to Japan to be re-read.

Other examples are shown in **Box 12.1**.

In Ethiopia, Ghana, Kenya, Lao People's Democratic Republic, Viet Nam and Zimbabwe, the NTP did not outsource any activities; rather, they fully organized and implemented the survey themselves with support from partners.

12.1.2 Survey coordinator

The day-to-day management of the survey is the responsibility of the survey coordinator, who is appointed by the steering committee, and is a critical member of the core survey team. In large countries or in a survey with a large number of teams, an assistant survey coordinator or a coordinating team (comprising the central survey coordinator and several regional coordinators for administrative subdivisions) may be needed to facilitate smooth operations. Although the main work of the survey coordinator is managing the implementation of the survey, it is strongly advised that this person be appointed as soon as possible so that they can be actively involved in the design of the study, and in subsequent planning of activities at the field and central levels.

The survey coordinator supervises the work of the different field teams that collect the data; this requires close collaboration between the survey coordinator and the team leaders. Thus, the survey coordinator needs to spend time in the field directly observing field operations and needs to review field reports submitted by the team leaders in a timely manner. The field reports are drawn up after finalizing the activities in a cluster and are sent to the survey coordinator. Many of the recent surveys with digital data collection (see **Chapter 16**) had dashboards with real-time data. Weekly (if not real-time) monitoring through tabulation of key indicators for all critical activities is key to ensuring the quality of a survey (see **Chapter 14**).

In addition to field reports, there is a need for a report that summarizes key logistical and staff-related issues, and discusses problems encountered and solutions implemented. The team leaders should also document and report key issues such as major protocol or SOP breaches, equipment breakdown and staff changes. Such incidents may help to explain deviations in expected survey results during the analysis. Attention

BOX 12.1
EXAMPLES OF SURVEY ORGANIZATION: ESWATINI, 2018–2019; SOUTH AFRICA, 2018–2019 AND CAMBODIA, 2023–2024

Eswatini, 2018–2019

The National TB Control Program (NTCP) of Eswatini was the main organizer of the survey, working together with the National Health Research Unit, Eswatini Health Laboratory Services/National TB Reference Laboratory and the Central Statistics Office. The survey was organized through the steering committee, which had the final responsibility for the protocol, data collection, data management, and analysis and dissemination of the results. A TB prevalence survey coordination team was responsible for all technical activities. The principal investigator and coordination team were the core group driving the day-to-day survey activities; they were supported by the steering committee and the technical advisory group (TAG). Technical assistance was provided by three consultants from KNCV Tuberculosis Foundation; the assistance focused on data management, and laboratory and overall support from an epidemiologist (including data analysis and reporting). All key technical partners – including the World Health Organization (WHO), the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) and multiple nongovernmental organizations (NGOs) – were members of the steering committee or TAG.

South Africa, 2018–2019

The South Africa National Department of Health handled some survey activities (e.g. community sensitization and engagement), but also outsourced parts of the survey to multiple organizations: the South African Medical Research Council (SAMRC), the Human Sciences Research Council (HSRC) and the National Institute for Communicable Diseases (NICD). HSRC was responsible for the survey field activities and data management, SAMRC was in charge of central-level activities (including central CXR reading and case management) and NICD was responsible for central laboratory activities. The three organizations worked hand in hand with the National Department of Health during survey preparation, survey implementation, and interpretation and dissemination of results. WHO South Africa also provided additional oversight and coordination support.

Cambodia, 2023–2024

Under the Ministry of Health, the National Center for Tuberculosis and Leprosy Control (CENAT) coordinates TB activities throughout Cambodia. CENAT led the surveys in 2002 and 2010–2011, but for the third survey, the Research Institute of Tuberculosis/Japan Anti-tuberculosis Association (RIT/JATA) and Institut Pasteur du Cambodge (IPC) were co-principal investigators. In addition to these three organizations, WHO Cambodia provided additional oversight and coordination support (in particular, for donor liaison). For the latest survey, each of the three field teams was individually led by CENAT and two other NGOs: Health and Social Development, Cambodia (HSD) and the Cambodia Anti-Tuberculosis Association (CATA). IPC led the DMS and laboratory testing (Xpert® MTB/RIF Ultra [Xpert Ultra] and culture). RIT/JATA had an in-country acting coordinator, who worked with CENAT focal points to solve managerial and technical challenges. CENAT led the financial management whereas RIT/JATA assisted with budgeting and reprogramming of funds. Overall technical support was led by RIT/JATA, with frequent visits by international experts.

should be given to the communication between the survey coordinator and the field-team leaders. Once a field team has left the cluster, it will be almost impossible to rectify structural mistakes in data collection from this cluster, because tracing the participants is often impossible. Therefore, it is advisable to have the survey coordinator, the QA officer and senior team leaders closely monitoring crucial parts of the data collection, especially in the early clusters. These individuals form the “eyes and ears” of the survey coordinator, and can ensure that field activities are properly supervised and that problems are addressed in a timely manner.

12.1.3 Central-level coordinators

Survey activities take place at both the field (cluster) and central levels. Although the actual data collection is largely happening in the field, the central-level procedures are an essential part of the survey and are critical for a successful survey. Central-level procedures are led by a group of central-level coordinators, each of

whom is responsible for a key area and reports to the survey coordinator or principal investigator (**Fig. 12.1**). These roles form part of the core survey team. Each central-level coordinator is responsible for activities centrally and for overseeing the related activities in the field. The responsibilities of the coordinators are as follows:

- **Data management:** The data manager of the survey manages and oversees all data management activities, at both the field and central levels (see **Chapter 16**).
- **Radiology:** All or a subsection of X-ray images will be re-read at the central level, reading for QA purposes but also to aid a diagnosis for those eligible to submit sputum (see **Chapter 7**).
- **Laboratory:** Depending on the adopted algorithm, a part of the laboratory testing may be done at the central level (see **Chapters 3** and **8**). However, for all surveys, QA of field laboratory procedures will be overseen from the central level.
- **Clinical management:** The survey medical panel oversees the management of all participants identified in the survey with TB or non-TB diagnoses, but the survey coordinator (or chair of the panel) has overall responsibility (see **Chapter 9**).
- **Finance and logistics:** Surveys are complex and they require organization to ensure that staff are hired, and materials (equipment and consumables) procured and are available onsite. Therefore, it is vital to have a dedicated person in the coordination team responsible for finance and logistics because a separate skillset is required for this role.
- **QA:** This is a useful additional role to oversee all aspects of the field and laboratory work survey, and ensure that quality indicators are maintained (see **Chapter 11**).
- **Communications:** This is another useful additional role to liaise between the survey team and the public, including the media. The role also assists the field teams with public health messaging and liaising with communities where the survey is being conducted.

12.1.4 Field-team leaders and members

Each field-team leader is responsible for implementing field activities in their appointed clusters. In most surveys, the field-team leaders also play a role in the presurvey visits, and are part of the group conducting these visits for the clusters assigned to their team. These leaders are the liaison between the community and the survey coordinator. Field-team leaders report to the survey coordinator but can be more directly supervised and supported by assistant survey coordinators, where these are appointed. If there are many teams or they operate in widely different areas of the country, overseeing all field teams can become logistically challenging; in such situations, assistant survey coordinators may assist the survey coordinator in their role. Field-team leaders can form part of the core survey team.

The number and composition of field teams may vary, depending on the design and size of the survey. It is recommended that each field team has a fixed component and a flexible component. The fixed component comprises those individuals who carry out the technical activities – this part of the team remains the same for all clusters. **Table 12.1** outlines the standard composition of a field team. The flexible component refers to those individuals who assist the survey team in their own cluster (or clusters in their responsible administrative area; e.g. a province or district), and these change for each cluster or group of clusters. The flexible component allows adaptation to local circumstances (e.g. assisting the enumerators (census takers), tracing participants and translation), whereas the fixed component guarantees standardized survey procedures across the clusters. For some key staff, there is often only one position in the team (e.g. a medical officer or field information technology [IT] officer); therefore, a backup plan should be developed as part of survey preparation, outlining what will be done when that particular person is absent (e.g. falls ill or has to take leave of absence).

The field team should meet at the end of each day to discuss the day's events, identify any challenges or incidents, and compile a list of participants who missed their appointment or have not completed all required study procedures (e.g. missed sputum collection despite being eligible, or missed HIV testing or a questionnaire). Contacting participants or visiting their home should be arranged to follow up these missed activities, where necessary.

12.2 Advisory functions

The steering committee and the survey coordinator need to be advised on a range of technical issues. This is best done by forming a TAG. In addition, there needs to be a clinical review panel overseeing case management (see **Chapter 9**). The place of these activities within the overall set-up of the survey is highlighted in **Fig. 12.1**.

12.2.1 Technical advisory group

The steering committee and the survey coordinator should be advised by a TAG. This group provides technical input (e.g. on enumeration (census), radiology, microbiology and epidemiology) for the activities of the steering committee, and it comprises experts in these fields. The TAG will be very busy and intense during the design of the survey and the SOPs. During implementation of the survey, communication with the TAG may be on a more ad hoc basis, although it is advisable to have members of the TAG present at the regular meetings of the steering committee, and to ensure that TAG members receive updates on survey progress.

Table 12.1

Field-team composition for the fixed component of a field team[a]

JOB TITLE	NO. PER TEAM	PRIMARY ROLE	REMARKS
Field-team leader	1	Coordinate all activities in the cluster, and manage and lead the field team	For each team, one of the team members should be assigned as assisting field-team leader who can act as field-team leader when needed
Medical officer	1	Read and interpret CXRs, and evaluate participants for referral	If human reading of CXR is not done, this role can be combined with that of field-team leader
Data manager or IT officer (field)	1	Responsible for functioning of the (digital) DMS	Additional field-data management officers are generally required
Receptionist	1–2	Welcome eligible individuals at survey site, confirm eligibility and obtains informed consent	Most surveys assign 2 receptionists (who can also rotate with interviewers)
Enumerator	4–6	Conduct listing of household and inviting of eligible individuals	The number will depend on the survey design; in turn, it determines the speed of operation[b] Depending on how enumeration is organized, all staff can assist with the enumeration activities
Interviewer	2–3	Administer questionnaires (screening and others as per the design) to eligible participants at the field site	The number will depend on the design and number of questionnaires
HIV counsellor	1–2	Conduct HIV testing of participants	The number will depend on the testing strategy used (see **Chapter 10**) and which participants will be offered HIV testing
Radiographer	1–2	Responsible for taking CXRs in the field	Most surveys assign 2 people, who interchange during the day
Field laboratory technologist	1–2	Responsible for sample collection and conducting of sample testing in the field (as applicable), and for packaging samples for transportation	The number will depend on the design and whether field Xpert testing is done; where needed, sputum collection could be done by a different cadre of staff
Driver	2–3	Drive field staff to and from the site and the mobile X-ray truck (if applicable), and provide logistical support	The number will depend on the size of the team and type of vehicles used; drivers can also assist with logistics and security

CXR: chest X-ray; DMS: data management system; HIV: human immunodeficiency virus; IT: information technology.

[a] The number of staff and job titles may differ, depending on the design and size of the survey; they will depend on available human resources and should be adapted to the local context. Some roles and responsibilities may be undertaken by the same individual (see **Annex 12.1**).

[b] Depending on the design, the enumeration (or census) may be conducted by the national census bureau or statistical office.

The role of the epidemiologist and statistician in the TAG deserves special mention. The involvement of such individuals is important to ensure that sampling and data analyses are implemented correctly. Also, during the implementation of the survey, issues can arise that need the attention of these experts; for example, an unexpectedly inaccessible cluster that needs to be replaced or a need to subsample within a very large cluster in the selected list (see **Chapter 5**).

12.2.2 Survey medical panel

The medical panel usually comprises the survey coordinator, one or two radiologists, one or two respiratory physicians, a laboratory expert, a survey data manager and an administrative assistant. This panel is responsible for medical decisions related to the management of survey participants, not just participants identified with TB but also any medical situation that occurs during the survey (see **Chapter 9** and **Section 12.3.9**).

12.3 Qualifications and tasks for survey staff

The scale of a prevalence survey calls for the implementation of multiple related activities within a short period of time. This requires an organizational framework that covers all managerial and advisory levels in terms of preparation, execution and reporting. Each level (and each individual) has specific terms of reference and responsibilities, which should be clearly agreed upon and described. This section provides general descriptions of the qualifications needed for each role – these can serve as broad job descriptions, but should be adapted for local circumstances.

Remuneration for the activities should be based on

the extent of the work performed and the practices in the country. Activities that need a full-time commitment of the individual (e.g. survey coordinator, central-level coordinators, field-team leaders and fixed team members) can be remunerated through specially drawn-up contracts that include appropriate details, including the amount of time expected to be spent in the field. Part-time activities (e.g. membership of the steering committee, TAG and flexible team) could be remunerated through a per diem system, if renumeration is required according to the country circumstances.

12.3.1 Principal investigator

Within the steering committee, the principal investigator is responsible for all survey activities. This function can be performed part time (e.g. 20%, although the task may be more time-consuming at particular points during the survey). In many countries, the principal investigator is typically the NTP manager, head of research institute, lead statistician or focal point from within the ministry of health, and there can be more than one principal investigator per survey. If the NTP manager is the principal investigator and dedicates a lot of time to the survey, it is important to ensure that this does not have a negative effect on other NTP activities. This principal investigator is part of the core survey team.

Qualifications

- Preferably at least 5 years of managerial experience in the field of public health.
- Strong managerial skills, including being able to delegate tasks.
- Extensive knowledge of TB.
- Extensive knowledge of population-based surveys.
- Working within or having access to an organization that has an infrastructure supporting population-based surveys.

Job description

- Assemble a survey team that has all the expertise needed to design and implement the survey, analyse the survey data and disseminate the results.
- Liaise with the ministry of health and other governmental departments to organize the survey.
- Work closely with internal and external technical consultants.
- Liaise with the survey coordinator on a frequent basis.
- Secure funding for the conduct of the survey.
- Lead publications of the survey.

12.3.2 Survey coordinator

The survey coordinator is the focal point for day-to-day management of the survey. This is a full-time position and is part of the core survey team (**Fig. 12.1**).

Qualifications

- Preferably at least 3 years of research experience in the field of public health.
- Strong managerial and communication skills.
- Knowledge of public health research and epidemiology.
- Knowledge of TB.
- Expertise in fieldwork (preferably with household or community surveys).

Job description

- Be involved in all preparatory stages of the survey, including its design.
- Prepare the field manual and SOPs.
- Prepare the training manual and study materials.
- Arrange the training of all staff.
- Plan the fieldwork.
- Arrange pilot testing and its evaluation.
- Supervise the fieldwork.
- Supervise data management.
- Assess monitoring reports from both survey teams (central and field).
- Assess monitoring reports from external technical consultants.
- Prepare monitoring reports for the principal investigator and steering committee.
- Liaise with the principal investigator and central-level coordinators on a regular basis.
- Liaise with local officials in the survey clusters (during presurvey visits and actual fieldwork).
- Promptly report any major problems in the preparation, execution or data management of the survey.

12.3.3 Central-level coordinators

Central-level coordinators are the leaders of their respective areas of work at the central level. They are responsible for the performance of technical activities in their specified area (i.e. data management, laboratory management, radiology, clinical management, QC, communications, finance and logistics). These positions are part of the core survey team. Some roles could be combined; for example, radiology and clinical management. Coordinators may be specifically recruited for the survey but could also be seconded, for example, from another department of the ministry of health.

With the survey coordinator, the central-level coordinators form the day-to-day management team of the survey.

Ideally, central-level coordinators should be recruited early on during survey preparations so that they can help to develop the protocol and SOPs, and undertake preparatory activities.

Qualifications

- Preferably at least 3 years of research experience in their area of expertise.
- Strong managerial and communication skills.

- Knowledge of public health research and epidemiology.
- Knowledge of TB.
- Expertise in their area of work

Job description

- Provide technical guidance to the survey team for their area of expertise.
- Ensure that technical work is implemented according to appropriate standards.
- Be responsible for logistics and organization for their area of expertise.
- Coordinate the day-to-day survey work – depending on survey workload, this may require a full-time position.
- Conduct monitoring missions to oversee field implementation.
- Provide regular field reports on the survey work to the survey coordinator and steering committee.
- Liaise with the survey coordinator on a regular basis.
- Promptly report any problems in implementing the survey protocol.

12.3.4 Field-team leaders

Field-team leaders supervise the fieldwork performed by the survey team; the aim is to ensure that all activities are carried out in full and according to the protocol. This is a full-time job and these leaders can be part of the core survey team. The total number of team leaders needed depends on how many field teams are deployed – this typically ranges from two to six teams per survey. The number of field teams ideally should be more than the number of teams actively working in the field at the same time.[1] Many countries opt to rotate field activities among teams, to allow for an adequate amount of rest for each field team, while the equipment is working continuously. (In Rwanda, 3 field teams were deployed using two sets of equipment and the survey calendar was organized in such a way that 2 teams were always in the field and one resting. Eswatini did the same with 4 teams and 3 sets of equipment.) There must be a balance between the number of field teams and the standardization of activities (including laboratory capacity), as well as of overall supervision.

Qualifications

- Preferably at least 2 years of experience in fieldwork for health-related research projects.
- Knowledge of TB.
- Excellent managerial and communication skills.
- Team player and motivator.
- Attention to detail and accuracy when conducting administrative procedures.

Job description

- Visit selected clusters before fieldwork.
- Provide final map of area to be sampled.
- Lead the field team.
- Be responsible for finances, logistics and organization during fieldwork.
- Coordinate the day-to-day fieldwork.
- Liaise with local, district and provincial authorities on issues regarding fieldwork.
- Provide a final field report to the survey coordinator at the end of fieldwork in each cluster.
- Liaise with the survey coordinator (and field supervisors) on a regular basis.
- Promptly report any problems in implementing the survey protocol in the field.

12.3.5 Fixed team members

The fixed team members for each field team implement all technical field activities. These are full-time functions. Some roles and responsibilities can be undertaken by the same person (e.g. enumerator and interviewer). During team member selection, especially selection of interviewers and enumerators, it is good to account for the main languages spoken in a country and ensure that those languages are represented in each team.

Qualifications

- Experience in fieldwork in a research setting.
- Experience in the assigned task.
- Good administration and organizational skills.
- Good communication skills, to interact with the survey population and to work as a team member.

Job description[2]

- Medical officer: Read CXRs, inform participants of screening results and undertake clinical management.
- Data manager (field): Set up IT and data system and undertake real-time monitoring of data and validation (see **Chapter 16**).
- Receptionist: Provide informed consent to participants and assist the data manager (e.g. barcoding and verification of data).
- Enumerator and interviewer: Administration, enumeration (census taking), reception and interviewing.
- Counsellor: HIV counselling and testing.
- Radiographer: Taking CXRs and undertaking QA (see **Chapter 7**).
- Laboratory technologist (field): Undertake sputum collection, packaging and processing (see **Chapter 8**).

[1] The number of active field teams operating at the same time will affect the number of samples received by the central laboratory (see **Chapter 8**). The laboratory's human resource and culture capacity will determine how many field teams there are. Rotation of field teams is also important so that teams can rest between every 2–3 clusters.

[2] For a detailed description, see **Annex 12.1**.

- Driver: Manage the transportation of people, equipment and, if required, laboratory samples; and provide logistical support.

12.3.6 Flexible team members

Flexible team members are those who work in a single cluster. These are usually individuals from the local community, who assist the survey team in implementing the survey in that single cluster.[1] This is a full-time job done for a short period of time (1–2 weeks of field activities within a single cluster).

Qualifications

- Preferably experience in fieldwork in a research setting.
- Knowledge of local language(s) spoken in the cluster.
- Knowledge of the area where the activities are carried out.
- Good communication skills, to interact with the survey population.
- Adequate leverage or representation of the community; for example, these could be members of a youth group, a committee or another group that is known and accepted by the community.

Job description

- Prepare the site.
- Assist with enumeration (or census taking).
- Assist with sensitization of the community.
- Guide participants between different stations at the field site.
- Assist with finding participants for follow-up.
- Assist with translation, where required.

12.3.7 Data manager

Special mention of the role of a data manager is warranted because their contribution to survey design and survey implementation has been underestimated in some surveys (also see **Chapter 16**). This function is a full-time job, provides overall guidance and supervision of the field data managers, and plays a key role in the core survey team. Some surveys implementing fully digital data collection have appointed an IT manager in addition to the data manager, with the data manager responsible for the actual management of the data and the IT manager responsible for the system and IT set-up.

Qualifications

- Team leader and motivator.
- Proven extensive experience with large-scale surveys.
- Appropriate skills for building and maintaining relational databases.
- Experience in monitoring and reporting of large datasets.
- Able to carry out merging of databases.
- Able to carry out and validate data-capture procedures.
- Analytical skills to provide summary statistics and identify systematic entry errors.
- Good administrative skills, including maintenance of adequate documentation.
- Good communication skills.

Job description

- Lead the data management unit, including overseeing IT and data clerks in the field.
- Coordinate all steps in data management.
- Prepare database and data-entry screens.
- Liaise with external companies if database development is outsourced.
- Be responsible for the validation of captured data.
- Ensure data are properly stored and backed up.
- Check validated data files regularly for systematic errors (cleaning).
- Be responsible for the production of regular data management reports.
- Liaise closely with members of the data management group.
- Liaise with the survey coordinator (and, where appointed, the IT manager) on a regular basis.
- Promptly report any problems encountered in data management.
- Participate in the medical panel (see below).

12.3.8 Technical advisory group

The TAG advises the steering committee and the survey coordinator on all technical aspects of the survey. The main focus is on the design of the protocol and the SOPs, but ad hoc advice during actual fieldwork should also be available. Members perform these activities on a part-time basis. Their workload may change in different phases of the survey, ranging from ad hoc meetings during the implementation phase to more intensive involvement during the design phase. The TAG should meet regularly during the full period of the survey, from design to field implementation, analysis, completion of the survey report and dissemination of results.

Terms of reference

- Advise on the survey protocol.
- Produce the technical parts of the field manual and SOPs.
- Advise on the procurement of equipment and supplies.
- Advise on the design, pretesting and production of study materials.
- Provide technical assistance for training and pilot testing.
- Provide ad hoc advice during survey implementation.
- Have representatives in the steering committee.
- Provide oversight during the full survey period, to

[1] If there are more clusters from the same community, then the same flexible team members can also work in the other clusters.

help ensure that the final survey report and a peer-reviewed journal article are produced.

12.3.9 Survey medical panel

The medical panel usually comprises the survey coordinator, one or two radiologists, one or two respiratory physicians, a laboratory expert, a survey data manager and an administrative assistant.

The panel is responsible for medical decisions related to the management of survey participants. This is a part-time activity (about 10%).

Terms of reference

- Review information from all survey participants who have at least one sample with *Mycobacterium tuberculosis (Mtb)* detected, and decide whether the participant can be classified as a survey TB case by applying the case definition (see also **Chapters 4** and **9**). The panel should meet regularly (e.g. weekly) and discuss, at a minimum, all participants with TB as indicated by their laboratory results (e.g. positive Xpert Ultra test or culture positive for *Mtb*), reviewing their CXR images, HIV status, treatment history and other available information. The medical panel should also discuss participants with an abnormal CXR, or with a high computer-aided detection (CAD) score, even if laboratory tests were not positive, or if culture results indicated non-tuberculous mycobacteria (NTM).
- Advise on management of medical conditions identified among survey participants that may also include those with non-TB-related findings on CXR (if these participants were not already advised in the field).
- For each participant discussed, compile a written individual panel's response for management and referral. This form should be promptly transmitted to a local-level TB coordinator, to ensure proper patient clinical management (i.e. linkage to care). For cases referred at field level, the team clinician or medical officer will be responsible for doing this, with oversight by the medical panel (see **Chapter 9**).

12.4 Staff recruitment

Staff recruitment should start well before the field operations begin. Identifying and recruiting staff – especially those in the field teams – can be a challenge, particularly for positions such as medical doctors and radiographers, for which there could be a shortage within the country. There should be ample time to train all staff before survey implementation, to ensure that staff know what is expected of them and are confident of conducting the required procedures. The central laboratory may also need to start hiring extra staff, depending on the anticipated volume of tests and how that volume may affect routine laboratory work (if this is not done, the survey's conduct and quality will be jeopardized).

Staff can be identified through routine recruitment procedures within the country. Given the temporary nature of the survey, it is worth assessing the possibility of recruiting staff on a secondment basis from universities, research organizations or NGOs for the period required. In some instances, international recruitment may be required if the requisite skillset is not available.

A challenge of many surveys is the staff turnover of those working in the field. As an incentive, some countries implemented a system whereby staff staying for the full duration of the survey would receive a bonus. Nevertheless, procedures should be in place for rapid replacement and training of newcomers, and incentives for retaining staff should be considered. In addition to adequate remuneration, future work prospects after completion of the survey should be emphasized. The survey can be seen as a capacity-building activity to allow for career opportunities within both the NTP and other research programmes.

12.5 Training of the survey team

Training can be considered in two sections: the pretesting by the core survey team (i.e. survey coordinator, central-level coordinators and field-team leaders) followed by the training of the full survey team (**Fig. 12.2**).

Before training of the full survey team can begin, all SOPs and the DMS should be pretested. After each test, revisions to the SOPs and DMS are generally required, so several cycles of pretesting are recommended (see **Box 12.2** and also **Chapter 13**).

The training of the full survey team is important, to ensure that procedures are fully conducted as per the SOPs and are standardized across all teams. The survey coordinator should arrange for such training, either in the institutions implementing the survey or at a location that has facilities to host training courses (**Fig. 12.3**). All

Fig. 12.2

Pretesting and training process

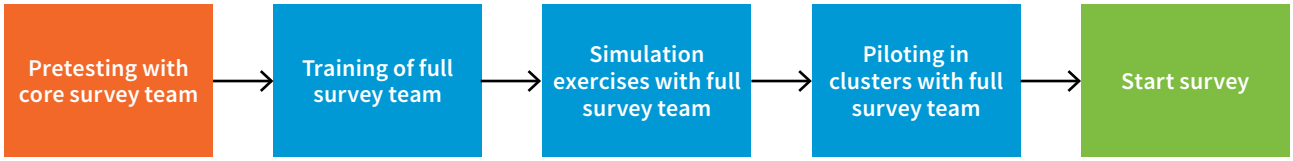


Fig. 12.3

Field team training for the national TB prevalence survey of the Philippines, 2016

Photo credit: WHO/Irwin Law.

staff members should be systematically trained and assessed before being declared suitable for the post to which they have been recruited. This is required for all staff including, for example, the field-team leaders, enumerators, interviewers, radiographers, field laboratory technicians, HIV counsellors and all other fieldworkers.

Staff from the central level should also be trained in survey activities. Technical day-to-day procedures at the central level can be substantially different to procedures in a survey setting. Therefore, the central-level staff involved in the survey should take part in the survey training and be aware of all survey procedures.

A distinction should be made between technical training and survey (field) procedure training. Before training in survey procedures starts, it is important to ascertain that all staff have acquired the technical skills for which they are hired. If new staff are recruited to perform technical skills (e.g. laboratory testing and X-ray taking) it should be ensured that before survey-specific training starts, the staff have acquired the right technical skills and experience to carry out their duties. For example, in Eswatini, staff were deployed in local clinics before the survey commenced, to help them gain additional experience before the survey-specific training started; this was done for laboratory technicians, radiographers and HIV counsellors.

Shortly after training, the full survey team should undergo simulation exercises (i.e. testing of all aspects of the survey in a controlled setting, such as a university or factory), then piloting within non-survey clusters must be conducted. **If amendments are required during this phase, then relevant SOPs and DMS should also be amended; therefore, it is important to ensure there is sufficient time to make such amendments before starting the actual survey** (see also **Chapter 13**). These activities will help to ensure that all survey procedures are well understood and can be deployed in a real-life situation – this will help to build capacity and confidence within the survey team.

In collaboration with the WHO Global Programme for Tuberculosis & Lung Health (WHO/GTB), the WHO Special Programme for Research and Training in Tropical Diseases (WHO/TDR) developed guidance to describe and explain how to apply the principles of good clinical practice (GCP) and good data management practice (GDMP) within the context of national TB surveys *(1)*. Specifically, the guidance aims to ensure the protection of the rights, safety and well-being of all survey participants and the integrity of the survey data, which is further described in **Chapter 11**. **All stakeholders involved in implementing a survey – especially the principal investigator, survey coordinator and survey team leaders – should undergo training in GCP and GDMP, and should understand those principles and be able to put them into practice before conducting a survey.**

12.5.1 Training set-up

The set-up of the training will depend on the proposed composition of the different parts of the survey team, with a central team and a field team. It is best to have all staff trained together at the same time, to facilitate team building and create awareness of the activities performed by others. Such training also makes it possible to conclude the training with a dry run of all procedures, which serves as a final test of the SOPs, DMS and other systems before the piloting begins.

The format outlined in the generic training manual is a 5-day workshop or training format. The first day is a plenary session for all staff that provides an introduction to the survey, and outlines the design and general overview of all procedures. The next 3 days are dedicated to the specific survey activities the different team members need to carry out. For this part, the team is split into smaller groups; several of these training activities can be run in parallel given that not all staff need to attend each module. Part of the final day is reserved for another plenary session, which is used for feedback from the training or for team-building activities. Additional time may be needed to cover all topics or build in more practice, depending on the capacity or prior experience of the survey staff. The pure technical training for the use of X-ray machines, X-ray reading and laboratory activities should be done in advance, to develop enough capacity before other training activities with the rest of the survey team.

The SOPs should be finalized and printed before the training begins, and each survey staff member should have a copy of the SOPs (or at least those that are relevant to the role to which the staff member is assigned).

A generic training manual that describes the objectives, content and methodology for training of survey staff should be developed.

BOX 12.2
PRETESTING OF SURVEY PROCEDURES: COUNTRY EXPERIENCES OF ESWATINI, 2018–2019 AND MOZAMBIQUE, 2018–2019

In Eswatini and Mozambique, table-top exercises were conducted with the core survey team before actual training commenced. This varied from testing the questionnaires with skip patterns[1] in the DMS, through to data collection and specimen collection. In Eswatini, the core survey team undertook exercises in which teams were asked to outline the different stations of the field site and simulate the activities within these stations (**Fig. B12.2.1**). This helped to understand the timing of each station, the participant flow and the resources needed.

In Mozambique, pretesting of the DMS included integration with the CXR system. This was done in a large clinic where all outpatient attendees were asked to volunteer their time to take the survey questionnaire followed by an X-ray and sputum test for TB. These pretests were useful; in particular, they helped in drafting realistic SOPs. This training of trainers was useful for finalizing the SOPs, pretesting the DMS and ensuring that the necessary resources were in place before the formal survey training of all staff commenced.

Fig. B12.2.1

Pretesting of survey procedures and simulation of participant flow by the survey team in Eswatini, 2018

Photo credit: Eveline Klinkenberg.

[1] A skip pattern refers to the situation where the sequential flow of a survey is changed, based on answers to one or more previous questions in the survey.

12.5.2 Training modules

The different roles of the survey will require generalised or specialised training using pre-specified training modules as developed by the survey team (**Table 12.2**).

Module A: Introduction to a prevalence survey

Module A describes the rationale and the design of the survey, as well as the roles and responsibilities of the different teams involved. It should have a strong emphasis on communication, standardized data collection methods and the role of SOPs, and should include content on GCP and GDMP practices. Ideally, all survey staff should complete ethics training and obtain a GCP certificate before the training begins. The training is done through presentations, discussions and group work. The responsibility for this module lies with the survey coordinator, in collaboration with a technical assistance consultant, who could help facilitate implementation of this module if necessary. All survey staff follow this module, whereas other modules are team specific.

Module B: Laboratory procedures

Module B is designed for all TB laboratory staff working as part of the survey, at both the field and central levels. The focus should be on survey-specific con-

Fig. 12.4

Observation of ongoing national TB prevalence surveys by teams from countries planning a survey: a) team from Lao People's Democratic Republic visiting Cambodia; b) teams from Bangladesh and Nepal visiting Indonesia.

a)

b)

Photo credit: a) WHO/Tytaart; b) WHO/Irwin Law.

ditions and issues, and where these will differ from routine procedures. Key issues to address, for example, are registering and labelling of samples, techniques to obtain quality sputum samples, handling of large volume of specimens for Xpert Ultra testing, repeat testing of samples in case of error, follow-up of participants with positive Xpert Ultra test results, sample packaging and transportation procedures, and QA procedures (both internal and external). The methodology used is a combination of presentations, discussions, groupwork and small-scale field testing and proficiency testing. The central laboratory coordinator is responsible for the conduct of this training.

Module C: Radiology

Module C is designed for all field and central staff involved in taking and reading X-rays; this includes the radiology technicians as well as those involved in QA of the field reading. The focus is on technical issues related to TB diagnosis through CXR, and technical issues involved in chest radiography, storage of images and administration. Also highlighted in this module are specific survey conditions with respect to administration, handling of large volume of CXRs, radiation safety regulations and QA procedures. The methodology combines formal presentations and practical exercises, and includes hands-on training in survey activities. In addition, the supplier of the X-ray equipment may also provide training for the survey's X-ray staff about operating the equipment, maintenance and problem solving. If CAD software is used, then specific training of radiologists and field readers is essential, depending on the use case of CAD in the survey (see **Chapter 7**). The central radiology coordinator is responsible for the implementation of this training.

Module D: Survey management

Module D is specifically for the survey coordinator and members of the core survey team. If there is a formal monitoring team, then these members should also receive training in this area. The principal investigator, in collaboration with the technical assistance consultant, is responsible for this training. The focus is on leadership, rapid identification of problems during the survey, assessing monitoring reports, financial management and communication with both the principal investigator and the steering committee. The methodology is mainly through discussions and role play. In addition to the training given in this module, it is of great value for some core team members to visit surveys that are already in progress in other countries, to gain hands-on experience (**Fig. 12.4**).[1]

As previously mentioned, the principal investigator, survey coordinator and survey team leaders should undergo training in GCP and GDMP.[2] They should ensure that all survey team members adhere to the principles, even if they do not take the training themselves.

Module E: Data management

Module E is geared towards the data management team, which includes the data manager at the central level and the members of each field team. The focus of this module is discussion of the formal data management plan

[1] Part of the survey preparation can involve the observation of ongoing surveys in other countries by key survey staff (e.g. survey coordinator, laboratory manager and data manager). WHO has previously organized visits from countries planning a survey to observe survey operations in another country to enhance learning and collaboration.

[2] An example online course can be found here: https://globalhealthtrainingcentre.tghn.org/ich-good-clinical-practice/

Table 12.2

Training modules by team

SURVEY TEAM	SUB TEAM	KEY TASKS	MODULES[a]	SPECIFIC CONTENT	METHOD
Central	Survey coordinator	Management	A, D	• Managerial skills • Identifying implementation problems • Assessing monitoring reports • Communication	• Presentations • Discussions • Group work
Central	Data management team	Data entry Data management	A, E	• Implementing data management plan • Administration • Identifying inconsistencies • Data entry, cleaning and validation	• Presentations • Practical exercises
Central	Laboratory team	Quality assessment of field laboratory Xpert Ultra Sputum culture	A, B	• Technical training • Specimen handling, storage and shipment • QC measures	• Presentations • Practical exercises
Central	X-ray team	Quality assessment of field X-ray Final diagnosis	A, C	• Technical training • Handling and storage of a large volume of images • QC measures	• Presentations • Practical exercises
Field	Team leaders	Management	A, D	• Managerial skills • Monitoring data collection • Identifying inconsistencies • Administration	• Presentations • Practical exercises • Group work
Field	Enumeration (census) team	Enumeration (census taking)	A, F	• Ethics • Population selection • Interview techniques • Administration	• Presentations • Practical exercises • Field visit
Field	Interview team	Interview taking	A, F	• Ethics • Population selection • Interview techniques • Administration	• Presentations • Practical exercises • Field visit
Field	Laboratory team	Sputum collection Xpert Ultra testing Sample packaging	A, B, G	• Technical training • Storage, packaging and transportation of specimens • Xpert Ultra in field conditions	• Presentations • Practical exercises
Field	X-ray team	Screening X-ray	A, C	• Safety • Technical training of radiographic images • Storage and shipment of images	• Presentations • Practical exercises
Field	Data and IT management team	Data management and IT maintenance	A, H	• Implementing data management plan • Data entry, cleaning and validation • IT systems	• Presentations • Practical exercises

IT: information technology.

[a] See **Section 12.5.2** for an explanation of Modules A–H.

(see **Chapter 16**), including administration of the DMS, creating back-ups, data entry and assessing inconsistencies in the data. Practical aspects relate to adequate data capture in the field and to monitoring of data collection through digital dashboards and reporting. There should be a strong emphasis on communication between the field-team leaders, data managers (central and field level) and the survey coordinator. The entire data management team should undergo training in GCP and GDMP before the survey begins. The methodology is explained through practical exercises with the survey database, overseen by the data manager and the survey coordinator.

Module F: Enumeration (census taking) and interviewing

Module F is designed for all staff in the field teams who are interviewing potential survey participants. The objectives are to be aware of ethical issues involved in performing such interviews, learn interviewing techniques, be able to select the appropriate study population (inclusion and exclusion criteria) and have

the necessary administrative skills. Apart from presentations and discussions, practical exercises, role plays and a field trip to "real households" could be used. The responsibility for this training lies with the survey coordinator; however, training in enumeration (census taking) might be best performed by somebody from the central bureau of statistics who has substantial field experience.

Module G: Field specimen collection

In Module G, specimen collectors are trained in approaching study participants, technical issues on specimen collection (e.g. sputum and blood [optional]), packaging and storage of specimens, preparations for specimen shipment and administrative issues. This module is mainly a hands-on training of survey activities, and is overseen by the head of the TB laboratory department. It should emphasize the need to collect sputum samples of good quality, communicate well with participants and create clear documentation. Most participants eligible for sputum collection may not be symptomatic and therefore will probably have more difficulty producing sputum than people seen in the clinical setting; thus, extra emphasis is needed and additional techniques such as physiotherapy should be explained. Survey samples do not become part of the routine QA activities in the country but will be subject to study-specific QA strategies (see **Chapter 8**).

Module H: Field data and IT management

Module H is intended for the data managers in the field (and IT managers, if these are used); it focuses on all activities needed for the adequate monitoring of data collection, administration and maintenance of IT systems. The methodology is a combination of presentations, discussions and practical exercises. There is a strong emphasis on communication between the field-team leaders and the survey coordinator. The survey coordinator in collaboration with the data manager is responsible for this training module.

12.6 Technical assistance and guidance from the Global Task Force on TB Impact Measurement

Countries conducting their first TB prevalence survey may require extensive technical assistance with all aspects of the design, implementation, analysis and dissemination of the survey. However, countries conducting repeat surveys may have sufficient capacity remaining in-country. For all countries, it is important to liaise with the Global Task Force on TB Impact Measurement *(2)*, which is led by WHO, and to ensure alignment to the latest global guidance around TB prevalence surveys, especially topics related to the screening and diagnostic algorithms, and case definitions for burden estimation. This ensures that surveys are designed and implemented in a standardized way. There are several technical agencies and consultants with experience in conducting surveys who work closely with the task force. This close cooperation also ensures that all involved have access to personnel with a wealth of survey experience, including the shared evidence generated from multiple surveys (see **Chapter 20**).

The choice of technical agency will be made by the organizing institution. Often, the agency chosen is one that is already involved with the NTP on a programmatic level or on other research activities. Depending on in-country capacity, a full-time external consultant may be required for specialized areas (e.g. laboratory or data management). South–south collaboration has been a key asset in several surveys, with survey coordinators or other staff from completed surveys assisting other countries with survey design and implementation.

An adequate budget line and associated funding are needed to accommodate external technical assistance (see also **Chapter 15**).

12.6.1 Role of the technical agency

The main role of the technical agency (whether this is one person or a team) is to assist in all stages of the prevalence survey; that is, from initial assessment, design and implementation to analysis and dissemination of results. All activities should be agreed upon within a formal memorandum of understanding (MoU). Despite the involvement of the technical agency throughout the survey, the organizing institution (through the steering committee of the survey) remains ultimately responsible for the survey. Also, the communication with all partners in the survey, including the technical agency, is part of the responsibility of the organizing institution. Proposed terms of reference (ToR) for the technical agency are to:

- identify (in collaboration with the steering committee and principal investigator) the possible bottlenecks in the progress of the survey at all stages;
- provide technical assistance or facilitate provision of such assistance by other identified partners;
- serve as a member of the TAG (or steering committee);
- assist in finalization of the protocol, SOPs, field manual, training manual and budget;
- assist the survey coordinator in the implementation of the survey at all stages;
- arrange regular monitoring visits of field activities; and
- assist in data analysis and dissemination of results.

References

1 Good practices guidance handbook for national TB surveys: how to apply good clinical and good data management practices for national TB surveys. Geneva: World Health Organization; 2022 (https://iris.who.int/handle/10665/360604).

2 WHO Global Task Force on TB Impact Measurement [website]. Geneva: World Health Organization; 2025 (https://www.who.int/groups/global-task-force-on-tb-impact-measurement).

Annex 12.1 Field-team composition: roles and responsibilities of the different fixed team members

The composition of the field team, and the associated roles and responsibilities, will depend on available human resources and the local context. Some roles and responsibilities may be undertaken by the same individual (e.g. enumerators can also be interviewers, radiographers or laboratory technologists).

JOB TITLE	NO. PER TEAM	ROLES AND RESPONSIBILITIES
Field-team leader	1	• Participate in and facilitate trainings • Communicate and coordinate with local, regional and national authorities on issues regarding the fieldwork • Coordinate with community leaders and secure community support • Lead the team at the cluster site • Conduct the presurvey visit • Coordinate and supervise day-to-day field operations, and ensure they are conducted as per the SOPs • Ensure completion of the field-data collection forms and field report • Provide a cluster summary report to the survey coordinator at the end of fieldwork in each cluster • Ensure that data collection is conducted according to the SOPs • Undertake blind rechecking of enumeration and the symptom-screening interview • Maintain an up-to-date referral directory
Medical officer	1	• Read and interpret CXRs taken of participants • Capture all CXR readings on the survey database • Communicate CXR findings to participants who would like to know the findings • Orient survey participants to the next step according to the sputum collection eligibility criteria • Provide leadership and direction to the field-team leader on medical issues that may arise
Data manager / IT officer (field)	1	• Lead the field-data management unit • Coordinate all steps in field-data management • Establish the IT set-up in the field • Prepare the cluster database and data-entry screens • Ensure that data are properly stored and backed up • Check validated data files regularly for systematic errors (cleaning) • Be responsible for completion of required data management reports • Liaise closely with members of the data management group • Liaise with the field-team leader on a daily basis • Promptly report any problems encountered in data management to the field-team leader and, where necessary, to the data manager (central)
Receptionist	1–2	• Provide accurate information at reception to participants about the survey process • Receive participants at reception to verify their identity and obtain informed consent before survey operations at the mobile field site start • Support the field-team members on all data collection, processing and reporting • Support the use of barcoding (e.g. printing barcodes and checking the correct use of barcodes) • Monitor and perform quality checks on the data collected by the field team for accuracy, completeness and consistency at the end of the day
Enumerator	4–6	• Verify the household listings and update as necessary • Invite eligible household members to participate in the TB prevalence survey, as per the SOPs • If required, administer the socioeconomic questionnaire at household level
Interviewer	2–3	• Interview all survey participants for symptom screening and, if required, administer the health care seeking behaviour questionnaire and risk factor questionnaire • Provide survey-specific and general health information to participants waiting at reception

JOB TITLE	NO. PER TEAM	ROLES AND RESPONSIBILITIES
HIV counsellor	1–2	• Provide counselling for HIV testing and inquire about current HIV status –based on the response, offer HIV counselling and testing as per the national algorithm or SOPs • Provide counselling before and after testing to participants accepting HIV testing services • Perform HIV testing as per the national testing guidelines • Ensure clients are referred or linked to care, as appropriate • Support field-data collection activities as the need arises
Radiographer	1–2	• Ensure that X-ray machines are in good functioning condition, perform preventive maintenance as per the training or SOPs, and ensure the appropriate storage of digital images taken • Set up the X-ray unit at the field examination site as per the SOPs and ensure that it is ready for use • Explain the X-ray procedure to all participants before conducting CXRs • Take quality X-ray images and forward them to the field and central X-ray readers • Adhere to the national radiation authority safety guidelines and the guidelines for the protection of participants from radiation
Field laboratory technologist	1–2	• Ensure that samples are collected (from people who screen positive and those who are Xpert Ultra positive), packed well, labelled and transported to the laboratories • Perform Xpert Ultra testing of samples in the field, where necessary, as per the SOPs
Driver	2–3	• Drive vehicles for transporting staff, participants and samples • Assist with setting up the field site and undertake ad hoc duties during field operations as needed (e.g. security, logistical support, and organizing food and lodging)

CXR: chest X-ray; HIV: human immunodeficiency virus; IT: information technology; QC: quality control; SOP: standard operating procedure; TB: tuberculosis.

CHAPTER 13

Field operations

To ensure that field operations for a national tuberculosis (TB) prevalence survey run smoothly, careful preparation, planning and management are essential, above what is included in the survey protocol. TB prevalence surveys require the close involvement of local government, local health service networks and communities. Also, the field operations for these surveys require extensive field testing of the various instruments, training of staff and close monitoring of activities to ensure adherence to standard operating procedures (SOPs). Countries often encounter unforeseen challenges during field operations; hence, the survey team needs to be agile, resourceful and able to communicate effectively.

This chapter explains the principles of field activities. It also provides practical insights on survey activities in the field, including planning, presurvey visits and field operations, and the importance of local government and community involvement.

13.1 Planning the schedule of field operations

A schedule for all the necessary field operations should be developed before the survey begins. The complexity of the schedule will depend on the number of days required for fieldwork in each cluster, the number of clusters, the number of field teams and laboratory capacity. In turn, these factors will depend on the available budget.

The choice of cluster size is based on statistical considerations and operational feasibility (see **Chapter 5**). Most surveys operate with a cluster size of 400–800 participants and aim to complete field operations in a cluster in about 5–7 days. Multiple teams should be working simultaneously, to ensure that all clusters can be surveyed within 12 months. Standardizing procedures across multiple teams can be a challenge, even with well-trained staff; therefore, most countries have only three to six teams for each survey.

The activities within each cluster should be planned carefully, with days allocated for presurvey visits, field set-up, enumeration (i.e. census), screening, sample collection and follow-up. **Box 13.1** summarizes the timelines of basic field activities for each cluster.

The number of screening days will depend on the number of participants that can complete field operations (per cluster) within a day. In turn, this will depend on several factors:

BOX 13.1
EXAMPLE OF A SCHEDULE OF FIELD ACTIVITIES

1. Previsit #1: Occurs 2–3 months before field operations. This is the survey planning and preparation stage. The aims are to inform cluster authorities and health facilities about the survey and obtain their agreement, and to evaluate the physical condition of the cluster.
2. Previsit #2: Occurs 3–5 weeks before field operations. The aims are to finalize the survey plans, decide the demarcation of the cluster, explain the survey steps to the cluster authorities, and decide the survey screening and laboratory sites.
3. Cluster survey operations:
   - Day 1: Arrival and setting up with local collaborators.
   - Day 2: Census – confirmation of household listing, and invitation of eligible individuals.
   - Day 3: Screening.
   - Day 4: Screening.
   - Day 5: Screening.
   - Day 6: Screening.
   - Day 7: Follow-up operations (after which the team moves to the next cluster or returns to base).
4. Feedback of survey results to local TB coordinator:
   - At the end of cluster operations: provide a cluster report with Xpert® MTB/RIF Ultra (Xpert Ultra), chest X-ray (CXR) and HIV results, including a list of referrals and the reason for each referral.
   - Within a few months: produce a report with culture results.
   - After completion of the survey: provide a thank-you letter and a comprehensive report.

- **Number of participants reporting to the survey site.** This is an important driver of the speed of survey operations. About 100–150 people should be invited each day over a 4–5 day period; however, the number of people invited each day may increase if the cluster size is larger or the number of days to be spent in the field is fewer.
- **Speed of flow of participants at the survey site.** This depends on the time each participant spends at each field station, and the number of interviewers available. Typically, the bottleneck is the CXR station because there is generally only one for each field team. Long waiting times may lower participation. It is important to practise the field flow and conduct simulation exercises for each station before the actual survey.
- **Number of CXRs that can be taken in one day.** Most portable CXR machines can take 150–180 CXRs per day, although experience from prevalence surveys in Myanmar (2009–2010, 2017–2018) *(1, 2)*, Rwanda (2012) *(3, 4)* and Viet Nam (2007) *(5)* shows that it is possible to achieve more than 200 CXRs per day.

It may be necessary to complete all the fieldwork from all clusters as quickly as possible (e.g. screening 200 participants per day in 2–3 days), but this creates an overload of work for staff, which in turn has a detrimental effect on staff morale and overall survey quality. Ideally, no more than 150 people should be invited to participate in the screening each day. Scheduling more days of screening in the field will necessitate a higher budget, but scheduling fewer days may compromise data collection and overall survey quality.

Other considerations when scheduling field operations are logistics (e.g. distance to field site, required time of travel, refuelling, supplies and accommodation), weather conditions, national and local events (e.g. elections), workload of field survey staff, time for reporting of the completed cluster work and preparation for the next cluster. Typically, a field team will survey two clusters in a row then take a week off.

The number of teams that can work at the same time often depends on the budget available for X-ray equipment and the availability of specialist staff (e.g. medical doctors and radiographers). Also, although the number of liquid cultures to be conducted is considerably less when using the latest screening and diagnostic algorithms (see **Chapter 3**), laboratory capacity (i.e. availability of human resources and equipment) will limit the number of samples that can be processed and tested at any one time (**Box 13.2** and **Chapter 8**).

Multiple field teams can work simultaneously; also, field teams often visit different clusters in consecutive weeks without returning to base, depending on the distance between clusters. For example, the survey in Cambodia (2010) *(6, 7)* had three field teams. Each week, two teams performed field operations while the third team took a break (rested) (**Fig. 13.1**). Each field team worked for 2 consecutive weeks (completing work in two different clusters) and in the third week the team summarized progress made, replenished materials and rested (for part of the time) and conducted presurvey visits of future clusters.

The 2012 survey in Rwanda *(3)* had a similar set-up, with three field teams recruited. The two teams working in the field at the same time worked in clusters near to the central base. This set-up facilitated supervision activities and sample transportation; also, it was useful when X-ray equipment broke down because, during the repairs, the two teams could share the remaining equipment, with it being used in one cluster in the morning and the other in the afternoon. Mozambique, 2018–2019 and Zambia, 2013–2014 *(8, 9)* also had three field teams, but in these surveys each team was assigned to different parts of the country. Local recruitment of some staff from the different geographical zones facilitated communication with participants who used the local language or languages.

When the survey plan involves blocks of multiple clusters, it is advisable to visit the most logistically difficult cluster last, to avoid postponement of operations in the other clusters (**Fig. 13.2**). For example, an extremely remote or densely populated urban cluster that may require additional days to reach or complete should be visited as the last cluster of a cycle (a cycle being clusters that are visited consecutively without returning to base). It is also advisable to conduct fieldwork in the densely populated urban clusters towards the end of

Fig. 13.1

Example of staggered scheduling for a three-team field operation for a national TB prevalence survey

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9
Team 1	Active	Active	Rest	Active	Active	Rest	Active	Active	Rest
Team 2		Active	Active	Rest	Active	Active	Rest	Active	Active
Team 3			Active	Active	Rest	Active	Active	Rest	Active

TB: tuberculosis.

BOX 13.2
SIMULATED CASE SCENARIO TO SHOW THE IMPLICATIONS OF THE NUMBER OF SURVEY TEAMS ON LABORATORY WORKLOAD

The required laboratory capacity to process samples depends strongly on the anticipated number of participants eligible for sputum collection, which in turn depends on the total number of participants seen on any given day, the sensitivity of screening tools (i.e. the computer-aided detection [CAD] threshold) and the selected screening algorithm (see **Chapter 3**).

For example, when implementing the diagnostic algorithm Option 1, a survey team planning to screen 500 people in 4–5 days will screen about 120 participants per day. Assuming that 15% of those people are screen positive, about 18 participants can be expected to submit sputum samples (see **Chapter 8**). Submitting two samples per participant means that 36 samples can be expected to be tested in the field with Xpert Ultra; hence, additional cartridges (about 5% of the original total) are likely to be needed for repeat testing of samples that have indeterminate results.

Participants who are Xpert Ultra positive will be required to submit two more samples for liquid culture. Positivity rates will vary by country but are likely to be about 5% of screen-positive participants; that is, about one in 18 participants who are screen positive are likely to be eligible for culture, and two samples for culture should be requested from those participants. If screening positivity rates increased from 15% to 30%, this would mean about 36 participants being screen positive, 72 samples being required for Xpert testing, and possibly up to eight additional samples (from four participants) needing to be taken for liquid culture.

If three to five field teams are working simultaneously, the number of samples will greatly increase (**Table B13.1.1**). Such an increase would affect the amount of Xpert Ultra testing in the field (and therefore the total number of machines and cartridges that need to be available); it would also affect the number of cultures that need to be processed within a short time, and the number of mycobacterial growth indicator tube (MGIT™) machines required to incubate the culture tubes. **Chapter 8** provides further information on capacity needs for the laboratory, which depend on the selected diagnostic algorithm.

Table B13.1.1

Projection of number of samples to be expected, based on the number of participants screened and the percentage anticipated to be screen positive if a country implements diagnostic algorithm Option 1

NUMBER OF PARTICIPANTS SCREENED PER DAY	% OF PARTICIPANTS WHO ARE SCREEN POSITIVE	NUMBER OF PARTICIPANTS WHO ARE SCREEN POSITIVE	NUMBER OF SAMPLES FOR TESTING BY XPERT ULTRA / LIQUID CULTURE[a] PER TEAM	NUMBER OF SAMPLES FOR TESTING BY XPERT ULTRA / LIQUID CULTURE FOR 3 TEAMS	NUMBER OF SAMPLES FOR TESTING BY XPERT ULTRA / LIQUID CULTURE FOR 5 TEAMS
80	15%	12	24/1.2	72/3.6	120/6
80	30%	24	48/2.4	144/7.2	240/12
120	15%	18	36/1.8	108/5.4	180/9
120	30%	36	72/3.6	216/10.8	360/18
160	15%	24	48/2.4	144/7.2	240/12
160	30%	48	96/4.8	288/14	480/24
200	15%	30	60/3	180/9	300/15
200	30%	60	120/6	360/18	600/30

[a] Two samples per participant to be collected for Xpert Ultra, plus an additional two if the participant is Xpert Ultra positive. For the purposes of this table, the positivity rate for Xpert Ultra was assumed to be 5%. For Xpert Ultra cartridge planning, it should be assumed that there could be 5% extra for repeat testing in case of indeterminate results.

Fig. 13.2

Careful planning of cluster operations for the national TB prevalence survey of Ethiopia, 2010–2011

Photo credit: Marina Tadolini.
TB: tuberculosis.

the survey once the teams have gained more experience with survey operations.

Annex 13.1 shows a survey calendar with different numbers of field teams, to estimate the entire survey duration. This can help in making a realistic timeline and can guide the final decision on the number of field teams, striking a balance between time and budget availability. Once survey operations start, the calendar can also be used as a monitoring and planning tool, and can be adjusted as the survey progresses.

13.2 Standard operating procedures

The field activities should be carried out according to SOPs, as described in **Chapter 2**. The SOPs should explain how different components of the survey's field activities link with each other because teamwork is essential and most procedures are interlinked. In the field, there is often no opportunity to quickly contact the survey coordinator when an unexpected problem arises; hence, the SOPs should give detailed descriptions of procedures and what to do in certain difficult situations that may arise. The SOPs form the basis for the training (see **Chapter 12**), and should be amended if survey procedures change after testing or training.

Features such as examples, case studies and frequently asked questions (FAQs) can help staff to understand the SOPs, which will be living documents. For example, during the survey itself, material will be added to SOPs to share the field teams' experiences and lessons learned from challenges in the field, and to ensure standardized responses across teams. Regular field supervision by the core survey team[1] is critical to ensure adherence to SOPs and standardization of procedures across field teams. **Chapter 14** provides more details on monitoring and supervision.

13.3 Mobilization and involvement of local government and communities

The success of fieldwork during a TB prevalence survey depends on close cooperation with the communities where the survey is conducted. Such cooperation is possible only when the project is supported by stakeholders beyond the public health services, community leaders are consulted by the research team, and community members are properly informed about the objectives and the conduct of the survey.

Full support for the survey from the ministry of health is vital, even though the survey itself may be carried out by a third party (e.g. a research institute) outside the ministry. This support should be communicated to all relevant authorities at the administrative levels that are involved in the implementation of the survey (e.g. states, provinces, districts and local communities). The goal is for the survey team to obtain full cooperation from the relevant authorities within the local administrative unit and the communities where the survey is being conducted. For example, the ministry of health may directly inform local health and relevant authorities, or the national TB programme (NTP) may use its decentralized infrastructure to notify peripheral levels.

In terms of communication, the most important aspect is direct contact with the community. Three occasions are often used to facilitate community involvement: the assessment visit, the previsit and the cluster operations themselves.

Even if local authorities and community leaders support the survey, this does not guarantee that community members will cooperate with the survey team. Several activities can help to improve community participation (much of this work can be done on arrival in the community):

- provide adequate information to the community; for example, by explicitly defining:
  - all target groups in the community that should be informed;
  - the message to be conveyed;
  - the means of conveying the message;
  - the timing of providing the information; and
- ensure that field activities create minimal intrusion and do not overlap with locally organized events or gatherings.

The message conveyed to the community should be simple and direct, and its phrasing should be carefully considered. It is best to use neutral phrasing and simple wording, and to include visual aids (e.g. a leaflet and poster). The essential parts of the message are:

[1] The core survey team, as described in **Chapter 12**, comprises the principal investigator, the survey coordinator, the central-level coordinators and the field team leaders.

- the objective or objectives, time frame and venue of the survey;
- an explanation of the methods to be used (CXR, questionnaires and sputum examinations);
- the benefits (early detection and treatment of TB) and risks, and possible disadvantages to the participant; and
- a clear description of the process that will be followed if any abnormality (TB or other disease) is detected.

A more detailed message about the survey and its processes will be given to individual participants during the process of obtaining informed consent (see **Chapters 6** and **11**). Ways in which these messages can be conveyed to community members include community meetings, leaflets, drama or song performances, church and other local leaders, community radio stations, and print and other media platforms. The research team should discuss with the community leaders which methods are most appropriate and effective for the community.

Having a focal person from within the community taking part in conveying the message will strengthen the community's trust in the survey team. Good community sensitization will increase participation and community engagement. This could be undertaken by the communication department of the ministry of health or by health-communication specialists. Having a high-level person (e.g. the minister of health or another influential figure) visit one of the first clusters in operation, with good media coverage, can also boost participation and demonstrate the national focus of the study.

Field activities must be designed to minimize inconvenience to community members, to ensure their cooperation. The best approach involves a careful trade-off between the need for certain activities and the convenience of the participants. Issues to consider in carrying out the survey activities are timing (including the season; e.g. rainy season, harvesting season and cultural activities) and location (i.e. the survey base).

The working hours of the survey team should be tailored to the activities of the community rather than the other way around. For example, in urban settings, residents may have fixed working hours during the week and be more available during evenings and weekends. Religious events (e.g. Friday prayers or Sunday services) should also be considered when planning operations in specific settings.

Fig. 13.3

Poster for the national TB prevalence survey of Myanmar, 2017–2018

TB: tuberculosis.
Source: National TB programme of Myanmar (reproduced with permission).

The national TB prevalence survey of Myanmar (2017–2018) *(1)* used the image of a famous Myanmar singer-songwriter and actor, Mr Sai Sai Kham Leng, on a poster (**Fig. 13.3**):

> *"Even though tuberculosis is a curable disease, it is still a public health problem in Myanmar. Therefore, we need to conduct a survey to understand the TB situation. From this survey, you and your family may be diagnosed with TB, provided with effective treatment, and prevent the spread of TB. In addition, we will know how many people have TB in the whole population. Based on this information we can plan effective strategies to control TB. You are cordially invited to participate in the national TB prevalence survey."*

In South Africa, a leaflet (**Fig. 13.4**) was distributed to illustrate the examinations that would be carried out during the survey operations. The leaflet also explained

Fig. 13.4

Explanatory leaflet and promotional material used during the national TB prevalence survey of South Africa, 2017–2019

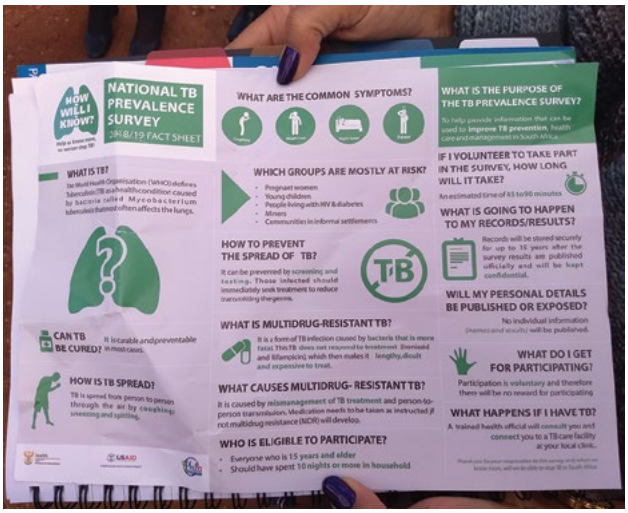


Photo credit: Eveline Klinkenberg.

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

that survey examinations would be free, as would treatment if TB was detected.

13.4 Field activities

The field activities of a TB prevalence survey should include the preparation and testing phase, the pilot survey, preparation visits (presurvey visits), field data collection and follow-up activities.

13.4.1 Survey readiness

It is important to delay the start of field operations until all preparations have been completed and a pilot has been successful. A checklist could be created to assess and score survey readiness, and to list key outstanding issues (**Table 13.1**). In addition to having tables for each subsection, a separate table could be prepared that details the status of all outstanding tasks.

13.4.2 Pretest and piloting

A pretest (or simulation) of survey procedures should be undertaken once SOPs are ready, equipment is available and the data management system (DMS) is in place. The pretest should take place in an environment where many people can voluntarily attend without the need for a household census; for example, in an office area or a university dormitory (see **Chapter 12**). The testing could also be done as a desk simulation exercise. The pretest ensures that the core survey team know their roles before they act as trainers for the full staff training. If the pretest shows that procedural amendments are needed, then the SOP should be amended accordingly.

Once the SOPs have been finalized, the DMS has been extensively tested (see **Chapter 16**) and training of staff is complete, a pilot survey with community participants should be carried out in at least two mock clusters. This pilot should take place a few weeks or a month before the anticipated survey launch. Although pilot clusters will be outside the list of chosen survey clusters they should be representative of the communities and areas to be visited. Where possible, the pilot survey should include two different settings (e.g. urban and rural), because of the different challenges in such settings; in such cases, the first pilot cluster should be selected from an area that is easily accessible. All survey instruments and all procedures should be tested during the pilot phase, especially the household enumeration, use of electronic data collection tools, taking of a CXR with the use of CAD (if implemented), testing of sputum specimens with Xpert Ultra in the field, and transportation of specimens. Additional staff (e.g. supervisory staff or trainers) should be put in place to provide direct monitoring or on-the-job training for the field teams during the pilot. The pilot should be run with the same number of staff that will participate in the actual survey field operations. Data collected during the pilot should not be included in the survey dataset but should be used to assess the pilot. Any participant in the pilot survey identified as having TB, HIV or requiring serious medical attention should be managed appropriately. Once the pilot is complete, additional time should be factored into the schedule to discuss any lessons learned, additional training of staff and amendments to be incorporated into the SOPs.

If there are still considerable problems after the first pilot (**Box 13.3**), then a second pilot should be planned.

Table 13.1

Example checklist to assess survey readiness

KEY SURVEY READINESS INDICATORS	STATUS	REMARK (EXAMPLES)
Has ethical clearance been obtained to start the survey?	Yes	National ethical clearance number is ERC123456
Have all permits from different authorities needed to start the survey been obtained?	No	Permits obtained from all district security officers and the national radiation authority, but permit from the head of subdistricts is pending
Is there an organizational structure for the survey (e.g. steering committee and technical committee)?	Yes	Check how often the committees are meeting
Have the core survey team undergone training in good clinical practice and good data management?	No	Only the data manager has undergone training
Have the clusters been selected and has a schedule been developed?	Yes	See protocol
Have the SOPs been finalized, including the data management plan?	No	Need to change laboratory algorithm in protocol
Is all equipment for all teams available; has it been tested, serviced and calibrated; and is it functioning?	No	Issues in power supply observed and a shortage of IT equipment (i.e. barcode printers)
Is the DMS accurately capturing all data at all stations, and are dashboards used?	No	DMS is functioning overall but some adjustments are still needed; central part has not yet been tested and not all dashboards have been developed
Have all survey staff been recruited and trained to carry out procedures as per protocol and SOPs?	No	Staff have been recruited but some refresher and additional training is needed
Has the central laboratory been assessed and approved to be ready to deliver the requested services?	No	The laboratory has been assessed but QA procedures for culture are not complete (i.e. positive control)
Is the central radiology team ready to deliver the capacity required?	Yes	Services will be outsourced to company X; an agreement has been drafted but the set-up needs to be tested and piloted
Is the data management unit ready? Have a simulation and a pilot test of the DMS been done?	No	Not all IT equipment has been delivered and set up
Is all procurement completed?	No	Critical IT items are still missing, especially some of those needed for full survey operation (there are only enough for the pilot test)
Is the sample transportation system (field to central laboratory) in place?	Yes	

DMS: data management system; IT: information technology; QA: quality assurance; SOP: standard operating procedure.

It is better to do this than to start survey operations while the team or teams are not ready, which would jeopardize the quality of the data collected and the conduct of the full survey. As an example, in Eswatini, a pilot done immediately following the training indicated that teams were not yet fully ready to start field implementation – they needed more practice. A second pilot was successfully conducted, after which field implementation could start immediately.

13.4.3 Presurvey visits

The local communities where the survey is being implemented should be visited by members of the core survey team and the local TB programme during the preparatory stage of the survey (Fig. 13.5).

Presurvey visit 1

The first presurvey visit is typically arranged well before the survey operation plan is finalized (e.g. 1–2 months before the second presurvey visit). A member of the core survey team should participate in these visits. The objectives of this first visit are to:

- explain the objectives and procedures of the survey to relevant local authorities and community leaders;
- obtain consent and confirm the commitment of local authorities and community leaders to implementing the survey;

Fig. 13.5

Schematic of the order of the two presurvey visits before the start of field operations

BOX 13.3
EXAMPLE OF PROBLEMS IDENTIFIED DURING PILOT SURVEYS OF NATIONAL TB PREVALENCE SURVEYS THAT WERE RECTIFIED BEFORE FULL FIELD OPERATIONS COMMENCED

Cambodia, 2002 *(10)*: Survey staff had difficulties in explaining the survey procedures to people who were illiterate or those who were absent during home visits. In response to this situation, visual aids with photos of the field operation were developed to explain survey procedures. Each household was given a small notebook that had photos of survey procedures on the front and back covers, and information on the survey rationale, benefits and risks on the first few pages. The rest of the notebook was empty and could be used by individuals or households for their own purposes. The usefulness of the notebook meant that it was less likely to be thrown away after reading, as is often the case with leaflets.

Cambodia, 2002 *(10)* and Myanmar, 2009–2010 *(2)*: National reference laboratories in both countries are internationally certified and have successfully completed national TB drug resistance surveys; nevertheless, some of the laboratory results from the pilot prevalence surveys were questionable. Laboratories were not accustomed to receiving a large quantity of specimens of poor quality. Systematic contamination was seen in Cambodia, whereas excessive decontamination processes were seen in Myanmar. In Cambodia, these problems were rectified by retraining staff and adjusting survey procedures, but this delayed the start of the survey by a month.

Ghana, 2013–2014 *(11)*: The field operation site was equipped with more than 10 laptops. Only by trialling the system in a pilot did the team realize the challenges of transferring data between laptops and accessing a protected power supply. In addition, effective communication with participants was found to be important because in one instance a participant provided a non-sputum specimen in the specimen container.

Philippines, 2016 *(12)*: The field teams' misunderstanding of certain terminology meant that the survey data collection tools were not correctly filled in during the pilot testing. In response, a retraining workshop was held, where the trainers also reminded the survey team to "smile" and engage more with the participants, rather than focusing solely on survey procedures. Another lesson learned centred around the unavailability of CXR machines during the pilot. Only when the team conducted the actual survey did they encounter CXR equipment that failed due to the extremely hot conditions (requiring a pause in survey operations until the CXRs cooled down and were functional again).

South Africa, 2017–2019 *(13)*: Lessons learned from the survey were mainly about participation. In the pilot, it was found that the proportion of screen-positive participants who returned the following day to submit a second sputum sample was lower than expected (59%). This necessitated a change in the protocol to collect both samples on the same day, an hour apart. Another major lesson learned was the need to conduct survey activities from early morning through to late in the evening (including during the weekend), to maximize participation in the household enumeration (census) and screening activities.

Indonesia, 2013–2014 *(14)*: During the pilot it was found that the number of survey team members was not sufficient for the allocated workload of the field operation in each cluster. As a result, the health facilities and the district health officers were asked to allocate more staff to support the screening operation. Following the pilot, the survey team also developed a system to trace participants who did not attend the field operations. This was achieved by identifying the invitees who did not attend until the last screening day, and by sending members of the survey team and local authorities to remind those who had been invited to come for screening.

- obtain a list of the population or households if available; and
- assess the situation for the survey team in terms of accessibility; the availability of electricity, food and water, and accommodation; security; timing of important local events (e.g. holidays or elections); and seasonal conditions.

The availability of population data from each survey cluster will assist in the development of the field operation schedule. Detailed population data may already be available from a recent national census. Planning of the survey census is best done in close consultation with the country's national bureau of statistics or equivalent. In some countries, the bureau has been involved in planning, training and recruiting field staff to conduct the survey census. Even in countries where vital registration data are not officially available, local community offices or public health facilities often keep household lists updated; for example, for the Expanded Programme of Immunization, the Maternal and Child Health Programme and agricultural development projects. It may be possible for local health workers to obtain population data and copy them onto the survey household forms in advance of the second presurvey visit. The field operation schedule should only be finalized after a full assessment of all the candidate clusters has been completed.

The first presurvey visit is vital in establishing a good working relationship between the local communities and the survey team. Hence, the core survey team and local TB programme must meet the right people within each community. At this stage, to avoid unrealistic expectations, the team should ensure that local authorities and community leaders are aware that:

- this is a (national) survey requested by the government;
- the survey is still at the planning stage;
- the survey may not be able to cover entire communities;
- the subset of the community (e.g. a particular village or household groups) that will receive examinations will be defined at a later stage;
- participation in the survey is free and voluntary;
- the survey is primarily focused on screening and testing for TB (and other comorbidities as defined by the survey protocol); and
- the survey results will help to improve TB control in the country; hence, community participation is critical.

After this first contact, local health authorities and the NTP should keep local authorities and community leaders informed about the progress of survey preparations and the tentative schedule of field operations in the specific area.

Presurvey visit 2

The second official contact will be a presurvey visit that typically occurs 3–5 weeks before the actual field operations. The field team leader should visit the cluster with the responsible local TB coordinator and district health officer or officers. One full day may be required for each cluster, and the visit should coordinate with ongoing field operations. The objectives of this second visit are to:

- discuss and finalize the survey operational plan (including logistics and the local human resource management plan) with local stakeholders;
- map the cluster areas and exclude some facilities (e.g. schools, correctional facilities and military institutions) from the sampling unit, according to the survey's inclusion and exclusion criteria;
- define the sampling area – when the sampling design does not require part of the final sampling unit to be included, the second presurvey visit is easier;
- identify the survey area where field operations will take place; usually, this will be a place that is well known to the community and easily accessible;
- discuss the community mobilization plan that will be used to facilitate participation in the survey;
- provide campaign materials (e.g. posters and leaflets for the community); and
- orient local health workers or equivalent personnel to prepare a population list within the households of the selected survey areas.[1]

The survey team should identify the community members who need to be engaged to ensure high community participation. These could be local health care providers (e.g. governmental, nongovernmental and private), community-based organizations and community leaders (e.g. religious leaders and teachers).

The team should explain the details of the survey operations to community leaders. First, it is essential to designate survey sampling areas (i.e. household groups) according to the survey sampling design as laid out in the protocol (see **Chapter 5**). This must be done in a transparent manner when only part of a cluster is included in the survey (e.g. where the population of a village is larger than the target cluster size). Next, in consultation with the community, the exact location of the mobile field site should be decided and local volunteers appointed. During this visit, orientation of local staff to prepare the household enumeration (census) can also be done, if necessary (see **Chapter 6**).

It is best to only inform the wider community about the survey shortly before the actual survey takes place.

[1] In countries where local population data are not reliable and local capacity to prepare the population list is doubtful, the previsit team may include enumerators (census takers), who extend their stay to complete a census for the survey. The enumeration (survey census) might be carried out independently from the survey operation days in a cluster.

Fig. 13.6

Examples of where survey staff were sleeping during field operations: a) camp site near the cluster during the national TB prevalence survey of Mozambique, 2018–2019; b) school hall during the national TB prevalence survey of Ethiopia, 2010–2011

a)

Photo credit: Eveline Klinkenberg.

b)

Photo credit: Marina Tadolini.
TB: tuberculosis.

This helps to prevent the bias of intentional survey participation by people who want to be screened (e.g. people may falsely declare TB symptoms, to seek further medical examinations and receive care from the survey team). Communication about the survey can be done by community leaders and health workers during the period between the presurvey visit and survey operations or it can form part of separate enumeration activities that take place before the arrival of the main survey team.

Where several of the cluster villages lack access to stable electricity and clean water, the survey team will need to bring a generator and water supplies. The capacity requirement of the generator should be assessed carefully by an electrical engineer. A bigger capacity is not always better, because the generator is probably the heaviest piece of equipment that the team needs to carry. Another option to consider is renting a generator from the local community. During the presurvey visit, the team should investigate the availability of a back-up generator from the local community and processes for renting that generator.

Access to local markets with bottled water and to local facilities with freezers to produce ice or ice packs for cold chain should also be examined in advance. Canopies and furniture (e.g. desks and chairs) are also usually available locally. In terms of accommodation, in Mozambique, the field staff sometimes camped because there was no accommodation, given the remoteness of some clusters, whereas in Ethiopia, survey staff were accommodated in schools when hotels were not available (**Fig. 13.6**).

13.5 Cluster operations (field data collection days)

13.5.1 Arriving in the community

The field team leader and the enumeration staff may arrive at the cluster either one day earlier than the CXR and laboratory units, or on the same day. Basic activities on the day of arrival are:

- greeting community leaders;
- meeting with relevant people including local volunteers;
- organizing a community meeting, if necessary;
- receiving prepared household lists;
- counting the number of individuals who may be eligible to participate;
- based on the expected number of eligible individuals in the household list, deciding whether it is necessary to add some village household blocks to reach the required sample size or to omit some blocks to stay within the cluster size;
- developing a precise household visit plan for the enumeration (i.e. who from the team will visit which block, in which order and with which local volunteers);

- setting up the survey site (e.g. with clear and visible instructions, posters and banners); and
- establishing a place for accommodation and supplies.

The survey team should wear some sort of uniform (even if it is just a T-shirt designed specifically for the survey) with a name tag. Local volunteers should receive a similar uniform but in a different colour, to distinguish them from the survey team members. To ensure security, the local police station should be contacted in advance; it may also be necessary to recruit night guards.

13.5.2 Enumeration (census) of the households

A complete list of all the people in the area demarcated within the cluster is critical for knowing who to invite and follow up, and to accurately define the denominator for when the survey is being analysed. The aim of the enumeration is either to physically verify the list received from the community leaders (or collected during the presurvey visits), or to develop a new list if this was not previously possible.

When household population lists are lacking or the local stakeholders have not had the chance to develop such a list beforehand, it may take the survey enumeration team 2 or more days per cluster to develop the list. Even in situations where a list has already been generated, the team still needs to visit all households to confirm the number and identities of the individuals in that list, and to distribute the survey invitations. This activity is a good opportunity for the survey team to establish effective communication and rapport with the community, and thus make follow-up activities easier to carry out.

The enumeration team – comprising the field team leader, receptionist, interviewers and others trained in the activity – in collaboration with the local community, should accurately enumerate the population of the cluster (**Fig. 13.7**). This activity is sometimes carried out together with staff from the national bureau of statistics. At a minimum, one field team and one local community member should form an enumeration team. A few teams may combine under the guidance of the survey team leader to visit different households within the same cluster. This can be done either at the start of survey activities or 1–4 weeks ahead of time, depending on the survey organization. The survey team must be accompanied by appropriate people trusted by the community members, such as health volunteers, as the team moves from house to house.

Countries vary in the way they organize the enumeration (**Fig. 13.8**):

- in Indonesia and Zambia, a separate team conducted the enumeration of one cluster 1–2 weeks before the rest of the field team arrived in that cluster;
- in Cambodia and Rwanda most, if not all, of the enumeration of one cluster was conducted in a single day, after which screening at the mobile field site commenced, with one or two field staff completing any outstanding areas of enumeration; and
- in Eswatini, Mozambique and South Africa, the enumeration and screening overlapped by a few days, with different field staff undertaking the two activities.

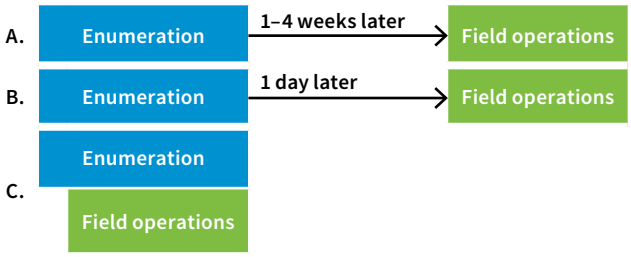
Fig. 13.7

Field team visiting households and inviting individuals to participate in the national TB prevalence survey of Myanmar, 2017–2018[a]

Photo credit: WHO/Irwin Law.
TB: tuberculosis.
[a] As illustrated, some households are harder to access than others.

Fig. 13.8

Different timelines used to enumerate a cluster before field operations



A. Enumeration conducted by a separate team before the field team arrives.
B. Enumeration conducted by the field team before the survey commences.
C. Enumeration conducted at the same time as the field operations.

The time needed to conduct the enumeration will depend on factors such as:

- cluster size;
- population density;
- terrain (e.g. flat areas, hills, mountains and rivers), road conditions and weather;
- availability of an updated household population list; and
- other survey components such as a household assessment of socioeconomic status.

A single day is usually enough to complete the listing of 150–200 households with 500–700 eligible subjects (1000 population). This can be achieved by three or four enumeration team members, provided the household list has been prepared in advance by local health workers or authorities. If more days are needed for larger sized clusters, this does not mean delaying other activities until the cluster census is complete. Instead, eligible individuals from the first few days of the enumeration can be examined on the following day while the enumeration continues in other parts of the cluster.

This activity is a key first step in enumerating the eligible survey population of each cluster, from which the eligible individuals are invited to attend the field site. Typically, an eligible person is someone who has lived in the household for the past 14 days and is aged 15 years and older.

The objectives of the enumeration (by means of household visits) are as follows:

1. In each household, to **brief a household member on survey activities** (information sheet or leaflet may be provided).
2. To complete or **verify** (if prepared in advance) **the household listing** by:
   — interviewing a household member to verify the household list;
   — deleting from the list those who have died, or who have not lived or stayed in the household for the duration defined in the protocol;
   — adding to the list those who stay in the household but do not appear on the initial household list, as prepared by community members; and
   — collecting socioeconomic information from each household to determine socioeconomic status, if required.
3. To **allocate a survey household number to each household** (this is a survey-specific unique number for each household in a survey cluster). The household number may be pasted on the entrance or wall of the house (with the permission of the household member). In recent digital surveys, household numbers have been automatically generated or manually assigned.
4. To **identify and invite eligible individuals** to attend the survey site, based on the completed household listing. In digital surveys this can be an automated process using age and residence criteria. The aims are to:
   — provide a unique individual survey number to all individuals including children (depending on the database design – see **Chapter 16**);
   — evaluate each person's eligibility for an invitation to participate in the survey according to the criteria defined in the survey protocol (the invitation should be issued, regardless of a person's expected availability on the survey day, or their willingness to participate);
   — issue individual invitation cards with the expected day and time slot, and venue to all eligible subjects (e.g. Wednesday 15 January 2025, 1.00 pm–5.00 pm, at the community hall):
     - if household members are not physically met during enumeration, then invitation cards can be left with the head of household or responsible person of the household; and
     - barcodes can be affixed to the invitation cards for easy and quick access to the individual's information at the screening site (the barcodes can be automatically generated in the household or can be prepared in advance and affixed to the invitation card in the household).

Several countries have used maps to identify predefined enumeration areas (**Fig. 13.9**). Maps can also be used to verify whether all structures have been surveyed, by plotting the geocoordinates of each listed household (including refusals) on Google Earth, to ensure that all households have been covered or that particular areas have been left out. This technique is especially helpful in areas of irregular settlements where there are no clear streets.

The survey team and local volunteers should wear a uniform (e.g. a T-shirt designed specifically for the survey) so that they are easily identifiable by the community.

Fig. 13.9

Map used to identify a demarcated enumeration area in the national TB prevalence survey of Lesotho, 2019

TB: tuberculosis.
Source: National TB programme of Lesotho (reproduced with permission).

The enumeration is a good opportunity to provide the community with information on the survey and to answer specific questions. Also, for those aged 15–17 years, the enumeration provides an opportunity to explain the necessity of obtaining both the person's assent and consent from a parent or a guardian (see **Chapters 6** and **11**).

After completing the enumeration of the cluster, the household lists are compiled from each enumeration team to determine the total number of eligible participants (invitees). During survey examination days, the receptionist can use the household list as a survey register. In digital surveys, data from all enumeration teams can be compiled electronically (see **Chapter 16**). During the Myanmar survey (2017–2018), the census was carried out on Sundays because the chance of meeting at least one adult in the household on Sundays was higher than on weekdays.

Once the enumeration has been finalized, the household and population list should be locked and should not be edited. Anyone presenting spontaneously to the survey site asking to be included in the survey should not be added to the survey population, because that person might not belong to the designated cluster area. It is important to explain this to the community leaders well in advance, so that the leaders can convey the message to villagers belonging to households outside the survey area and to people living in other villages.

13.5.3 Mobile field site set-up

The mobile field site should be constructed in such a way that participant flow is as smooth as possible, with stations set up in a logical order. **Fig. 13.10** outlines a schematic flow of a mobile field site and **Fig. 13.11** shows examples of field sites.

13.5.4 Screening days

Before welcoming the survey participants, the team leader should ensure that everything is ready for starting operations for the day. Each station should be checked by one or more of the team members using a checklist as per the SOP; if any issues are found, the

team leader should be alerted. The field data manager should ensure that all aspects of the digital data collection system (especially the local area network [LAN]) are operating correctly (**Fig. 13.12**). The roles of all team members and volunteers should be reconfirmed – they need to understand the flow of participants as well as the survey instruments, because the location of each station may vary from one cluster to another. A banner in front of each field site will help to inform the community about the survey (**Fig. 13.13**).

Reception

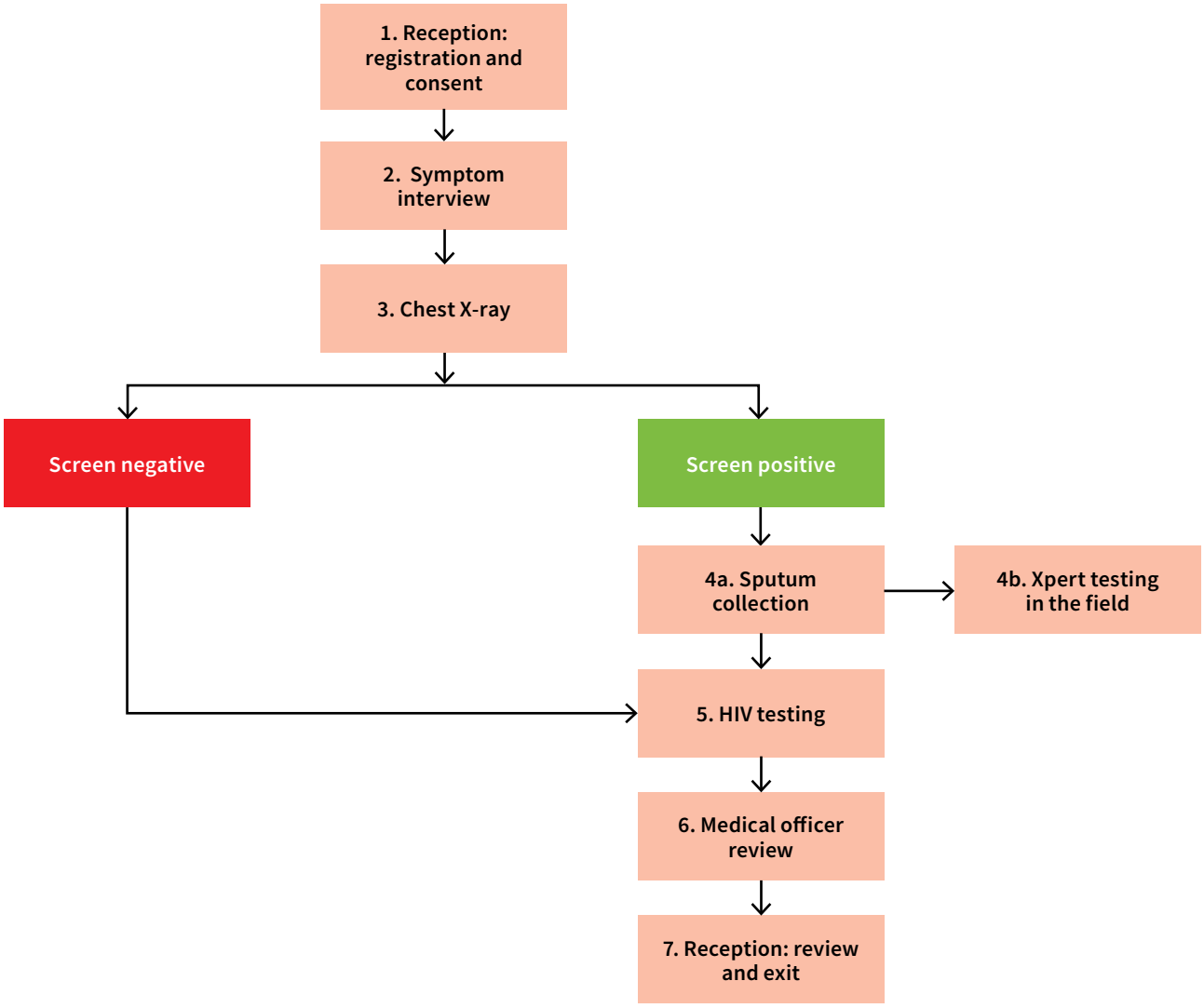
A receptionist welcomes survey participants to the field operation site (**Fig. 13.14**). A local health worker may assist the receptionist, and local volunteers will help participants to create a queue if many people arrive at the same time. The receptionist checks the participant's invitation card (containing the survey identification [ID] number) against the enumeration listing (survey registry) to confirm eligibility and identity based on name, age and sex. The receptionist should use a barcode scanner to scan the invitation card; this registers the individual in the database (see also **Fig. 16.9** in **Chapter 16**) and is a critical step in the data management process because it forms the list of participants.

Many previous surveys have issued a paper tracking form at reception (or integrated as part of the invitation card), listing all the stations of the field site. Survey staff then tick the paper form at each station to indicate that the participant has attended (**Fig. 13.15**). This approach can be helpful in managing the participants onsite and cross-checking against the database. Also helpful is providing all participants with a lanyard that can hold printed information, including a chronological participant number based on when the person arrives at reception – this can help with crowd management, participant flow and data quality.

Informed consent (or assent) can be obtained at recep-

Fig. 13.10

Schematic of participant flow through the mobile field site of a national TB prevalence survey



HIV: human immunodeficiency virus; TB: tuberculosis.

Fig. 13.11

Mobile field sites in national TB prevalence surveys of a) Lesotho, 2019; b) Myanmar, 2017–2018; c) South Africa, 2017–2019; and d) Eswatini, 2018–2019

a)

Photo credit: WHO/Irwin Law.

b)

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

c)

Photo credit: South Africa TB prevalence survey team.

d)

Photo credit: Eveline Klinkenberg.

tion, but in some surveys consent has been obtained at a separate station after reception (**Fig. 13.16**) or by the interviewer of the symptom-screening station (see **Chapters 6** and **11**). Also, some surveys have included a group information session for participants at which a team member explained survey procedures, risks and benefits in addition to an information sheet. The session can occur before or after the reception area when participants are waiting at the survey site (**Fig. 13.17**). In the Philippines survey (2016), each individual attending reception was provided with a tablet computer and asked to watch a short video describing the survey procedures explained in the local language, before being asked to sign the consent form (see **Fig. 6.3** in **Chapter 6**).

Participants who need more explanation should be can meet a team leader or other designated staff if they would like further information. People aged 15–17 years need to sign a separate assent form; they also need to have consent from a legal guardian.

Where a person has disabilities that limit or prohibit their ability to provide informed consent, if a country's ethical review allows, the guardian's consent is sufficient to involve that person in the survey. In this situation, screening information may be provided by family members instead of the participant. If it is difficult for a person with disabilities to participate in an interview or receive a CXR, that person should not be forced to participate.

Fig. 13.12

Field data manager doing a routine check of the IT system during the national TB prevalence survey of Cambodia, 2023–2024

Photo credit: WHO/Tytaart.
IT: information technology; TB: tuberculosis.

Fig. 13.13

Example of banners used in the national TB prevalence surveys of a) the Gambia, 2012 and b) Viet Nam, 2017–2018

a)

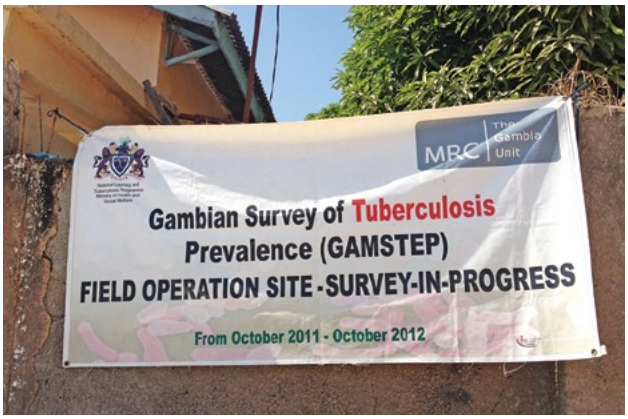


Photo credit: Marina Tadolini.

b)

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

Fig. 13.14

A participant's details are being verified at the reception of the field operation in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

Individuals from outside the cluster or other non-eligible people may arrive at the field site seeking medical examinations. When this occurs, it may be appropriate to ask local community leaders to communicate with these individuals, to explain why they cannot be included in the survey; also, if these people are unwell, local health workers should be consulted. If a non-eligible person presents as an emergency, a local health worker may ask the survey team's medical officer to see that patient. The team leader or a medical officer may decide on humanitarian grounds to undertake a CXR, especially in remote areas where such examinations are rarely available; they may also decide to undertake a CXR for political or psychological reasons. Such instances should be recorded and, importantly, the information on the patient should clearly identify them as being non-eligible and their results should not be included in the survey dataset.

Individual screening interview

During data collection, both name and survey number are often used as identifiers and verified at every station. Ideally, both male and female interviewers will be available, and female participants will have the opportunity to choose a female interviewer. However, when interviewers are medically qualified, it may not be possible for a participant to have an interviewer of the same sex; in such situations, an interviewer of a different sex is usually acceptable to the participant. In some settings, it is important to have interviewers or translators who speak the local language or dialect. Often, older people do not speak the official national language, and some countries have more than one official language.

Confidentiality during interviews is critical; therefore, the survey site should be set up in a way that avoids exposing participants to other community members while answering the questions (**Fig. 13.18**). For example, an interviewer should not be able to hear a neighbouring participant interview. Local volunteers and translators must keep all information received confidential, exactly as survey staff do. This can be assured by having all local volunteers, translators and other sur-

Fig. 13.15

Participant tracking card used in the national TB prevalence survey of South Africa, 2017–2019

Participant Survey ID Tracking Card

(Ikhadi Lokulandelela Inombolo Yokuhlola Yomhlanganyeli)

Sequential number *(Inombolo elinganiselwe)*

BARCODE

Participant Name *(Igama lomhlanganyeli)*: _____

Cluster Name: _____ **Cluster No:** _____ **Date:** _____

Age *(Ubudala)*: _____ **Sex** *(Ubulili)*: **Male** ☐ **Female** ☐

Race: ☐ **African** ☐ **White** ☐ **Coloured** ☐ **Indian/Asian** ☐ **Other**____

Stations and Eligibility *(Iziteshi kanye nokufaneleka)*	**Yes** *(Yebo)*	**No** *(Cha)*	**Refused** *(Wenqatshelwe)*	**NA**
Invitation slip presented at the reception *(Isitifiketi sommemezelo esethulwe ngesikhathi sokwamukelwa)*				
Demographic information confirmed *(Ulwazi lomdabu luqinisekisiwe)*				
Group Information session completed *(Isikhathi Sokwaziswa Seqembu sigcwalisiwe)*				
Informed Consent signed (*i-Consent eyaziwa isayinwe)*				
Consent for CXR given (*i-Consent ye-CXR enikeziwe)*				
Consent for HIV testing given (*Isivumelwano sokuhlolwa kwe-HIV sinikeziwe)*				
Individual interview completed (*Ingxoxo yomuntu ngamunye yaqedwa)*				
Sputum eligibility (based on symptoms) *Ukufaneleka kwe-sputum (ngokusekelwe ezimpawu)*				
CXR done (*i-CXR yenziwe)*				
CXR reading completed (*Ukufundwa kwe-CXR kugcwaliswe)*				
Spot Sputum collected *(i-sputum iqoqwe lapho)*				
2nd sputum given (*Isampuli yesi-sputum yesibili eqoqwe)*				
HIV testing completed (*Ukuhlola i-HIV kugcwaliswe)*				
All applicable procedures completed (*Zonke izinqubo ezisebenzayo ziphelile)*				

Remarks(*Amazwana)*:_____

TB: tuberculosis.

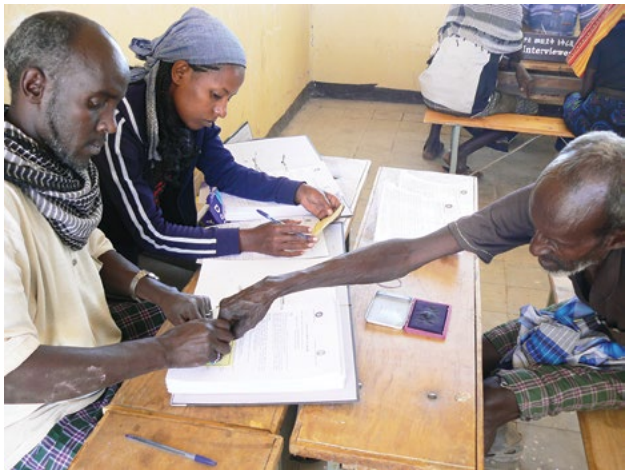


Fig. 13.16

Participant signing his consent form with a thumbprint during the national TB prevalence survey of Ethiopia, 2010–2011

Photo credit: Marina Tadolini.
TB: tuberculosis.

Fig. 13.17

Participants provided with information in a group session as part of the national TB prevalence survey of Ethiopia, 2010–2011

Photo credit: Marina Tadolini.
TB: tuberculosis.

Fig. 13.18

Participants being interviewed in separate rooms of a tent in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

vey staff sign confidentiality agreements pertaining to the survey.

One of the advantages of conducting interviews at the central survey site is that if the interviewer cannot judge a participant's response to key questions, they can call on a medical officer from the survey team. This is a common problem when participants report that they are currently receiving "TB treatment" because they may confuse TB treatment with other treatments or with TB preventive treatment. Generally, there will be only a few people receiving TB treatment per cluster; hence, it may be possible for all those reporting that they are receiving TB treatment to be interviewed by a qualified physician or clinical officer. In some instances, showing a participant the TB medication may help to ascertain whether they have been or are currently being treated for TB (**Fig. 13.19**).

For healthy interviewees, the screening interview can be completed within a few minutes. For individuals who have symptoms on screening, a further interview about treatment-seeking behaviour should be carried out, either by the same interviewer or by another interviewer (e.g. a qualified medical professional). After the screening interview, the participant is guided to the CXR station.

Other details about the interview can be found in **Chapter 6**.

Chest X-ray

CXR equipment may be installed in a truck, a bus, a shielded container or, if standalone equipment is used, in a building, house or even a tent (**Fig. 13.20** and **Chapter 7**). The installation needs to comply with the rules of the national radiation regulation authority, although it is not realistic to expect every survey cluster to be inspected by that authority. The area where the CXR is being conducted should be clearly distinguished from other areas, and it should be restricted, to protect people other than radiology staff and examinees from unnecessary radiation exposure.

Some participants may never have received a CXR before; therefore, effective communication is important. Visual aids (e.g. a poster) to show what having a CXR involves can help to prepare participants and facilitate participant flow. Specific practical points include the following:

- instruction may be given to participants in groups while they are waiting;
- it is ideal to have two spaces for dressing or undressing, with curtains;
- a female assistant may help female participants to prepare for their CXR;
- participants could change into gowns, but some surveys have provided T-shirts to each participant that they then could keep (the shirts could be printed

Fig. 13.19

An interviewer in the national TB prevalence survey of Indonesia, 2013–2014, asking a participant whether they have ever taken TB medication

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

with TB messages and could also serve as a token of appreciation for participation);

- participants should be told beforehand to not wear metal jewellery when coming to the survey site (this avoids the longer changing time required for removing such jewellery);
- longsleeved gowns may be required for female participants in certain countries, in accordance with local customs; and
- the time it takes for a CXR to be taken and read is usually only a few minutes; the field reader (**Fig. 13.21**) may call the team leader when an abnormality is detected that needs urgent medical intervention and referral of the participant to an appropriate medical facility (see **Chapter 9**).

More details on CXR implementation in the field and other practical tips can be found in **Chapter 7** (**Sections 7.10** and **7.11**).

Sputum eligibility

Once the results of the screening interview and CXR are available, eligibility to submit sputum samples can be determined. For digital systems, this is often done electronically to avoid manual errors. Participants who are classified as screen positive are eligible for a sputum examination (see **Chapter 3**) and are referred to the sputum collection station. When a participant is not eligible for sputum examination, that person should be informed about why they do not need to submit specimens. Also, they should be told that their participation is complete and they should be referred to the exit station, pending review by the medical officer (**Fig. 13.10**).

Fig. 13.20

A participant undergoing a digital CXR in the national TB prevalence survey of Viet Nam, 2017–2018

Photo credit: WHO/Irwin Law.
CXR: chest X-ray; TB: tuberculosis.

Fig. 13.21

A medical officer reviewing a digital CXR in the national TB prevalence survey of Nepal, 2018–2019

Photo credit: Marina Tadolini.
CXR: chest X-ray; TB: tuberculosis.

Sputum collection (field laboratory)

The sputum area of the laboratory section should be clearly distinguished and positioned in such a way that it provides privacy for participants (**Fig. 13.22**). Clear instructions (according to SOPs) should be given to participants on how to produce sputum (see also **Chapter 8**) – visual aids are often helpful. Even during busy times, the laboratory section will have, at most, five or six participants eligible for sputum examination per hour (about 10–20% of survey participants). Producing sputum can be difficult for some participants, especially for those who do not have symptoms such as a cough. Physiotherapy techniques can be used to stimulate production of a quality sputum sample. When participants are seen to be trying hard to produce a sample, even saliva-like specimens should be accepted. Laboratory staff should not refuse or discard such a specimen (see **Chapter 8**).

After collecting a spot specimen, staff will provide instructions on how to collect a second specimen, either 1 hour later or, especially if diagnostic Option 2 is chosen, on the following morning. If a morning specimen is requested, it is important to clarify the process; the options are that the participant will bring the specimen to the collection site, the participant will produce the sputum specimen at the collection site in front of staff, or staff will visit the participant's home to collect the specimen (see **Chapter 8**).

If several members of a single household are asked to produce morning sputum specimens, it is necessary to clearly indicate which sputum container belongs to which person. Small stickers of different colours on sputum cups for a single household may help to avoid confusion, especially when some participants cannot read.

Many surveys undertaken during the past 5 years have performed Xpert testing at or near to the cluster site (see **Chapter 8**). Both diagnostic options – Option 1 and Option 2 – include Xpert testing in the field, which allows rapid clinical management (i.e. referral) of those with a positive test and collection of additional samples for further investigations. The Xpert testing can be done physically at the survey site if Xpert machines are available (e.g. installed in the truck) or in a nearby health facility laboratory.

Fig. 13.22

Field laboratory used in the national TB prevalence survey of Indonesia, 2013–2014

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

HIV and other comorbidities

HIV testing is often placed as the last station at the field site or is done between collection of sputum samples for those eligible for sputum testing. The station offering HIV testing should be staffed by people who are experienced in providing counselling before and after tests for HIV (see **Chapter 10**). As with all stations, it is important to establish an area that provides privacy and ensures confidentiality.

If other measurements are being taken (**Fig. 13.23**), then separate stations may need to be inserted before or after screening. For example, staff in reception can measure participants' height and weight, and fasting blood glucose could be tested after screening.

Medical officer review, data check and completion of screening

Before the participant is allowed to leave the field site, they should be offered the opportunity to talk to and ask questions of the medical officer. For example, participants may have questions about the results of the screening tests, follow-up and referral, or aspects of the survey itself.

Once all stations have been completed, participants visit the final "check out" station where staff check that the participant has completed all required survey procedures and there are no missing data or samples. If additional samples are required (e.g. pending Xpert Ultra results, to decide whether additional specimens are required for liquid culture) then it is important to ensure that participants know what is being asked of them and to reconfirm their contact details.

Some countries provide a small amount of compensation (**Box 13.4**) for transportation costs or time spent at the site before the participant leaves. For tallying participants, it is good practice for staff at the exit station to collect all the tracking sheets (and lanyards) for all those who have completed procedures.

The exit station can also be used to identify household members who have not yet visited a survey site. The digital data system could be programmed in such a way that, at the exit station, eligible household members who have not yet attended the survey site are listed; this means that participants can be asked to alert other household members to visit the survey site.

Follow-up operations

The DMS for each field team should include a live dashboard that can be used to monitor the participation of eligible individuals. This will allow the survey team to identify anyone who has not participated in the field

Fig. 13.23

Measurements such as a) blood pressure, b) weight and c) height were measured in the national TB prevalence survey of Cambodia, 2023–2024

a)

b)

c)

Photo credit: WHO/Tytaart.
TB: tuberculosis.

operations. Some people who are eligible may not know where and when the survey operations are taking place; those who are older or unwell may be unable to come even though they are willing to participate; and those who missed their appointment may believe they can no longer participate. Follow-up operations should be conducted daily to increase the participation rate as much as possible; for example, through door-to-door visits by the survey team, announcements made by community volunteers and text message (SMS) reminders (if mobile phone details are available).

A survey team car could be used to bring people who are unwell, older, pregnant or disabled to the survey site if required. If some people are unable to come to the survey site, interviews and sputum sample collection could be carried out in their home.

Survey hours may be extended on a specific day of the week or over the weekend to increase participation, especially for people who work during the week. This is particularly true in urban or suburban areas, but also in farming areas where people tend to start work early in the day.

Transportation of sputum samples

Both diagnostic algorithms, Option 1 and Option 2, require transportation of sputum samples to a regional or central culture laboratory (see **Chapter 8**). In many countries, it has been necessary to establish the survey's own transportation system for sputum specimens, because of the lack of a reliable and regular courier system with effective cold chain systems.

Where each team has several vehicles to move staff to the cluster site, one of those vehicles could be used to transport sputum specimens to the laboratory under cool conditions every few days, if feasible (**Fig. 13.24**). In larger countries, depending on the location of laboratories, an air courier might be necessary for some clusters. When public transportation is used, the most reliable and feasible option could be for local laboratory staff to carry samples inside a cold box.

Samples often arrive at a referral laboratory during the weekend or outside working hours. It is therefore important to ensure that laboratory staff are present to receive those samples and that enough space is

BOX 13.4
COMPENSATION

Compensation includes any payments made to participants to compensate them for time, travel or inconvenience. Participants should not be expected to pay out-of-pocket expenses if participation in the survey requires them to travel or take time off work; however, any compensation should be reasonable so that it does not induce someone to take part in the survey simply for financial gain. Decisions on whether any compensation will be provided and, if so, the amount of compensation, should be taken during the design of the survey. If compensation is to be offered, it must be budgeted for and clearly explained in the information sheet given to the participant. Whether a country provides some form of compensation for survey participants will depend on country guidance, ethical approval and local customs. Some examples of compensation from previous surveys are a T-shirt in Cambodia; reimbursement of transport costs in Mozambique (~200 meticas/US$ 2); a food package in Lesotho; a notebook that also provides TB information in Ethiopia; and soap, mobile phone or supermarket vouchers in South Africa (~50 rand/US$ 3) (**Fig. B13.4.1**).

Fig. B13.4.1

Tokens of appreciation provided as part of the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

available to store the samples safely at the correct temperature.

Community involvement beyond data collection

Local community volunteers often assist during enumeration and survey operations at the field site; however, additional community involvement (i.e. beyond data collection) often leads to a much higher acceptability of survey activities by the community and hence to a higher participation rate. During the national survey in Cambodia in 2002, survey teams hired the services of the local community to cook meals for the team, and to wash uniforms and gowns used during X-ray examinations. In South Africa in 2017–2019, tents were sourced from local suppliers in some field sites. These activities do not violate the general principle of "minimal intrusion" into the community but do give something back to the community.

Feedback of survey results

Effective feedback of the survey results is an important duty of the survey team. Activities conducted during the fieldwork should be reported to local authorities and the community when a survey team leaves a cluster. A summary report may include numbers of the following items (taking into account the need for confidentiality): households visited, eligible individuals invited, participants, CXRs taken, subjects eligible for sputum examinations, subjects who submitted sputum specimens and subjects referred for care.

Given that prevalence surveys study healthy individuals in a community, it is important to do everything possible to avoid "false positive" diagnoses. The team leader and medical officer should review all available information for any survey participant who has indications of TB (e.g. *Mycobacterium tuberculosis* detected in a sputum sample or a CXR that is suggestive of TB) before deciding on the appropriate referral instructions

Fig. 13.24

Motorbike transportation of sputum specimens by "Riders for health", as used in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

(see **Chapter 9**). Such a review may find errors (e.g. a mix-up of sputum cups within a household).

After a team leaves a cluster, several reports will be sent from the survey central unit to the relevant local health unit. Individual examination results will be communicated to participants before official dissemination reports are published. The method of communicating individual results, particularly to those who need further medical intervention (e.g. treatment for TB or other serious non-TB conditions) should be clearly defined in the survey's SOPs.

Quality TB treatment should be available globally; however, access to the diagnostic centre may vary considerably among clusters. The team leader should discuss how results will be delivered and how further action will be taken with the local TB programme officer and with community leaders. On average, only about five people will need these arrangements in a typical cluster of 400–500 participants. It is also important for the central team to send a "zero" report to the local TB coordinator and community if there are no diagnoses of TB.

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Annex 13.1 Example of a survey calendar using a different number of field teams to complete 80 clusters[a]

THREE-TEAM FIELD OPERATION					FOUR-TEAM FIELD OPERATION					FIVE-TEAM FIELD OPERATION					
WEEK	TEAM 1	TEAM 2	TEAM 3	CUMULATIVE NUMBER OF CLUSTERS COMPLETED	TEAM 1	TEAM 2	TEAM 3	TEAM 4	CUMULATIVE NUMBER OF CLUSTERS COMPLETED	TEAM 1	TEAM 2	TEAM 3	TEAM 4	TEAM 5	CUMULATIVE NUMBER OF CLUSTERS COMPLETED
1	1	0	1	2	1	0	1	1	3	1	0	1	1	0	3
2	1	1	0	4	1	1	0	1	6	1	1	0	1	1	7
3	0	1	1	6	0	1	1	0	8	0	1	1	0	1	10
4	1	0	1	8	1	0	1	1	11	1	0	1	1	0	13
5	1	1	0	10	1	1	0	1	14	1	1	0	1	1	17
6	0	1	1	12	0	1	1	0	16	0	1	1	0	1	20
7	1	0	1	14	1	0	1	1	19	1	0	1	1	0	23
8	1	1	0	16	1	1	0	1	22	1	1	0	1	1	27
9	0	1	1	18	0	1	1	0	24	0	1	1	0	1	30
10	1	0	1	20	1	0	1	1	27	1	0	1	1	0	33
11	1	1	0	22	1	1	0	1	30	1	1	0	1	1	37
12	0	1	1	24	0	1	1	0	32	0	1	1	0	1	40
13	1	0	1	26	1	0	1	1	35	1	0	1	1	0	43
14	1	1	0	28	1	1	0	1	38	1	1	0	1	1	47
15	0	1	1	30	0	1	1	0	40	0	1	1	0	1	50
16	1	0	1	32	1	0	1	1	43	1	0	1	1	0	53
17	1	1	0	34	1	1	0	1	46	1	1	0	1	1	57
18	0	1	1	36	0	1	1	0	48	0	1	1	0	1	60
19	1	0	1	38	1	0	1	1	51	1	0	1	1	0	63
20	1	1	0	40	1	1	0	1	54	1	1	0	1	1	67
21	0	1	1	42	0	1	1	0	56	0	1	1	0	1	70
22	1	0	1	44	1	0	1	1	59	1	0	1	1	0	73
23	1	1	0	46	1	1	0	1	62	1	1	0	1	1	77
24	0	1	1	48	0	1	1	0	64	0	1	1	0	1	80
25	1	0	1	50	1	0	1	1	67						
26	1	1	0	52	1	1	0	1	70						
27	0	1	1	54	0	1	1	0	72						
28	1	0	1	56	1	0	1	1	75						

Annex 13.1 Example of a survey calendar using a different number of field teams to complete 80 clusters[a]

THREE-TEAM FIELD OPERATION					FOUR-TEAM FIELD OPERATION					FIVE-TEAM FIELD OPERATION					
WEEK	TEAM 1	TEAM 2	TEAM 3	CUMULATIVE NUMBER OF CLUSTERS COMPLETED	TEAM 1	TEAM 2	TEAM 3	TEAM 4	CUMULATIVE NUMBER OF CLUSTERS COMPLETED	TEAM 1	TEAM 2	TEAM 3	TEAM 4	TEAM 5	CUMULATIVE NUMBER OF CLUSTERS COMPLETED
29	1	1	0	58	1	1	0	1	78						
30	0	1	1	60	0	1	1	0	80						
31	1	0	1	62											
32	1	1	0	64											
33	0	1	1	66											
34	1	0	1	68											
35	1	1	0	70											
36	0	1	1	72											
37	1	0	1	74											
38	1	1	0	76											
39	0	1	1	78											
40	1	0	1	80											

[a] These examples do not account for holidays, intentional breaks (e.g. for reviews or national holidays) or unintentional breaks (e.g. machinery malfunction, staff unwell or security issues) in scheduling that need to be factored in. A team should implement two clusters, then take a break.

CHAPTER 14

Survey monitoring

Close monitoring of all aspects of a tuberculosis (TB) prevalence survey is of paramount importance to ensure that high-quality data are collected. Monitoring should be an ongoing and continuous process, supplemented with supervisory visits by the senior survey team and external independent assessors. A dedicated quality assurance officer at the central level can help with oversight of the monitoring process, and a well-functioning information technology (IT) dashboard is needed to actively monitor for any major discrepancies that might need to be remedied. This chapter describes the need for regular monitoring of the survey and the activities required to conduct monitoring, and lists the key indicators used to assess survey progress.

14.1 Overview

The objective of survey monitoring is to ensure consistent adherence to the survey protocol and standard operating procedures (SOPs), which in turn means that the data collected for the final analysis will be of high quality and survey conduct adheres to ethical values (**Chapter 11**). As described in the data management chapter (**Chapter 16**), low-quality data give rise to results that may not be representative of the survey population, which may lead to potentially misleading conclusions.

Monitoring of a national TB prevalence survey is similar to the process of public health surveillance, which was defined by Thacker et al. *(1)* as the:

> *Ongoing, systematic collection, analysis and interpretation of health-related data essential to the evaluation of the task with timely and effective reporting of any tasks that do not adhere to defined benchmarks.*

The process of survey monitoring is outlined in **Fig. 14.1**. Each part of the survey should be carefully and regularly reviewed to identify any errors (i.e. results that go beyond a set benchmark). An analysis of why the errors occurred should then be conducted, followed by development of a plan and communication about how to correct the errors. Timeliness of monitoring is crucial; if an issue is reported late, then it is probably too late to correct it.

The key areas that require monitoring in a survey are the field operations (including census and household enumeration), laboratory, radiology, clinical management, overall organization, and data and IT management which underpins all aspects of the survey (**Fig. 14.2**). All

Fig. 14.1

Process of survey monitoring

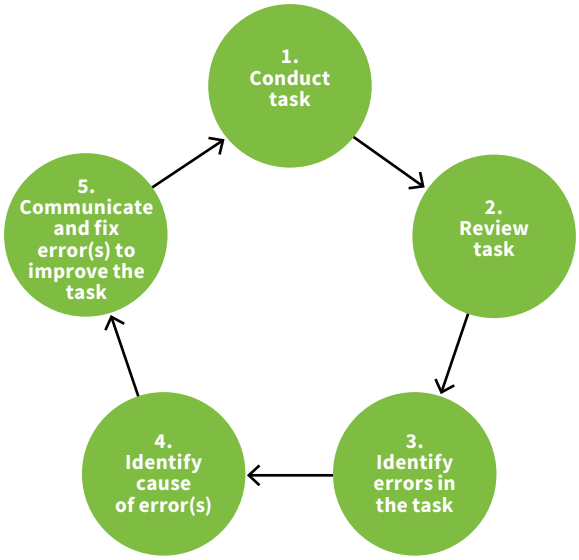
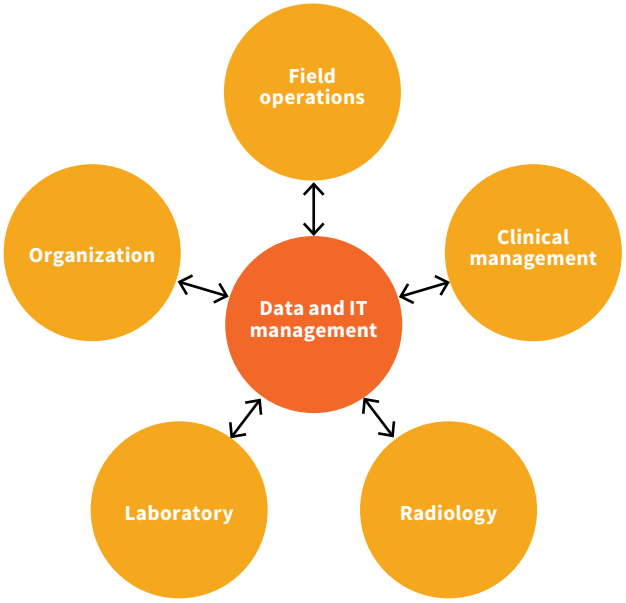


Fig. 14.2

Components of a survey that require regular and ongoing monitoring



aspects have functions at the field and the central operational level. These elements are interlinked; hence, the ongoing and continuous analysis of data is crucial for evaluating the survey team's performance and identifying areas of weakness or lack of standardization. Close monitoring of data can also be done remotely.

The key monitoring activities for a survey are:

- continuous monitoring of activities related to field operations, radiology, and the central laboratory;
- supervisory visits by in-country focal points; and
- monitoring missions with external technical assistance.

14.2 Monitoring activities

14.2.1 Continuous monitoring

Key areas of a survey that require continuous and ongoing monitoring include activities related to field operations, radiology and the central laboratory. More specific considerations are outlined in **Section 14.2.4**. Many of the activities within these key areas can be automatically monitored with established process and output indicators, using an effective data management system with real-time dashboards (see **Chapter 15**). A list of key indicators, provided in **Tables 14.1**, **14.2** and **14.3**, can also assist with standardizing protocols among field teams.

Table 14.1

Key indicators to monitor progress during field operations (by cluster and overall)

NO.	INDICATOR
1	Number of households visited
2	Number of individuals enumerated[a]
3	Number of individuals eligible for participation
4	Number of individuals not eligible for participation • Aged <15 years • Not resident (but ≥15 years)
5	Number of participants who consented to participate • Number of participants aged 15–17 years who provided assent • Number of parents or guardians who provided consent for the participation of those aged 15–17 years
6	Number of participants who were interviewed
7	Number of participants who were not eligible to participate who were interviewed
8	Number of participants who had a CXR taken
9	Number of participants who were not eligible to participate who had a CXR taken
10	Number of participants who did not have a CXR taken
11	Number of participants with a "normal" CXR result[b]
12	Number of participants with a CXR result of "abnormal, eligible for sputum collection"[c]
13	Number of participants with a CXR result of "abnormal/other, not eligible for sputum collection"[d]
14	Number of participants eligible for sputum collection (total) • Number of participants eligible for sputum collection (interview only) • Number of participants eligible for sputum collection (CXR only) • Number of participants eligible for sputum collection (both interview and CXR) • Number of participants eligible for sputum collection (other)[e]
15	Number of participants eligible for sputum collection who submitted sputum specimen 1
16	Number of participants eligible for sputum collection who submitted sputum specimen 2
17	Number of participants eligible for sputum collection who submitted two sputum samples for Xpert® MTB/RIF Ultra[f]
18	Number of participants eligible for sputum collection who submitted only one sputum sample for Xpert Ultra
19	Number of participants eligible for sputum collection who did not submit any sputum sample for Xpert Ultra
20	Number of participants with at least one positive Xpert Ultra result[g]
21	Number of participants with Xpert Ultra result[g] – specimen 1 positive
22	Number of participants with Xpert Ultra result[g] – specimen 2 positive
23	Number of participants with Xpert Ultra result – specimen 1 negative
24	Number of participants with Xpert Ultra result – specimen 2 negative
25	Number of participants tested with Xpert Ultra but result not available (specimen 1)[h]
26	Number of participants tested with Xpert Ultra but result not available (specimen 2)[h]
27	Number of Xpert Ultra results available more than 24 hours after collection
28	Number of participants with at least one positive Xpert Ultra result who submitted at least one sputum sample for TB culture (MGIT™) • Number of participants with at least one positive Xpert Ultra[g] result who submitted two sputum samples for TB culture (MGIT) • Number of participants with at least one positive Xpert Ultra[g] result who submitted only one sputum sample for TB culture (MGIT)
29	Number of participants with at least one positive Xpert Ultra[g] result who did not submit a sputum sample for TB culture (MGIT)
30	Number of participants who submitted samples for Xpert Ultra but were not eligible
31	Number of participants who self-reported being HIV-positive
32	Number of participants who were offered testing for HIV
33	Number of participants tested for HIV in the field

NO.	INDICATOR
34	Number of participants who had an HIV test result in the field
35	Number of participants tested for HIV who are HIV-positive
36	Number of participants tested for HIV who are HIV-negative
37	Number of participants tested for HIV who are HIV-inconclusive
38	Number of participants requiring immediate referral to a health facility (for any reason)

CAD: computer-aided detection; CXR: chest X-ray; HIV: human immunodeficiency virus; MGIT: mycobacterial growth indicator tube.

[a] Indicators 2–11 can also be disaggregated by gender and age group.

[b] If only CAD is used, this will be a value below the assigned threshold.

[c] If only CAD is used, this will be a value at or above the assigned threshold.

[d] If only CAD is used, this category may not be available.

[e] This can include participants who did not have a CXR taken, or who meet other predefined screening criteria.

[f] Indicators related to Xpert Ultra results are applicable where diagnostic option 1 is used (see **Chapter 4**).

[g] Including trace, very low, low, medium and high.

[h] Including error, invalid result or no result available due to premature termination of the test.

Table 14.2

Key indicators to monitor progress of radiological activities (by cluster and overall)

NO.	INDICATOR
1	Number (%) of participants who had a CXR taken
2	Number of normal CXRs yet to be read by the central reader
3	Number of abnormal CXRs (eligible[a]) yet to be read by the central reader
4	Number of abnormal CXRs (other, not eligible) yet to be read by the central reader[b]
5	Number (%) of normal CXRs (field) read by the central reader
6	Number (%) of abnormal CXRs (eligible[a]) read by the central reader
7	Number (%) of abnormal CXRs (other, not eligible) read by the central reader
8	Number (%) of normal CXRs (field), but abnormal (eligible) read by the central reader
9	Number (%) of abnormal CXRs (other, not eligible), but abnormal (eligible[a]) read by the central reader
10	Number (%) of abnormal CXRs (eligible[a]) read by the central reader, but normal or abnormal CXR (other, not eligible) as read by the field reader
11	Number of times CXR machine malfunctioned (i.e. at least 30 minutes without operation) during the cluster[c]

CAD: computer-aided detection; CXR: chest X-ray.

[a] Eligible for sputum examination.

[b] If only CAD is used, this category may not be required.

[c] Please document why this happened, and what was done in the field during the malfunction (e.g. all participants were asked to produce sputum samples).

Table 14.3

Key indicators to monitor progress of central laboratory operations (by cluster and overall)

NO.	INDICATOR
1	Number (%) of batches where the temperature of received specimens is <8 °C [a]
2	Number (%) of samples rejected at reception
3	Number (%) of sputum specimens that arrived in the culture laboratory >3 days since specimen collection
4	Number (%) of sputum specimens that took longer than 42 days from date of reception to final culture result
5	Number (%) of participants who provided only one specimen for MGIT testing (and specimen was received by the laboratory)
6	Number (%) of participants who provided two specimens for MGIT testing (and specimens were received by the laboratory)
7	Number (%) of positive MGITs that are *Mtb*[b]
8	Number (%) of negative MGITs[b]
9	Number (%) of other positive MGITs[b] • with AFB (i.e. bacteria and AFB present) • with NTM (based on morphology, ZN staining and identification) • with other bacteria only (i.e. no AFB present)
10	Number (%) of negative MGITs among participants with a history of TB treatment (within 5 years)[c]
11	Number (%) of negative MGITs among participants with a trace Xpert Ultra result (highest available semiquantitative category)[d]
12	Number (%) of negative MGITs among participants with a very low Xpert Ultra result (highest available semiquantitative category)[d]
13	Number (%) of negative MGITs among participants with a low Xpert Ultra result (highest available semiquantitative category)[d]
14	Number (%) of negative MGITs among participants with a medium Xpert Ultra result (highest available semiquantitative category)[d]
15	Number (%) of negative MGITs among participants with a high Xpert Ultra result (highest available semiquantitative category)[d]
16	Number (%) of positive–negative MGIT pairs
17	Number (%) of positive–positive MGIT pairs
18	Number (%) of negative–negative MGIT pairs

AFB: acid-fast bacilli; MGIT: mycobacterial growth indicator tube; *Mtb*: *Mycobacterium tuberculosis*; NTM: non-tuberculous mycobacteria; TB: tuberculosis; ZN: Ziehl–Neelsen.

[a] Ideally, temperature monitors (e.g. log tags) should be included to allow for continuous monitoring of the cooler being used to transport specimens from the field to the laboratory for culture.

[b] This refers to one tube of MGIT.

[c] This is 5 years (60 months) after the final medication taken to treat TB.

[d] A positive Xpert Ultra result is categorised as trace, very low, low, medium or high. Highest available semiquantitative category refers to the highest category from two Xpert tests. For example, if result 1 is trace and result 2 is negative, the highest available category is trace; similarly, if result 1 is medium and result 2 is high, the highest available category is high.

Good communication is an important part of effective monitoring; hence, important activities to ensure effective monitoring of the survey include the following:

- Development of a **summary report of each cluster** by the field team leader for the survey coordinator and the central survey team. Aside from monitoring process indicators, it is important to document and discuss problems related to key logistical and staff issues, and implement solutions to address them. It is also important that the team leaders keep incident reports of key issues that occur during fieldwork, such as breakdown of equipment, breaches of protocols or SOPs, low staff morale and security issues at the field site. This information may be helpful during the analysis to explain unexpected indicator results; for example, high rates of liquid culture contamination could be due to a long delay in the transportation of sputum specimens from the field to the central laboratory.
- **Daily meetings** by the field team at the end of each day to discuss field operations and identify any challenges such as low participation rate, incorrectly screened individuals, missed collection of samples, Xpert module failure, chest X-ray (CXR) machines not functioning, database not synchronizing or inadequate accommodation.
- **Weekly meetings** by senior technical survey staff to ensure that all aspects of the survey are regularly reviewed and solutions are sought for any issues arising.

Use of mobile communication applications has changed the nature of monitoring and consultation. Recent surveys have created groups within messaging apps (e.g. field team, field team leaders, central coordination, data management and laboratory teams) to communicate almost daily, to share experiences and provide feedback, including via photos.[1]

Many prevalence surveys using digital data collection have incorporated real-time digital dashboards of key process indicators to allow for continuous monitoring (see **Chapter 16**). Separate dashboards can be developed for the field level and for different central-level (survey coordination and central laboratory) monitoring requirements. Digital dashboards can generate progress and error reports, and alerts for protocol violations or for corrective actions that need to be taken. For example, unexplained changes in indicators such as participation rate, sputum eligibility rates, sputum submission rates, HIV test acceptance or detection rate of *Mycobacterium tuberculosis* can point to challenges in field operations that can be immediately addressed.

[1] Although sharing of information via mobile applications has increased efficiency, survey teams should be aware of the ethical and confidentiality issues related to sharing photos and videos with personal identifiers and data.

Table 14.1 lists a minimum set of indicators to be monitored by cluster. Continuous analyses of data can show patterns of inconsistencies; therefore, analyses should be done as soon as possible rather than delayed until the end of the survey.

As described in **Chapter 17** on analysis and reporting, some of the key descriptive analytical indicators (at the cluster level and overall) that warrant close attention during monitoring include participation rate, screening rate by modality, specimen collection rates and availability of valid laboratory results.

14.2.2 Supervisory visits by in-country focal points

The roles and responsibilities of in-country focal points for key areas of the survey (**Fig. 14.2**) should include regular onsite monitoring visits and continuous analysis of data. Monitoring of the key process and performance indicators (in **Tables 14.1**, **14.2** and **14.3**) will help in assessing overall survey quality and compliance with the survey protocol; such monitoring will also ensure adherence to principles related to good clinical management and good data management practices, and ethical values (**Chapter 11**). Direct observation of survey practices may allow reviewers to highlight best practices and practices that may be deemed misconduct. Aspects of field operations that are not necessarily quantitative in nature can also be assessed; for example:

- Is a participant given enough information to provide informed consent that is not obtained under coercion?
- Is the interviewer asking the correct questions to the participants in an unbiased way?
- Are participants provided with adequate space to change clothes in privacy before having a CXR?
- Are confidentiality and privacy of participants provided when screening results are returned to them?
- Is sufficient effort being made to collect sputum samples from participants who are eligible after screening?
- Do participants understand the instructions given to them well enough to provide a good-quality sputum sample?
- Are staff satisfied with the environmental conditions in which they work (and sometimes sleep)?

Frequent supervisory visits are required in the initial phase of the field operations, but the frequency can then decline once field and central teams are comfortably aligned with the SOPs.

As was done in the 2016 Philippines survey *(2)*, a dedicated person to oversee survey quality assurance and monitoring could be recruited to coordinate and provide further oversight.

As previously mentioned, good communication will ensure better survey quality. Those undertaking mon-

itoring should provide both positive and negative (but constructive) feedback (written and oral) to the survey coordinator and the survey teams after each visit. Survey team members should also be able to honestly communicate to their supervisors and survey monitors. Attention should also be given to the communication between the survey coordinator and field team leaders. After a field team has left the cluster, it will be almost impossible to rectify structural mistakes in data collection, because tracing participants from the cluster may be difficult or impossible. Therefore, it is advisable to have the survey coordinator and focal points in the field, especially in the early clusters, to conduct close monitoring. Field team leaders can then provide daily supervision and ensure that problems are addressed in a timely manner.

14.2.3 Monitoring missions with external technical assistance

It is advisable for a survey to be reviewed by an external monitoring team (e.g. international experts) at least two or three times during the field operations. Ideally, the review should take 5–7 days, and the monitoring team should include people who are experienced in conducting all aspects of a prevalence survey, and are knowledgeable about those aspects.

In addition to these two or three monitoring missions, a major, and more intensive, review by a larger external monitoring team is recommended once 10–20% of clusters have been completed.[1] As with all monitoring activities, the primary aims of such a review are to ensure protocol adherence, identify challenges and make recommendations to improve survey operations.

The major review monitoring team (usually 4–8 people) should include at least one reviewer per field team, and other people to assess areas related to data management, laboratory, radiology and overall organization; some of these roles could be undertaken by one person. Ideally, all reviewers should be impartial and should not be part of the survey's technical or steering committee. Reviewers are generally international advisors, but the funder may sometimes participate in the major review as well.

The major review can take 7–10 days depending on the number of reviewers, number of field teams and geographical distances required to travel to review the field sites and central operations. Data should also be made available before the review itself, to allow for the generation of monitoring indicators (**Table 14.1**), assessment of missing data (e.g. non-participation, specimens not submitted and lack of availability of laboratory results) and some provisional analysis – all of which can provide insights into ongoing survey challenges.

At the end of the major review, the monitoring team should present to the survey team and discuss all the strengths and weaknesses of the survey, including practical advice on how to improve the survey. If there are any major recommendations, field operations should be halted until these issues are resolved. Examples of such issues include incorrect screening practices, inability to match participant data to laboratory results due to poor data management, or breakdown of laboratory equipment. In extreme circumstances, surveys have been cancelled because of major protocol deviations that would not have been able to fulfil the objective of estimating the prevalence of bacteriologically confirmed pulmonary TB.

The major review can be funded by the survey itself (if already budgeted for), or by external technical agencies with donor support. The review can also be used as a learning opportunity for survey teams from other countries who are preparing for their own prevalence survey.

14.2.4 Monitoring of specific areas

Specific details related to radiology, laboratory, clinical management, overall organization and data management are given in other chapters (**Chapters 7**, **8**, **9**, **12** and **16**), but monitoring of these areas is just as critical as monitoring field operations. Other aspects to be aware of when monitoring these areas are outlined below.

Radiology

Monitoring of CXR performance includes assessing the safety of taking CXRs in the field and the correct use by the field reader of criteria for screening participants (depending on the use case, see **Chapter 7**). In the field, the main priority is to ensure that sensitivity is high enough to not miss people with potential TB or significant pathology that requires immediate referral to a health clinic. A central team of experienced radiologists should re-read field CXRs to ensure that field readers (especially if not using computer-aided detection [CAD]) are appropriately screening participants; that it, ensuring few false negatives and thus a high sensitivity.[2] If there is poor concordance between field and central readings, further training of field readers may be required. The central reading of CXR results can also help with the verification of laboratory results. If CAD is being used, monitoring of CXR readings and laboratory case load may determine whether the cut-off threshold is of the required sensitivity (**Chapter 7**). In addition, even when a country is experienced in the use of digital CXR technology, taking CXRs in a stressful, high-throughput community setting could differ from the experiences in clinical or high-risk group settings.

[1] In the past, these more intensive reviews were termed "mid-term reviews" even though they were conducted earlier than the name suggests.

[2] Ideally, all CXRs should be reviewed centrally (both for quality control and for data analysis), although some countries may only centrally review all field abnormal CXRs and at least 10% of normal CXRs, depending on the number of central readers.

Laboratory

Monitoring of the central laboratory (or laboratories) conducting culture tests requires an extensive system of standardized quality controls to be in place before a survey commences (**Section 8.4.5**). The laboratory must participate in an external quality assurance programme, and all laboratory staff must be well trained in good laboratory practices and quality assurance, to ensure that work is of high quality. If more than one laboratory is being used, standardization becomes even more essential.

Quality indicators that can be used are described in the World Health Organization (WHO) practical guide to TB laboratory strengthening *(3)*. Minimum requirements and indicators are provided in **Chapter 8** (**Boxes 8.3** and **8.4**). A supervisory visit by a WHO TB supranational reference laboratory team should be conducted before the survey starts and at regular intervals during the survey.

The best way to monitor the efficiency of culture is through performance indicators *(4)*. For example, if the contamination rate is higher than expected, a careful review of in-laboratory procedures, including sterile technique, should be undertaken and staff retrained if necessary. In extreme situations, a pause in the survey may be needed; for example, if the laboratory contamination rate is a persistent problem affecting consecutive clusters.

Adherence to biosafety, waste management, laboratory inventories and data management are also key considerations that require monitoring.

Clinical management

Appropriate and timely clinical management of survey participants is a crucial parameter of survey quality, and it deserves careful preparation and monitoring throughout the survey (**Chapter 9**). Monitoring teams should ensure clear levels of responsibility and adherence to clinical management protocols, especially ensuring that participants diagnosed with TB, or with other serious comorbidities, are referred and linked into care. Establishing good lines of communication between the survey coordinator, the medical panel and the national TB programme (with direct involvement of local TB officers or district health officers) is extremely important to ensure smooth linkage of participants into the health system. Biosafety within the field screening site is another aspect of monitoring requiring due consideration.

Overall organization

A critical responsibility of the survey team is the overall organization of the survey (**Chapter 12**). All survey team members should be aware of the functions involved in such organization, but sometimes an external monitoring team is best able to review these areas, including:

- **Effective communication:** How often and how frequently do meetings take place? Are there clear channels of communication? Are steering and technical committees in place, and do they meet on a regular basis with active participation?
- **Human resource management:** Are all positions filled with the best-available skilled personnel? Are all positions necessary? What plans are in place for when someone leaves the survey? Are funds in place to support all staff throughout the entirety of the survey? What plans are in place to support salaries if there are delays in field operation and the survey is extended? Is there support for technical assistance?
- **Financial and procurement management:** Are there enough funds for the survey to complete its primary objective? If not, why? Is there a dedicated financial officer for the survey? Is the reporting mechanism to donors too arduous? Are all necessary resources procured before the survey begins? Are there service contracts for capital equipment? Can some activities be outsourced to offer cost savings?

Data management

It is possible to rely too strongly on IT and related data management tools, and assume that they will prevent many errors (**Chapter 16**). As mentioned above, even when a country has good experience with new technologies, using them in a stressful, high-throughput community setting such as a prevalence survey could be different from the experiences observed in other settings. Although thorough testing and simulation of the equipment and processes should be undertaken before the survey begins (**Chapters 12** and **13**), errors can still occur because of human error (e.g. scanning the incorrect barcode or making manual transcription errors such as entering the incorrect age or sex, presence or absence of symptoms, or incorrect laboratory result). Therefore, it is important for monitoring teams to observe how data are entered at all steps of the survey process, perhaps even re-interviewing some participants to ensure that their answers match what was recorded in the tablet computer in the field. Using source documents to validate laboratory results in the survey database is a key method of monitoring.

References

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3 Practical manual on tuberculosis laboratory strengthening (2022 update). Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/365134).

4 MGIT™ procedure manual. Geneva: Foundation for Innovative New Diagnostics (FIND); 2006 (https://www.finddx.org/wp-content/uploads/2023/02/20061101_rep_mgit_manual_FV_EN.pdf).

CHAPTER 15

Budgeting and financing

A national tuberculosis (TB) prevalence survey needs to be carefully budgeted; all sources of financing should be identified before the survey starts, to prevent any risk of the survey being interrupted. The funds required for the entire survey period (preparation, implementation, analysis and dissemination) should be included in the survey budget, and consideration should be given to how the survey will be funded (e.g. from domestic sources or co-funding, as discussed in **Section 15.5**). All survey protocols should include a clear description and justification of the budget and sources of funding, including a plan for how to use any procured items that have a lifetime that extends beyond the end of the survey (e.g. X-ray or laboratory equipment).

This chapter provides an overview of the reported budgets for national TB prevalence surveys implemented between 2007 and 2024, and how these budgets compare with the total amount of funding available for the TB response at country and global levels. It also discusses how the financial costs included in a survey budget can underestimate or overestimate the true economic cost of a survey. The chapter then describes the main items that need to be included in a survey budget and the main cost drivers, as well as potential ways to optimize the use of survey resources (including for future, non-survey-related applications) and minimize costs. The final section discusses how surveys have been funded in recent years.

15.1 Total budget required for a national TB prevalence survey

The reported budgets for 35 national TB prevalence surveys conducted between 2007 and 2024 (all converted to US$ values for 2022, to allow for fair comparisons) ranged from just over US$ 1 million (in Timor-Leste) to US$ 15.6 million (in India, for a large survey designed to also provide subnational estimates) (**Table 15.1**). The overall average was US$ 3.8 million and the median was US$ 2.9 million.

Overall, the average survey budgets in African and Asian countries were similar: US$ 3.5 million and US$ 3.3 million, respectively. The average budget (in constant US$ values for 2022) per cluster was about US$ 25 000 in Asian countries and US$ 50 000 in African countries, with the approximate cost per cluster ranging from as low as US$ 11 000 in Mongolia (2014–2015) to as high as US$ 82 000 in Zambia (2013–2014).[1]

When survey budgets were annualized over a 10-year period (the recommended duration between surveys), the survey budget was equivalent to between less than 0.1% and 9.4% of the total amount of annual funding available for the national TB response, with a median of 1.3% (**Table 15.1** and **Fig. 15.1**). That is, when the cost of the survey is spread across 10 years, a survey accounts for about 1% of the available funding for TB. In general, the larger the country (geographically and population wise), the lower the percentage.

The total budgets of the 35 surveys implemented between 2007 and 2024 (again, in constant US$ values for 2022)[2] amounted to US$ 128 million, with an annualized value of US$ 15 million. This is equivalent to about 1.5% of the international donor funding provided for TB each year, and about 0.3% of the total funding for the TB response in all low- and middle-income countries.

Of note, the report budget for a national TB prevalence survey may understate or overstate the true cost of a survey. The full economic cost of a survey is defined as the market value of all resources used in that survey. The survey budget will be less than the true cost of the survey if a survey budget does not include the value of the time of staff needed to manage a survey and implement field operations. This value may be omitted from the budget if those staff are already employed by the national TB programme (NTP) or ministry of health, or the survey makes use of volunteers who are not paid, or the survey budget does not include technical assistance provided by international agencies or consultants (which might be funded from separate funding sources and budgets). It is useful to define and list all in-kind contributions, to help to identify domestic contributions to the survey that might otherwise be missed.

When the budget does include the full purchase price of equipment (e.g. laboratory equipment and X-ray machines), vehicles and other items with a useful life that extends beyond the completion of the survey, the

[1] The budget was very high in Zambia because external technical assistance costs were included in overall field operations.

[2] With the exception of the Democratic People's Republic of Korea (2015–2016), Myanmar (2009) and Zimbabwe (2014), for which current values in the year of the survey were used, as explained in the footnotes to **Table 15.1**.

Table 15.1

Reported budgets[a] for 35 national TB prevalence surveys implemented between 2007 and 2024

COUNTRY	YEAR(S) OF FIELD OPERATION	NUMBER OF SURVEY PARTICIPANTS	NUMBER OF CLUSTERS	SURVEY BUDGET IN MAIN SURVEY YEAR, US$ MILLIONS (CURRENT VALUES FOR THE SURVEY YEAR)	SURVEY BUDGET, US$ MILLIONS (2022 CONSTANT VALUES)[b]	ANNUALIZED SURVEY BUDGET, US$ MILLIONS (2022 CONSTANT VALUES)[c]	ANNUALIZED SURVEY BUDGET PER CLUSTER, US$ (2022 CONSTANT VALUES)	AVAILABLE FUNDING FOR THE TB RESPONSE, US$ (2022 CONSTANT VALUES)[d]	ANNUALIZED SURVEY BUDGET AS A PERCENTAGE OF AVAILABLE FUNDING FOR THE TB RESPONSE IN 2022
Bangladesh	2015–2016	98 710	125	3.6	5.1	0.60	40 958	126 120 335	0.48%
Cambodia	2010–2011	37 417	62	1.0	1.3	0.16	21 656	27 616 682	0.57%
Cambodia	2023–2024	34 836	84	3.3	3.3	0.39	39 286	27 616 682	1.4%
China	2010	252 940	176	5.6	7.6	0.90	43 416	762 621 837	0.12%
Democratic People's Republic of Korea	2015–2016	60 683	100	1.4	–	–	–	57 058 511	–
Eswatini	2018–2019	24 356	70	3.8	3.5	0.41	49 532	12 114 550	3.4%
Ethiopia	2010–2011	46 697	85	2.8	4.7	0.55	54 941	65 623 061	0.83%
Gambia	2011–2013	43 100	80	1.9	2.0	0.24	23 750	–	–
Ghana	2013	61 726	98	2.2	1.8	0.21	18 226	7 964 693	2.6%
India	2019–2021	322 480	443	15.1	16.6	1.95	37 582	531 323 222	0.37%
Indonesia	2013–2014	67 944	156	4.6	4.6	0.54	29 703	212 382 342	0.26%
Kenya	2015–2016	63 050	100	5.2	6.2	0.73	62 197	48 645 759	1.5%
Lao People's Democratic Republic	2010–2012	39 212	50	1.3	1.4	0.17	28 566	3 416 834	4.9%
Lesotho	2019	21 719	54	2.8	2.8	0.33	51 509	3 461 496	9.4%
Malawi	2013–2014	31 579	74	2.2	3.4	0.40	46 287	19 647 116	2.0%
Mongolia	2014–2015	50 309	98	1.1	1.2	0.14	12 373	12 233 689	1.2%
Mozambique	2018–2019	32 445	72	5.8	6.6	0.77	91 497	34 890 431	2.2%
Myanmar	2009–2010	51 367	70	0.90	–	–	–	34 787 328	–
Myanmar	2017–2018	66 480	138	2.0	2.9	0.34	21 183	34 787 328	1.0%
Namibia	2017–2018	29 495	68	5.5	5.4	0.63	78 997	10 154 478	6.2%
Nepal	2018–2019	54 200	99	4.1	4.4	0.52	44 634	20 449 740	2.5%
Nigeria	2012	44 186	70	3.1	2.5	0.30	36 234	122 354 463	0.24%
Pakistan	2010–2011	105 913	95	4.4	4.6	0.54	48 657	41 405 703	1.3%
Philippines	2016	46 689	108	2.4	2.5	0.29	22 702	142 297 938	0.20%
Rwanda	2012	43 128	73	2.4	2.3	0.27	31 147	10 240 315	2.6%
South Africa	2017–2019	35 191	110	5.1	5.1	0.60	46 373	229 832 329	0.26%
Sudan	2013–2014	83 202	114	1.9	1.5	0.18	13 404	6 069 670	3.0%
Thailand[e]	2012–2013	62 536	100	1.9	2.0	0.23	19 731	60 137 223	0.38%
Timor-Leste	2022–2023	15 267	50	1.1	1.1	0.13	22 000	57 47 350	2.2%

COUNTRY	YEAR(S) OF FIELD OPERATION	NUMBER OF SURVEY PARTICIPANTS	NUMBER OF CLUSTERS	SURVEY BUDGET IN MAIN SURVEY YEAR, US$ MILLIONS (CURRENT VALUES FOR THE SURVEY YEAR)	SURVEY BUDGET, US$ MILLIONS (2022 CONSTANT VALUES)[b]	ANNUALIZED SURVEY BUDGET, US$ MILLIONS (2022 CONSTANT VALUES)[c]	ANNUALIZED SURVEY BUDGET PER CLUSTER, US$ (2022 CONSTANT VALUES)	AVAILABLE FUNDING FOR THE TB RESPONSE, US$ (2022 CONSTANT VALUES)[d]	ANNUALIZED SURVEY BUDGET AS A PERCENTAGE OF AVAILABLE FUNDING FOR THE TB RESPONSE IN 2022
Uganda	2014–2015	41 454	70	2.8	2.7	0.32	38 651	34 643 793	0.92%
United Republic of Tanzania	2011–2012	50 447	62	3.4	4.2	0.49	67 091	36 876 839	1.3%
Viet Nam	2006–2007	94 179	70	1.0	2.4	0.28	34 225	83 518 842	0.34%
Viet Nam	2017–2018	61 763	82	2.0	2.2	0.26	26 950	83 518 842	0.31%
Zambia	2013–2014	46 099	66	5.4	4.2	0.50	64 143	23 861 420	2.1%
Zimbabwe	2014	44 951	75	3.5	–	–	–	20 672 356	–

TB: tuberculosis.

[a] Survey budgets were obtained from the first Ethiopian national population-based TB prevalence survey *(1)* and personal communication with survey teams from Cambodia, 2023–2024; Eswatini, India, Lesotho and Myanmar, 2017–2018; and Mozambique, Nepal, South Africa, Timor-Leste and Viet Nam, 2017–2018. A budget was not available for the Philippines, 2007.

[b] The survey budget from the main year of the survey was inflated to the value of 2022 US dollars by using published gross domestic product deflator values and conversion from local currency to US$, using published official exchange rates for 2022 (Source: The World Bank database *(2)*). Values could not be calculated for surveys conducted in the Democratic People's Republic of Korea and Myanmar, 2009–2010; or Zimbabwe. For Malawi and Myanmar, exchange rates for 2020 were used, and for the United Republic of Tanzania, exchange rates for 2021 were used, because values for 2022 were not available.

[c] The annualized survey budget was obtained by dividing the survey budget (in US$, constant values for 2022) by the annualization factor (8.53) that applies for a discount rate of 3% and an assumed lifetime of 10 years (i.e. assuming that surveys are undertaken about once every 10 years).

[d] Available funding was obtained from the Global Tuberculosis Report, 2023 *(3)*. Data were not available for the Gambia.

[e] Thailand's survey originally had a sample size of 90 000 but this was reduced to 74 700, which excluded the Bangkok area. There were 62 536 participants from the non-Bangkok area.

survey budget will be higher than the real cost of the survey. For example, if a survey takes a year to complete but the useful life of X-ray machines, vehicles and laboratory equipment is 8 years, the real cost of these items for the survey itself will be only a fraction more than one eighth of their purchase price (i.e. the total cost is divided by a factor that allows for the need to pay the full cost of these items upfront, rather than spreading the payment over time, and that allows for their full useful life). This is the reason for showing annualized budget values in **Table 15.1** and **Fig. 15.1**.

15.2 Typical components of a budget for a national TB prevalence survey

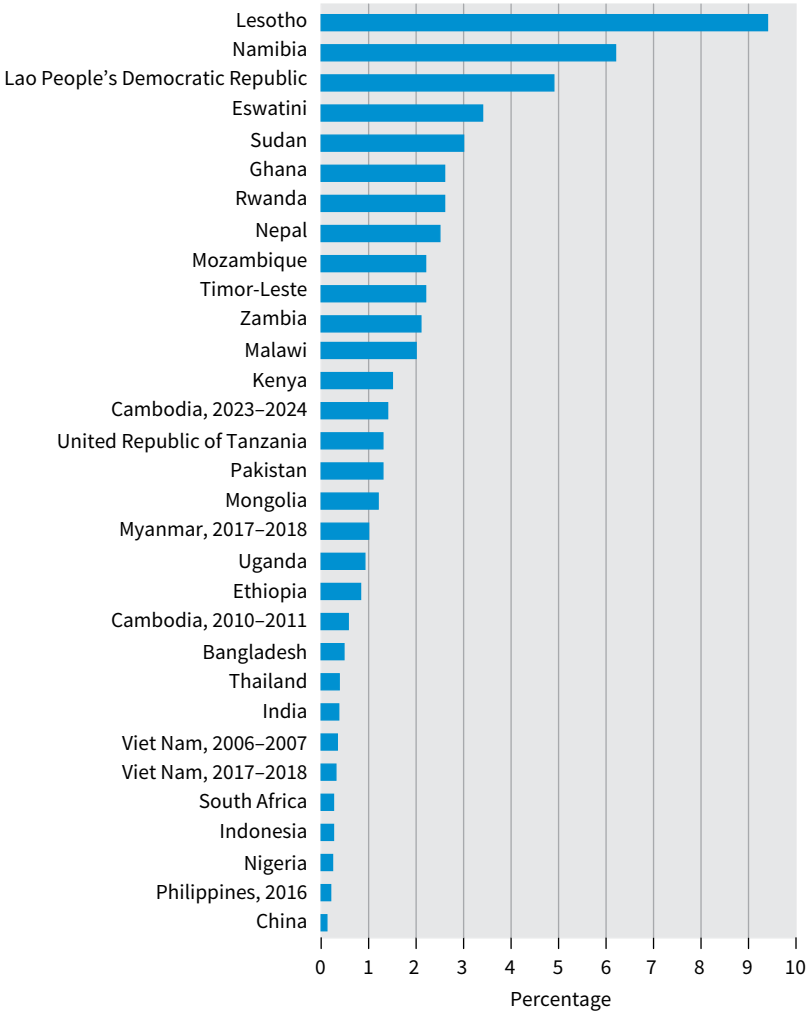
When the budget line items of surveys are analysed, there are usually three major categories of cost: field operations (excluding staff costs), with the total budget closely related to the number of survey clusters; staff costs, especially the salaries or fees of the staff responsible for overall coordination and implementation of field operations; and procurement of survey equipment and supplies, including chest X-ray (CXR) machines, laboratory equipment, information technology (IT) equipment and laboratory consumables. Each of these three categories generally accounts for about 30% of the total budget (**Fig. 15.2**).

The main subcomponents of these major categories of cost are as follows:

- **Staff.** A central survey team is needed at the national level to lead and manage survey operations and logistics. Staff at the central level are also needed to supervise field operations, and radiology and laboratory processes; manage and analyse data; write the survey report; and disseminate findings. Additional human resources (often including community volunteers) are required at the local level for field operations; in addition to salaries or fees for their time, per diems for food and accommodation are usually required. Government stipends and fees may be appropriate, but if non-NTP staff are used, other stipends and fees may be required.
- **X-ray equipment and accessories.** X-ray equipment and related accessories and consumables are essential to implement the screening strategy required in a survey, which always includes CXR screening for the entire eligible adult population (**Chapter 3**). The survey budget will be influenced by various factors: the type of digital technologies chosen for use, whether capital equipment and service contracts are purchased or leased, whether computer-aided detection (CAD) is used (including associated IT services such as DICOM® licences and data storage); and whether staff (e.g. radiographers, drivers and radiologists) are hired individually or as part of an overall leasing pack-

Fig. 15.1

Annualized survey budget (in constant US$ values for 2022) as a percentage of the total amount of funding available for the TB response at the country level in 2022, 31 national TB prevalence surveys implemented between 2007 and 2024[a]



TB: tuberculosis.

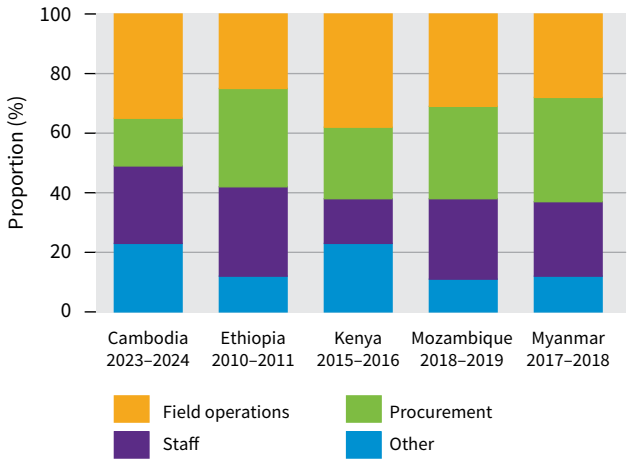
[a] The annualized budget assumes an expected lifetime of a survey of 10 years and applies a discount rate of 3%.

age. Many countries routinely use X-ray equipment and accessories as part of active TB case-finding and screening activities, so there may be scope for such equipment to be temporarily used or borrowed for a survey.

- **Laboratory equipment and supplies.** Depending on the existing availability and capacity of laboratories, the equipment to be budgeted for could include mycobacterial growth indicator tube (MGIT™) culture and GeneXpert® platforms (or equivalent), incubators, deep freezers, centrifuges and autoclaves. The survey will need to include a budget for laboratory consumables, for both molecular and culture testing. A specific budget will also be needed for the transportation of sputum samples from the field to a central laboratory, and for external quality assurance (QA) for the main laboratory.
- **IT equipment and data management.** Surveys that are fully (or almost fully) digitalized require digital resources such as tablets, laptops and servers, including internet access and mobile connectivity. The time and effort required to configure and maintain these devices should be included in the survey budget. The devices will be needed for the field teams as well as the central survey, laboratory and radiology teams, and are essential for ensuring a high quality of survey data management, analysis and communication.
- **Survey documentation and field supplies.** Examples of documentation and field supplies include logbooks, banners, T-shirts, hiring of tents and chairs, and cooling fans. Translation of documents may also be required.
- **Training.** Training is required for all aspects of the survey including reading of CXRs, how to conduct interviews, laboratory operations, and survey and data management. Refresher training may also need to be budgeted for, especially if there are adjustments to the protocol and standard operating procedures. Training of key survey staff in good clinical practice and good data management practices should also be considered.
- **Field operations.** These include one or more pilot surveys, visits to clusters in advance of full survey operations (presurvey visits), and the conduct of the survey itself. Vehicles could be leased (or borrowed) rather than procured, especially given that many NTPs have previously bought vehicles for other projects. Fuel should also be budgeted, along with internal flights if the distances between survey clusters and laboratories for culture testing are large and other forms of transportation are too slow. Travel costs can account for a large share of the total cost of field operations. Budget line items for community sensitization activities and materials to communicate with the public should also be included.
- **Workshops and meetings.** There will be a need for workshops and meetings for the central survey team and associated committees to prepare a survey, to provide survey oversight, to raise awareness and to conduct advocacy, and for data analysis.

Fig. 15.2

Distribution of survey budgets by major category for six selected national TB prevalence surveys[a]



TB: tuberculosis.

[a] "Other" accounts for training, dissemination, workshops, meetings and administration. Field operations may include field staff salaries. Source: Survey reports from Ethiopia *(1)* and Kenya *(4)* and personal communication.

- **Technical assistance.** Technical assistance is often required throughout the survey, especially in countries where some of the expertise required for a survey may be relatively scarce and in countries implementing a survey for the first time. In the early planning phases, technical assistance may be needed to draft and finalize the protocol, and to develop an implementation plan. At a later stage, assistance may be needed for activities such as selection of clusters, previsits to selected clusters, training of survey teams, provision of advice on data management and laboratory practices, and provision of advice during the pilot survey and field operations. It has also been standard practice to involve international experts in mid-term reviews, analysis of data and dissemination of survey findings.
- **Ethical review.** In some cases, a fee may need to be paid for the review and clearance of a survey protocol by relevant ethical committees.
- **Dissemination.** Dissemination includes preparation of a survey report, final review and agreement of results, followed by workshops to disseminate results, and publication of findings in international conferences and peer-reviewed scientific journals. This should be a high priority but is often a neglected part of a survey.
- **Additional studies.** Provided that they do not reduce overall survey quality, additional studies could be nested within a national TB prevalence survey to take advantage of the survey design (**Chapter 10**). Depending on the study objective, this will probably require additional staff and equipment.

It is also useful to structure the budget into four main parts, in terms of inputs and activities that are needed:

- throughout the survey;
- in the preparatory phase;
- during the implementation phase; and
- after field operations have been completed.

In this categorization, the main budget items that need to be included are as follows:

- **Throughout the survey:** staff salaries and associated costs (e.g. staff insurance) for the central survey team and technical assistance.
- **Preparatory phase:** any vehicles, equipment and supplies that need to be procured (or leased) for field operations, maintenance of equipment and vehicles, recruitment of survey teams, training, meetings, awareness-raising and advocacy, development and printing of documentation (e.g. forms, questionnaires and interviewer guides) and ethical clearance.
- **Implementation phase:** staff needed for the field operation survey teams, transportation costs (e.g. fuel) for activities such as a pilot survey, previsits to clusters and full survey operations, and data management.
- **Post field operations phase:** analysis of data and preparation of a report to summarize survey methods and results, a workshop to discuss and finalize results, a workshop to disseminate results, and the preparation and submission of manuscripts for peer-reviewed journals.

Budgets for all items are best created using the so-called ingredients approach, in which the quantity of units of each item is first specified separately from the items unit price, and the total budget is then calculated by multiplying quantities by unit prices.

The cost of a survey sometimes ends up being higher than anticipated; for example, if:

- there are unforeseen circumstances (e.g. severe weather, national strikes, staff resignations or national elections) that interrupt and cause delays in field operations;
- certain items increase in price between the planning and implementation of the survey (e.g. due to inflation within the country, or changes in exchange rates for imported items); or
- the value of donor funding falls between when it was initially provided and when it is used (due to exchange rate fluctuations).

There may also be some breakdowns of equipment that could delay field operations. For these reasons, some contingency funding (e.g. about 10% of the total for other items) should be included in the survey budget, to allow for such eventualities.

A detailed example of a template that could be used (and adapted as necessary) to develop a budget for a

national TB prevalence survey is provided as online supplementary material. The example is not intended to provide a fully comprehensive or exhaustive list; however, it does identify the most important items for which a budget is likely to be needed. For specific components of the survey, the central survey team should consult with relevant experts (e.g. experts in radiology, laboratory work and data management) to ensure that all necessary items are included and are budgeted at the appropriate unit costs.

15.3 Major factors that influence the absolute size of the required budget

The major factors that influence the absolute size of a survey budget include:

- **sample size**, number of clusters and nature of the terrain – these affect the number of survey teams needed, the length of field operations and the form of transportation required;
- **CXR equipment** – different technologies are available for screening survey participants, and these vary in cost (see **Chapter 7**); the type of equipment that can be used is also determined by national regulations on radiation exposure; and
- **human resources** – a specific budget is required for staff to manage the survey and conduct field operations; levels of staff salaries and per diems vary among countries, and are usually closely related to the average income level of a country; an additional budget may be required for external technical assistance.

15.3.1 Sample size, number of clusters and nature of the terrain

The sample size and the number of clusters (see also **Chapter 5**) affect how many survey teams are required, how much equipment is needed (e.g. vehicles, IT equipment, X-ray machines, Xpert® machines and cartridges), and the duration of field operations. Typically, a survey will require at least three survey teams, but more may be required if field operations are to be completed within 6–12 months. The larger the number of clusters that are in relatively inaccessible areas with difficult terrain, the higher the budget for items such as vehicles or other forms of transportation. Also, severe weather and challenging seasonal weather conditions combined with difficult terrain may necessitate some rescheduling of field operations. One reason why survey costs were higher in African compared with Asian countries was the geographically large sizes of countries relative to population,, on average, and the comparative geographical inaccessibility of large areas.

As stressed in **Chapter 1** and **Chapter 5**, the primary objective of a national TB prevalence survey is to obtain a reliable estimate of the prevalence of bacteriologically confirmed pulmonary TB **at the national level**. In countries where the production of **subnational estimates** is a secondary objective, additional clusters will be required at one or more specific subnational levels (e.g. province or state) to ensure that any subnational estimates have an adequate level of precision. There may be as much as a doubling of the number of clusters in the survey if subnational estimation is planned, which in turn will considerably increase the overall cost. If subnational estimation is considered, the central survey team should consult with relevant experts in TB disease burden estimation.

15.3.2 CXR equipment

Investment in X-ray equipment for each field team typically accounts for a large share of the survey budget. The transition from analogue to digital CXR systems has greatly improved the portability, delivery, reading and storage of the CXR equipment needed for mass population screening, as is used in a national TB prevalence survey. However, such systems do require a significant outlay. The cost for one unit of X-ray equipment is about US$ 95 000 (at 2024 prices) if direct digital radiography is used.[1] Details of the different types and costs of X-ray equipment used in surveys are given in **Chapter 7**.

In addition to the type of equipment selected for use, factors that affect the required budget for X-ray equipment include the following:

- **The number of X-ray systems needed per survey.** For the ideal survey duration of 6–8 months with three to five survey teams, the number of X-ray machines corresponds to the number of survey teams. Some countries may decide to purchase an additional back-up machine, to avoid delays to field operations if one unit breaks down. For geographically challenging regions, an extra and more portable X-ray machine might also be required. It may be feasible to negotiate prices below those officially quoted if multiple items are bought in bulk or via a specified vendor.
- **Service contracts (and warranties).** Given the large number of X-rays to be performed in a short space of time, sometimes in hot and dusty environments with inconsistent electricity sources, X-ray machines may break down. Therefore, it is important that the budget includes service contracts (and warranties) for in-country servicing of equipment by local engineers.
- **Available choice of X-ray equipment.** The choice can be constrained by national regulations related to radiation. For example, national or regional regulations may preclude the use of X-ray machines in open spaces, meaning that either containers must be pur-

[1] The unit cost includes hardware, CAD software, installation, training and warranty (1–3 years) based on the 2025 Global Drug Facility catalogue for diagnostics, medical devices and other health products *(5)*.

chased or infrastructure in which to conduct X-ray screening must be identified. Budgets need to reflect both the equipment and associated infrastructure needed to comply with these regulations.

- **Staff for reading of X-rays.** The staff needed to maintain and read CXRs include radiographers, radiologists and IT technicians. Even after field operations have been completed, radiologists are required to provide QA and re-reading of CXRs. If not available at the local level, a radiologist might be able to help remotely (i.e. at a distance, in the country or even outside the country), provided that digital technology is used and images are transmitted electronically.
- **Licensing.** Digital systems have the advantage and utility of rapid storage and archiving of CXRs. However, funding may be required to access these images if they are stored on a professional server. Access to images and associated licensing costs may require discussions with the vendor to ensure that DICOM images can be accessed, both during and after field operations.
- **CAD.** A recent advance in the use of digital radiography is the recommended use of CAD *(6)*. The costs of CAD vary depending on the vendor, specifications, licences (e.g. per-use or perpetual), volume usage and various add-on services. The Stop TB Partnership and the Foundation for Innovative New Diagnostics (FIND) have developed a resource to compare different CAD products *(7)*. The Stop TB Partnership's Global Drug Facility also provides more details in its diagnostics catalogue *(5)*.
- **Logistics.** Considerations include the transportation of equipment with each field team, and additional power sources (e.g. a generator, if electricity is limited at the field site). Protective transportation cases for X-ray equipment will require extra space in a vehicle. In cases where a mobile CXR van is used, a dedicated driver may be required.
- **Leasing.** As an alternative to procurement of X-ray equipment, the **leasing** of X-ray systems –including vehicles, radiologists and other support as a complete package – may be feasible. This could save on the outlays that would otherwise be required for X-ray equipment, with the drawback being that the equipment will be available only for the duration of the survey (and not then subsequently available to be deployed for non-survey uses).

15.3.3 Human resources

A survey requires a central survey team that leads and manages survey design and implementation. Staff are also needed to manage and implement field operations. Whether or not a specific budget is needed for such staff varies among countries.

In several countries, surveys relied on staff already employed by the NTP or local staff at the community level who were employed by the ministry of health (or equivalent), with no staffing budget required for the survey per se. Some other countries have had a specific budget for an outsourced central survey team (e.g. based at a university or research institute) and associated field teams. Such outsourcing generally reduces the level of effort expected from the NTP staff during survey implementation, allowing them to continue to focus on implementation of routine NTP activities. This approach was often used for national surveys in African countries, and is one reason why survey budgets were typically higher than in Asian countries (**Section 15.1**).

Staff need to be paid even when survey operations are not going to plan. More generally, ensuring that staff are always paid on time, throughout the survey, is good for team morale and helps to ensure a high-quality survey. If the survey needs to be extended, then staff need to be paid for any extra time that is required.

15.4 Potential ways to minimize costs and optimize the use of survey resources, including for future non-survey-related activities

During the preparatory phase of the survey, a sustainability plan should describe how any newly purchased capital equipment will be used once the survey has been completed. For example, X-ray equipment could be used for future active case-finding activities.

For items such as X-ray equipment with a useful life that extends beyond the end of the survey, survey managers should, wherever possible, purchase models that will be useful once survey operations have been completed. For example, if X-ray equipment has been purchased, it is important to select models that can be used within health facilities or for active case-finding once the survey has been completed, and for which maintenance contracts can be obtained.

The benefits of a survey may also extend beyond the survey itself. For example, national TB prevalence surveys can help to build skills and expertise in data management, X-ray reading and data analysis; they may also catalyse the expansion or improvement of laboratory capacity. The sustainability plan should highlight how human resource capacity (within and beyond the NTP) will be developed through survey activities.

Some countries usually conduct repeat surveys about 10 years after the previous one, which means that there are generally no specific items that could be reused from the last survey, to save costs. However, ideally, some of the people who were closely involved in the previous survey would be engaged to support the repeat survey. Such experience and "institutional memory" can be invaluable for successful avoidance (or otherwise anticipation and navigation) of common challenges, and for ensuring that the survey is planned and implemented smoothly, effectively and efficiently.

BOX 15.1
POTENTIAL WAYS TO OPTIMIZE THE USE OF RESOURCES REQUIRED FOR NATIONAL TB PREVALENCE SURVEYS

1. Aligning with existing plans for equipment procurement (e.g. of X-ray equipment, MGIT culture and GeneXpert platforms), so that such equipment can be used for survey field operations as well as routine activities.
2. Using resources that already exist wherever possible, rather than purchasing new items, provided this will not be detrimental to existing activities; examples include vehicles, mobile vans for transportation of GeneXpert machines, and portable X-ray equipment and computer servers.
3. Using in-country technical expertise from other government institutions, academia, national laboratories and technical partners wherever possible. There may also be opportunities to draw on expertise available in neighbouring or nearby countries that have already conducted a survey.
4. Ensuring good coordination, collaboration and communication among stakeholders (domestic and external) to avoid potential duplication of effort.
5. Exploring the potential incorporation of already planned minor activities into the design (and protocol) of the national TB prevalence survey, rather than conducting two separate activities, if this could make both activities more efficient. However, the added value, feasibility and benefits should be carefully considered, because addition of other activities could risk a delay in implementing the survey or could affect survey quality.

Other examples of ways in which the use of resources can be optimized are described in **Box 15.1**.

15.5 Sources of funding for prevalence surveys

High-level political and administrative commitment is essential for successfully undertaking a national TB prevalence survey. Surveys need to be viewed as a priority at both national and subnational (e.g. province and region) levels, to mobilize the necessary funding and ensure the quality of survey design, preparations, implementation and analysis. Domestic funding or co-funding should be strongly considered, and is arguably a prerequisite, for initiating survey preparations and planning.

The main sources of funding for national TB prevalence surveys include domestic budgets, international donor agencies (via bilateral or multilateral mechanisms) and foundations.

In surveys implemented from 2007 to 2024, the single biggest source of funding for national TB prevalence surveys was the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). The importance of the Global Fund in financing surveys in Africa and Asia from 2010 onwards is especially striking; in most countries that implemented a survey, the Global Fund was the only, or by far the most important, source of funding (**Fig. 15.3**).

The total budgets of the 35 surveys implemented from 2007 to 2024, at US$ 135 million (in 2022 US$ values), were still a very small share (less than 1%) of the total funding allocated by the Global Fund for the TB response during this 18-year period.

Bilateral donors that have contributed funding for national TB prevalence surveys include the governments of Australia, France, Japan, the Netherlands and the United States of America.

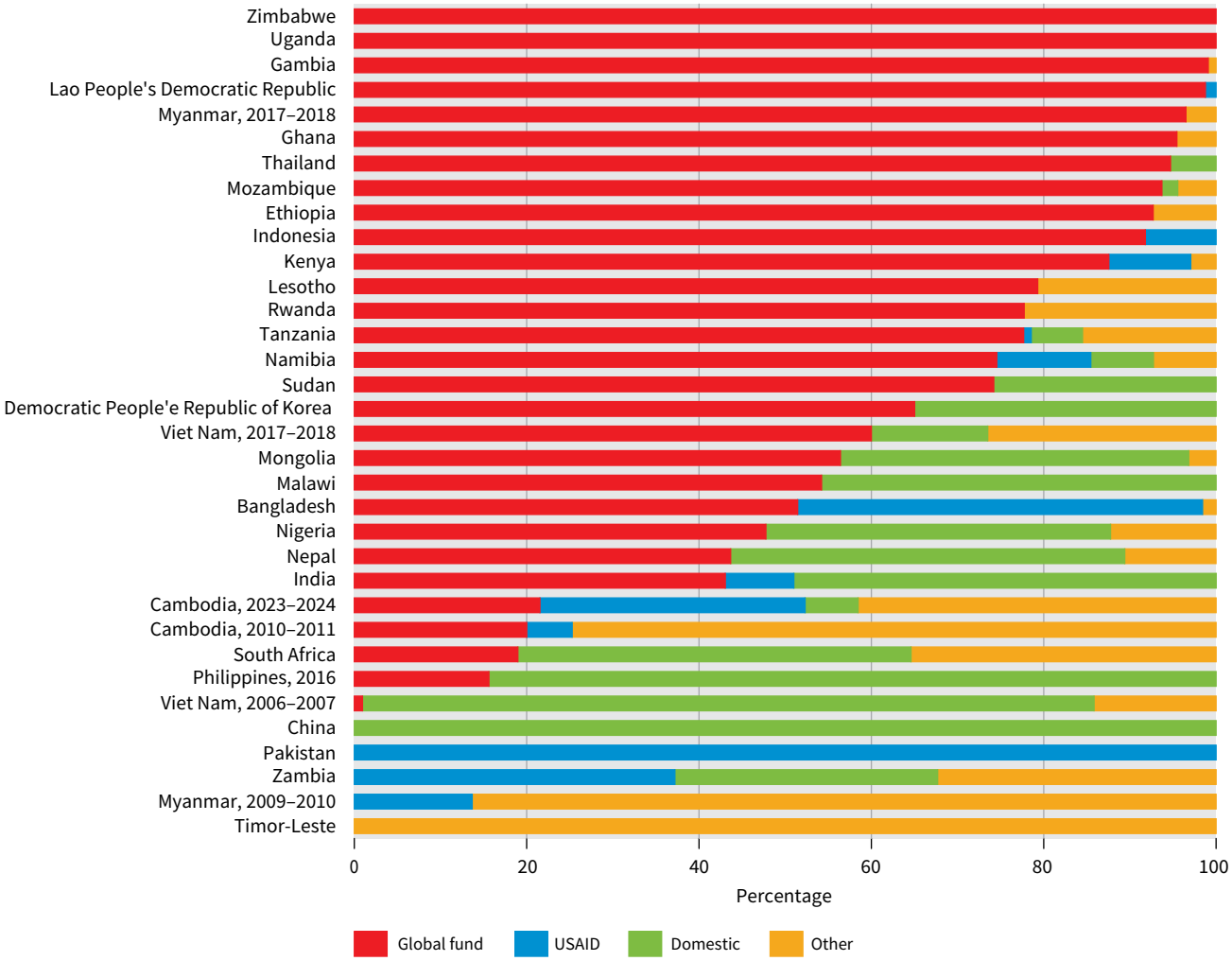
National governments that made significant contributions to their own surveys include China (2010), the Philippines (2016) and Viet Nam (2007).

To mobilize funding for national TB prevalence surveys from national governments and donor agencies, the importance of undertaking a survey must be demonstrated, and supported with a technically sound proposal, a detailed workplan and a budget. The budget should be clearly presented and the budget items – in particular, the items that account for the biggest share of the total survey budget – clearly justified.

Where appropriate, demonstration of cost-sharing and use of existing resources will be helpful. Resource mobilization efforts will also be facilitated if the budget justification includes an explanation of how the inputs and activities included in the budget (e.g. X-ray equipment and laboratory strengthening) will have benefits that extend beyond the survey itself.

Fig. 15.3

Sources of funding for national TB prevalence surveys (expressed as a share of the total reported budget[a]), 2007–2024



Global Fund: Global Fund to Fight AIDS, Tuberculosis and Malaria; TB: tuberculosis; USAID: United States Agency for International Development.

[a] Budget at the time of the survey. "Other" refers to financial contributions from partners not listed (e.g. Bill & Melinda Gates Foundation, KNCV Tuberculosis Foundation, Japan International Cooperation Agency, Population Services International, Three Diseases Fund, United States Centers for Disease Control and Prevention, World Health Organization and World Bank), other external government funds (e.g. Australia, France and the Netherlands), or a mixture of contributions that could not be disaggregated. These proportions are an approximation based on survey reports and personal communications. There were instances where in-kind contributions or survey staff who were seconded from other funded projects are not documented. A budget was not available for the Philippines (2007); budget breakdowns were not available for Eswatini and Mozambique.

References

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CHAPTER 16

Data management

Data from a tuberculosis (TB) prevalence survey must be collected and managed using a standardized, systematic and robust process. This must be done by experienced and well-trained personnel, to ensure that the data are accurate, reliable, precise and complete, and that staff will maintain confidentiality and data integrity. The final consolidated survey database should be free from duplicates and errors, and should have as little missing data as possible. Quality assurance (QA) measures need to be in place, to ensure that any problems with data are identified and fixed, so that the data can be used to make accurate decisions.

This chapter first explains the importance of data management in population-based surveys, based on experience from TB prevalence surveys conducted between 2010 and 2019. It also provides key recommendations to address common problems associated with data management. The chapter then describes all the components that must be in place in preparation for data collection; for example, appropriate staffing and training, development of the survey data management system and development of a data management plan (DMP). The process and content of data collection during field operations are described, as are the procedures and processes that need to be in place to ensure data quality. Finally, the chapter outlines key analyses and uses of survey data, both during and after field survey operations.

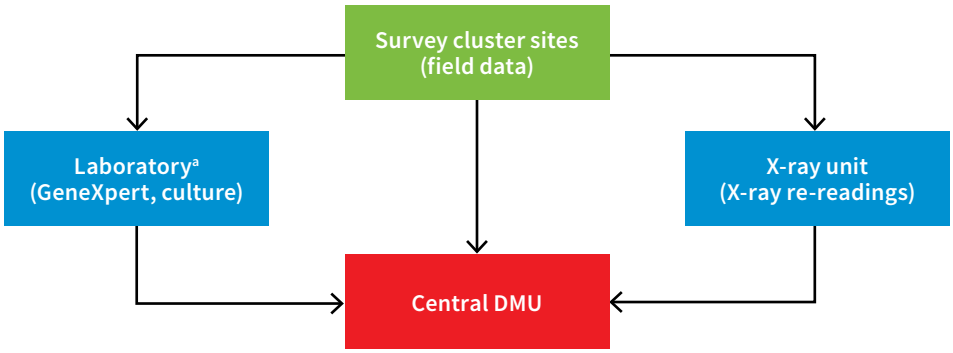
16.1 Overview

Data management consists of the processes and procedures for collecting, validating, processing and archiving data from the planning phase of a survey to the survey's implementation and completion, including analysis and publication of results. The aim of data management is to produce a reliable and high-quality consolidated dataset, so that prevalence survey data can be analysed, and the survey results reported and used as specified in the protocol and described in **Chapters 17**, **19** and **20**.

Data generated as part of a national TB prevalence survey are collected and linked across various locations (**Fig. 16.1**). These locations typically include all the survey cluster sites where field operations are conducted, a central chest X-ray (CXR) unit where CXRs are re-read (for QA and to inform survey objectives that require these data for their case definition), and all the laboratories that process sputum specimens collected from eligible survey participants and produce bacteriological test results. Within survey cluster sites, data on the same individuals are recorded at multiple positions and at different times. The recommended data collection tools are provided in **Chapter 6** and the details of all field operations conducted in each cluster site in **Chapter 13**. All survey data are ultimately consolidated into a final survey dataset that is managed by a central data management unit (DMU).

Fig. 16.1

Illustrative flow of data in a national TB prevalence survey using the recommended screening strategy



DMU: data management unit; TB: tuberculosis.

[a] Xpert test results could also be transmitted to the central DMU if Xpert testing occurs in the field.

Table 16.1

Sample size, number of clusters and number of enumerated individuals from selected national TB prevalence surveys

COUNTRY	YEARS	PLANNED SAMPLE SIZE	NUMBER OF CLUSTERS	NUMBER OF ENUMERATED INDIVIDUALS
Bangladesh	2015–2016	100 000	125	148 126
Ghana	2013	64 000	98	101 772
India[a]	2019–2021	500 000	625	354 541
Indonesia	2013–2014	78 000	156	112 350
Kenya	2015–2016	72 000	99	126 389
Myanmar	2017–2018	69 000	70	93 806
Pakistan[b]	2010–2011	133 000	95	131 377
Philippines	2016	54 000	106	89 663
South Africa	2018–2019	55 000	110	68 771
Sudan	2013–2014	91 131	109	150 490
Viet Nam[b]	2017–2018	82 000	82	87 207

TB: tuberculosis.

[a] During the course of the survey, the sample size was revised downwards.

[b] Only those aged 15 years and above were enumerated.

16.1.1 The importance of data management in population-based surveys

TB prevalence surveys are complex, involving the recording of data for tens of thousands of elements, with survey operations spread over many months and occurring at hundreds of locations. A survey's final dataset can contain over 100 000 individual records, each containing over 100 variables. **Table 16.1** summarizes the scale of selected surveys carried out between 2010 and 2019, in terms of their planned and actual sample size, and number of clusters in which field operations were conducted.

All survey data must then be brought together into a coherent whole that accurately represents the operations undertaken during a survey. This requires systematic and careful management so that survey operations can be monitored properly (preferably close to real time, to allow for corrective actions where needed) and the final dataset can be used to produce the specified analyses. Data management is an essential part of each survey.

Data management was one of the top five challenges in the 25 national TB prevalence surveys implemented between 2007 and 2016 *(1)*. **Box 16.1** provides recommendations to address common problems associated with data management that surveys have faced in the past.

16.2 Preparation and planning for data collection

This section describes the various elements that must be developed or put in place before data collection. These are the specialized human resources required to undertake the complex job of TB prevalence survey data management, the selection of software for use in the development of the data management system, and the reference document (i.e. the DMP) that describes all data management activities for the full life cycle of the survey data.

16.2.1 Staffing and responsibilities

The successful planning, implementation and management of a TB prevalence survey depends on the staff who collect, analyse and use the data; it is these staff who ensure the effectiveness and ethical conduct of the survey. This section presents the key personnel required at the central level, the cluster level (where field operations take place) and all other locations where data for the final consolidated survey database are generated.

DMU at the central level

The DMU is where the central data manager and their team are located and manage the central survey database. The DMU receives data generated from the field, the central CXR unit and the laboratories where sputum specimens collected during survey operations are processed. The DMU must ensure that these data from different locations and data systems are transferred into the consolidated survey database accurately, completely and in a timely manner. The data transfer mechanism or mechanisms can be automated as part of an interoperability solution between data systems (this is the recommended approach) or can be done manually.

The DMU is also responsible for capacity-building among all staff collecting data for the final consolidated survey database, according to the survey protocol and associated standard operating procedures (SOPs), as described in **Chapter 12**. Ultimately, it is the DMU that is responsible for the completeness, validation and high

BOX 16.1
RECOMMENDATIONS TO ADDRESS THE MOST COMMONLY OBSERVED PROBLEMS ASSOCIATED WITH DATA MANAGEMENT, FACED BY NATIONAL TB PREVALENCE SURVEYS, 2007–2016

Preparation and planning for data collection

Staffing

- Establish a DMU headed by an experienced data manager to take overall charge of data management activities. The survey data manager should be involved from the early planning stages of the survey, including contributing to the design and development of data collection tools, and developing the survey data management system and DMP.
- Ensure that the DMU has all the relevant specialized skills, such as data management, software and database development, information technology (IT) and data visualization.
- Appoint a team of experienced and competent field data managers and IT engineers. Each survey field team should include at least one data manager assigned to data validation and transfer, and one IT person assigned to ensure that all digital equipment is working properly in the field. Ensure that field data managers have backup (if needed) and support from the rest of the field team.
- Ensure that staff managing field data have a data-related background. Train data managers thoroughly in the use of the data management system before the start of survey operations and conduct one or more refresher trainings when needed.

Developing the survey data management system

- When developing the data management system and choosing the software, be guided by the expertise of the data manager and local software developers. Ensure that the software selected supports offline data collection and works on a local area network (LAN), so that survey operations can continue even when internet connectivity is limited or disrupted. Do not use Microsoft Excel® because it is not appropriate software for the management of the types of large datasets produced in these surveys.
- Establish software development procedures. The software developers should use version control and bug-tracking software to manage development, along with a standard process to distribute software updates.
- Thoroughly test and pilot all data management equipment, software, tools and procedures (e.g. data collection forms, data entry screens, transfer of data and feedback loops) to ensure that the system behaves as expected. Identify and correct bugs, and illogical or missing steps.
- Develop a backup system for data collection in the field using paper forms that can be used in an emergency (i.e. if digital tools and processes are unavailable or not working) to avoid delays.

Other

- Develop a DMP documenting all data collection tools and data management processes for the whole life cycle of the survey data.
- Procure appropriate equipment such as servers, tablets, laptops and digital CXR machines with monitors, barcode printers and scanners.

Data collection during field operations

- Set up regular, two-way communication channels (e.g. groups in messaging applications) between the DMU and field data managers.
- Use a LAN during field operations to establish proper communication between computers used at the different cluster stations. Upload data from a field server to the central server at a time that does not affect survey operations (e.g. at the end of a day). Even in countries with excellent mobile phone network coverage, the internet may not work well in remote areas. Poor internet connection can cause delays, especially for surveys that use a web-based data management system with real-time data transfer.
- Ensure that enumeration (census) data are fully available at the reception cluster station before cluster operations begin. If such data are not available, this can severely hamper the registration of participants arriving for screening.
- Have backup equipment in the field, and ensure that experienced IT staff are assigned to each field team for troubleshooting of equipment when needed. If these measures are not in place, delays in cluster operations may be experienced.
- Hire a guard to protect staff and equipment 24 hours a day in remote or insecure areas. Train data collectors on security measures. There have been some cases of violence against survey data collectors who were using tablets; such incidents can lead to delays in operations and require re-sensitization of the local communities where field operations take place.

Continued

BOX 16.1
RECOMMENDATIONS TO ADDRESS THE MOST COMMONLY OBSERVED PROBLEMS ASSOCIATED WITH DATA MANAGEMENT, FACED BY NATIONAL TB PREVALENCE SURVEYS, 2007–2016

Ensuring data quality

- Design and implement a system to allocate a unique personal identification number (PIN) to each survey participant. The system should not use handwritten PINs; instead, it should use scannable stickers and forms with barcodes or quick-response (QR) codes.
- Build data validation and consistency checks for use at all levels: cluster sites, laboratories, central CXR unit and DMU. This includes check-codes for data entry, a dashboard for data visualization and a built-in data validation tool for data QA.
- Pay particular attention to the field data validation tool, which should be a built-in component of the survey data management system. Field data validation and cleaning are important to identify errors and clean the data while the team is still in the field. If data validation and cleaning are not undertaken in the field, then they have to be done at the DMU, which can delay the final analysis and report writing.
- To avoid human errors during data entry, develop and use interoperability solutions between the survey database and systems holding data on survey participants (e.g. systems for data on CXR readings or laboratory results).
- Ensure that data are checked and verified daily at all the locations where they are being collected.
- Ensure that all essential documents and digital files are stored securely.
- Ensure that all survey staff handling data (both digital and paper-based) respect the confidentiality of the information collected.
- Ensure that the survey management team restricts access to all devices used to collect data to authorized staff, and use password, facial or other controls to enforce this.

BOX 16.2
EXAMPLES OF DATA MANAGEMENT PROCESSES AT THE CENTRAL LEVEL OF NATIONAL TB PREVALENCE SURVEYS

Nepal, 2018–2019

The survey data management system was installed at three laboratories for specimen registration and recording of test results. All laboratory staff were trained to use the system. Barcode labels and readers were used at all stages of sputum processing. Smear and culture results were entered directly into the system immediately after reading by laboratory technicians. Results from Xpert® MTB/RIF were exported from the GxAlert system to Excel files and transferred via USB memory sticks to the laboratory computer, where the files were imported into the survey data system.

The system was also set up at the central survey radiology department. Field CXR images were transferred to the central unit on the same day or the next day, depending on the internet connection in the field. Two radiologists read the images independently of one another and recorded their readings. The software identified and listed discrepant reading results between the field and central levels. Field data managers were notified of discrepancies and were able to take action, whilst in the field, according to the SOPs (e.g. modifying the sputum eligibility status of survey participants and contacting them to request sputum specimens).

Myanmar, 2017–2018

Sputum smear and culture results were received from the central laboratory on paper forms and entered into the survey data management system at the central DMU. The Xpert Ultra results were extracted as Excel files from the national GxAlert system, transferred via encrypted emails to the central DMU, and then imported into the survey data management system. Central CXR readings were received on paper from the central CXR unit and entered into the survey data management system at the central DMU. The three datasets (i.e. smear and culture results, Xpert results and central CXR readings) were validated, cleaned and merged into the central database by the central survey data manager.

quality of all data in the final consolidated survey database.

Box 16.2 provides examples of data management processes at the central level from two previous surveys.

The DMU should be headed by an experienced survey data manager, who takes overall responsibility for the management of all survey data required for the final consolidated survey database. The survey data manager must be part of a dedicated core survey team that is involved from the initial stages of protocol development and planning for the survey until the final consolidated survey database is analysed, and the results are fully disseminated and used.

The responsibilities of the **survey data manager** include the following:

- coordinate all data management procedures and processes at DMU;
- coordinate the development of the DMP, including all survey data collection tools;
- oversee the development of the survey data management system, including liaising with external companies if database development is outsourced;
- understand and, if necessary, troubleshoot major problems associated with the survey data management system;
- develop SOPs for data collection, validation and use;
- define the roles and responsibilities of all staff involved in data management activities;
- hire competent field data managers;
- train all staff who are involved in data collection, validation and use;
- supervise field data managers and IT staff, and monitor field data management through regular communication and field visits;
- provide feedback to field data managers on the quality and completeness of collected data;
- monitor data at the central level through data visualization dashboards and built-in data validation tools, to ensure data are complete, reliable and de-duplicated;
- oversee linking and merging of all survey data generated in multiple locations in the consolidated survey database;
- regularly extract the list of all sputum eligible cases for TB case identification and clinical management;
- advise the survey coordinator on data management issues;
- ensure that all paper documents are safely stored, and that all digital data files are securely stored and backed up;
- ensure that all necessary equipment and software are purchased and installed;
- report on progress with data collection and data management to the survey coordinator and the survey committee;
- attend survey management and implementation meetings, including those related to clinical management of patients; and
- contribute to the writing of the survey report and any associated peer-reviewed papers.

The DMU should also include one or more **IT managers or engineers**, to liaise with the survey's software development team in overseeing the establishment of interoperability solutions to other data systems that hold information on survey participants (e.g. a laboratory information and data management system [LIMS], GxAlert for making Xpert results available and digital readings of CXRs) and to be responsible for troubleshooting.

The **system software developers** should be directly involved in the survey planning. They should provide recommendations for the selection of the most appropriate software (or combination of different software) for the development of the survey data management system, participate in designing the data collection forms and thoroughly testing the system, and be involved in the development of reliable and secure data transfer mechanisms.

The DMU can also include **data entry clerks** if required, depending on the data entry SOPs.

Field data management teams

Each field team involved in cluster operations should include at least one data manager and, preferably, one IT person, depending on the complexity of the data management system. Some field data managers can combine both roles (i.e. data management and IT) if they have appropriate training. Field data managers should report to the central data manager and visit the DMU between field operations, to resolve any pending issues and prepare for field operations of subsequent clusters. **Chapter 12** provides details on the composition of the field survey teams.

The responsibilities of the **field data managers** include the following:

- participate in pilot testing of survey tools and processes;
- ensure that the data management system is working properly by the start of field operations in each cluster;
- ensure that all field staff are appropriately trained in data collection;
- validate and clean data daily during field operations, using built-in routines of the data management system;
- report problems and other issues with the data management system or IT, identified by any members of the field team, to the DMU and field team leader;
- back up data according to the agreed frequency;
- transfer data to DMU daily and at the end of operations in each cluster;

- produce cluster summary and survey progress reports; and
- enter data from paper forms into the digital system, if required.

The responsibilities of the **field IT staff** include the following:

- set up the digital data management system at the survey site, including connections to barcode printers and readers, and other data systems if required;
- troubleshoot problems and other issues with the data management system;
- support field data managers with data transfer and storage; and
- report IT associated problems and other issues with the data management system to the field data manager.

The responsibilities of other field or central staff involved with data collection (e.g. for CXR screening readings or laboratory results from sputum specimens collected from eligible survey participants) include the following:

- collect relevant data directly into the survey data management system or in other dedicated information management systems according to data collection SOPs; and
- report problems and other issues with the data management system to the field data manager.

Training on data collection

All survey staff responsible for data collection, analysis and use, either in the field or at the central level, must be fully trained before the first survey pilot.

- Field data managers should understand how the data management system works, including how to use the data visualization dashboards, validate and clean data, generate reports, transfer and backup data and provide some troubleshooting services to other field team members. They should also understand the data management SOPs, including those related to communication with the central DMU.
- IT field staff should understand how the data management system works, including how it is installed locally (e.g. connecting all devices to a LAN) and how to identify and fix problems. They should understand the data management SOPs, including communication with DMU and software developers.
- All personnel at the cluster stations, laboratories and central CXR unit should be familiar with their respective data entry screens, including validation rules and the relevant data visualization dashboards. Field operations data collection personnel should understand how all components of the survey system are related to each other.

16.2.2 Developing the survey data management system

There is currently no single out-of-the-box survey data management system that is recommended for use in national TB prevalence surveys. Each survey team, led by the DMU, must decide which software to use for developing the survey database (both at the back and front ends) and which tools to use for data collection. Decisions should be guided by suitability for meeting survey needs, and the DMU's existing experience, skillset and familiarity with specific software. When DMU and local experts are familiar with the chosen software, this facilitates the provision of technical support and troubleshooting. Other important considerations are the availability of dedicated financial resources for data management and local infrastructure (e.g. the availability, type and coverage of mobile phone networks).

The general stages of development and use of a survey data management system are shown in **Fig. 16.2**. It is important to plan for and establish clear activities to carry out for each of these stages. For example, the developers should use version control and bug-tracking software, including bug-fixing, to manage the design and development phase. The system must then be thoroughly tested – during development, during simulation exercises and as a part of survey piloting – to ensure that all components are working properly in operational conditions. After the survey pilot, the DMU should produce reports on the problems identified that need to be fixed before the survey can start. Finally, a standard process for the distribution of software updates should be developed, to ensure that the correct software version is used on all devices.

The survey data management system must include several components. All these components should be tested to ensure that they accurately capture the

Fig. 16.2

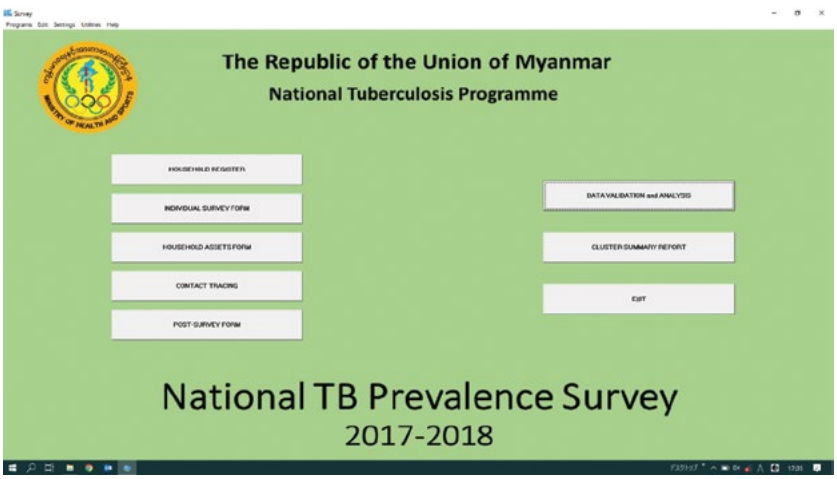
Stages of development and use of a survey data management system

required information and are logical and fit-for-purpose. The most important components are:

- user-friendly data entry screens, for each cluster site station, with built-in data validation (Fig. 16.3);
- an automated decision-making algorithm for participant flow and management (Fig. 16.4);
- data visualization dashboards, at cluster and central levels, for monitoring progress and taking action as necessary;
- automatically generated reports, at cluster and central levels, for data validation and monitoring of progress or other decision-making needs; and
- data linkages and interoperability solutions between the survey system and data systems for central CXR readings and laboratory results; where such dedicated data systems are lacking, the survey data management system will need separate modules to record each of these (such modules should be installed in the survey laboratories and the central CXR unit).

Fig. 16.3

Menu for the data management system of the national TB prevalence survey of Myanmar, 2017–2018



Source: National TB programme of Myanmar (reproduced with permission).
TB: tuberculosis.

Digital data collection in the field

Rapidly expanding use of digital technologies for TB, coupled with improvements with network and IT infrastructure globally, have opened the path for direct digital capture of health data in the field. The collection of data during field operations of TB prevalence surveys is no exception. Direct digital capture allows for the collected data to be monitored and validated for completeness and accuracy in real time.

This section describes two approaches to digital data collection in the field that have been used in recent surveys: directly digital and hybrid digital surveys (Table 16.2). Directly digital surveys are those where data are collected in real time from survey participants as they participate in cluster operations. Hybrid digital surveys are those where data from survey participants are initially collected in paper forms during cluster operations and are subsequently captured digitally by the field data manager (and data clerks) while the team is still at the cluster. Whichever approach is chosen, prerequisites of success are a comprehensive DMP, sufficient human and financial resources, and appropriate training of all staff involved in data collection processes. Table 16.3 lists the main advantages and disadvantages of the two approaches to digital data collection in the field.

Fig. 16.4

An automated decision algorithm to determine sputum eligibility in the TREATS project

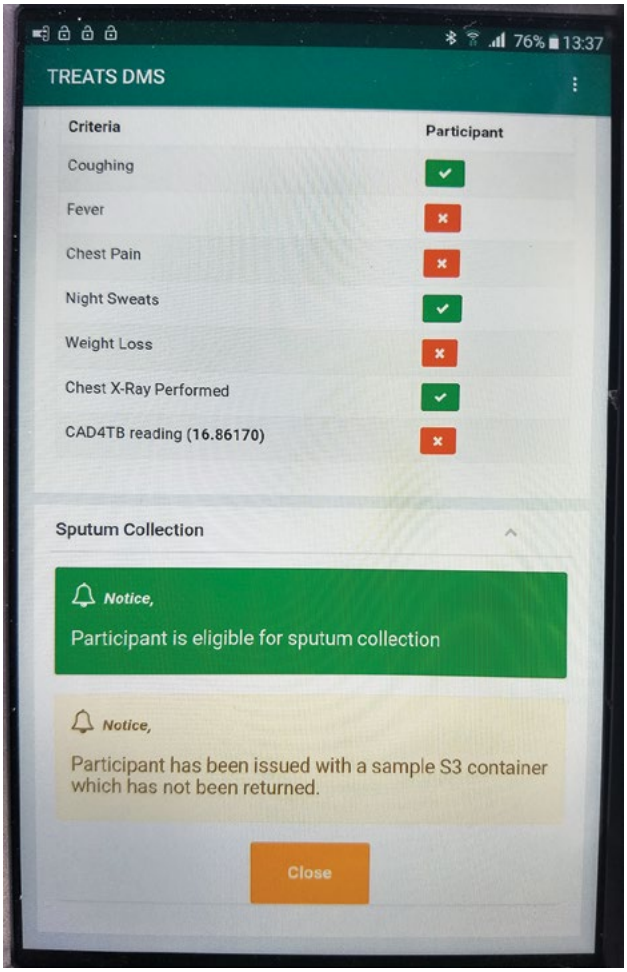


Photo credit: Eveline Klinkenberg.
TREATS: Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB.

Table 16.2

Approaches to data collection and software used for national TB prevalence surveys, 2016–2019

COUNTRY	YEAR	MODE OF DATA COLLECTION	SOFTWARE
Philippines	2016	Hybrid digital	Epi Info™ *(2)*
Myanmar	2017–2018	Hybrid digital	Epi Info™
Viet Nam	2017–2018	Directly digital	Custom-built software
Namibia	2017–2018	Directly digital	Custom-built software[a]
South Africa	2017–2018	Directly digital	REDCap *(3)*
Mozambique	2018–2019	Directly digital	Custom-built software
Eswatini	2018–2019	Directly digital	Custom-built software using ODK *(4)*
Lesotho	2018–2019	Directly digital	REDCap
Nepal	2018–2019	Directly digital	Custom-built software

TB: tuberculosis.

[a] Household data were collected using KoboToolbox *(5)*. Field operations data were collected using NAMTBCollect, developed using PHP software *(6)*, with MySQL *(7)* as the database backend and Apache *(8)* as the webserver.

Table 16.3

Advantages and disadvantages of the directly digital and hybrid approaches for data collection in the field for TB prevalence surveys

MODE OF DATA COLLECTION	ADVANTAGES	DISADVANTAGES
Directly digital	• Facilitates the management of survey operations and participant flows by automated decision algorithms. • Eliminates the need for paper forms to collect required data for the final consolidated survey database. • Improves quality and completeness of field operations data. • Expedites data collection. • Allows for real-time data capture, validation and fixing at cluster sites during field operations. • Provides easy and real-time access to data by authorized users for decision-making. • Facilitates the updating of data collection tools during the field operations stage of the survey.	• Additional cost of the equipment (e.g. handheld devices). • Increased risk of theft of equipment. • Failure of equipment can affect survey field operations, requiring a "plan B" of switching to paper forms if the data system fails. • Requires highly skilled human resources that might be unavailable or hard to find in each setting. • Requires internet and LAN connectivity.
Hybrid	• Survey operations will continue even when the digital system is down. • Not necessarily dependent on staff with IT skills or IT resources in the field.	• Requires large space for storage of paper forms and registers at central DMU. • Human error or illegible handwriting on paper forms. • Duplication of data entry effort (i.e. completion of paper forms, followed by capturing data digitally in the database). • Delays and additional effort required for data validation and data cleaning. • Lack of automated decision making during field operations provides potential for human error in the management of survey operations.

DMU: data management unit; IT: information technology; LAN: local area network; TB: tuberculosis.

Directly digital surveys

Directly digital, real-time data capture in the field is the recommended approach for TB prevalence surveys. Some paper forms might still be required; for example, for informed consent and specimen referral, dispatch and participant tracking forms. However, these forms are needed only to manage survey operations and flow of participants in cluster sites – not for capturing data that will be included in the final consolidated survey database for analysis. **Box 16.3** describes a directly digital survey in Nepal in 2018–2019.

Hybrid surveys

Although directly digital, real-time data collection is preferred, a hybrid approach could be used provided that data from paper forms are captured digitally while

BOX 16.3
A DIGITAL DATA COLLECTION SYSTEM USED IN THE NATIONAL TB PREVALENCE SURVEY OF NEPAL, 2018–2019

Each survey field team was equipped with five tablet computers and nine laptop computers, a local server, mobile internet devices, printers, barcode printers and barcode readers. The system was installed and tested (using mock participant data) 1 day before the actual screening day in each cluster. All stations were connected to the local server via a LAN. An electrician with support from IT officers ensured proper connections and functioning of all devices during enumeration days. All team members were trained to use the system according to their roles.

A dashboard with the latest status of survey operations was available on each station's computer. This allowed all field team members to cross-check their activities. For example, the number of specimens collected had to correspond to the number of participants eligible for sputum collection (**Fig. B16.3.1**).

Data from the tablets used for the enumeration activity were uploaded to the field server at the end of each enumeration day, ensuring that information about all eligible participants was available at the reception station on the first screening day. Global positioning system (GPS) data were collected during the enumeration and were available to create a map.

Fig. B16.3.1

A cluster-level dashboard from the national TB prevalence survey of Nepal, 2018–2019

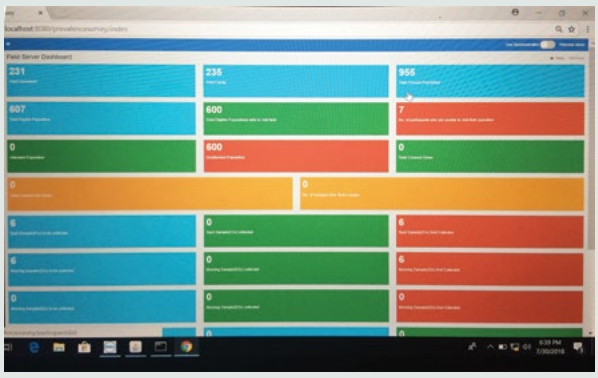


Photo credit: National TB Programme, Nepal.
TB: tuberculosis.

CXR images were read by a field reader and were also electronically transferred daily to the central level for a second reading. Discrepant results (e.g. images that were considered normal by the field reader but abnormal by the central reader) were automatically detected and sent back to the field for relevant action. The field data manager then modified the sputum eligibility status of those participants, and specifically assigned team members contacted them to request sputum specimens.

Several successful innovations were proposed by the team. For example, invitation cards were colour-coded to mark the day of the week the participant was invited to participate in cluster operations (in line with the survey SOPs, cluster operations were carried out over a period of 3 days) (**Fig. B16.3.2**).

Fig. B16.3.2

Colour-coded invitation cards corresponding to different days of the week used during the national TB prevalence survey of Nepal, 2018–2019

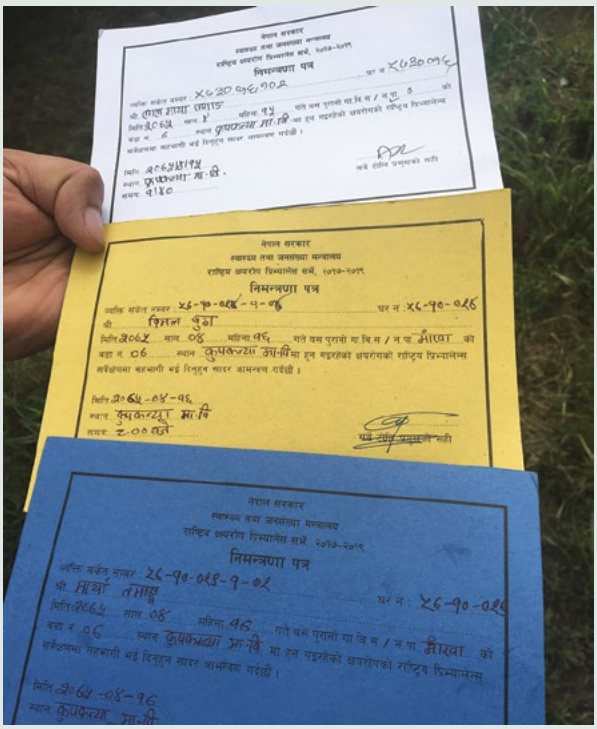


Photo credit: National TB Programme, Nepal.
TB: tuberculosis.

BOX 16.4
A HYBRID DIGITAL DATA COLLECTION SYSTEM USED IN THE NATIONAL TB PREVALENCE SURVEY OF MYANMAR, 2017–2018

Owing to data confidentiality concerns, the Myanmar survey team decided to use a hybrid digital mode of data collection, to avoid placing data on external agency cloud servers. The DMU of the Myanmar survey consisted of the survey data manager and their assistant, as well as two data entry clerks. Six field data managers (one per team) worked at the cluster sites.

Field data managers and their data entry clerks processed data captured on about 200 paper forms each day into the survey data management system. They also used a data validation tool at the end of each day to generate a list of issues such as duplicates, unmatched records (e.g. between the enumeration listing and individual questionnaire), missing data and other inconsistencies (e.g. participants aged <15 years, those who were ineligible but participated in the survey and those who were ineligible for sputum examination but submitted sputum). These issues were listed by the participant's PIN and serial number (the number based on the order in which the participant was screened) so that the paper forms could be found and checked. If the problems also appeared on the paper form, the participant was contacted so that the problem could be fixed while the team was still at the cluster site.

Verified electronic data were transferred to the server at the central DMU at least once during each cluster, and again after completion of the cluster. The laboratory and central CXR reading data were entered into the survey data system at the central DMU from received paper forms.

the field team is still in the cluster. This would allow close to real-time onsite data checking and cleaning.

The most common reasons for choosing a hybrid approach include insufficient funding, poor infrastructure and internet connection, lack of staff capacity, concerns regarding storage of survey data in the cloud, and concerns for the physical security of team members when using electronic equipment in the field (e.g. using tablets during a household enumeration).

Box 16.4 describes the example of a hybrid digital survey in Myanmar in 2017–2018.

16.2.3 DMP

The DMP is a critical document that describes all stages of the life cycle of survey data (**Fig. 16.5**); it should be developed before the start of a survey. The survey data manager should lead the development of the DMP, under the overall supervision of the survey coordinator. An example DMP is provided in online supplementary material.

The DMP should include at least the following components:

- staffing and responsibilities of the DMU, survey field teams and all staff involved with data collection;
- content and schedule of training for survey staff involved in all data management activities;
- data flows during survey operations (at both central and cluster levels);
- data collection tools (questionnaires and registers);
- description of data confidentiality and safety procedures and processes, including the participant consent form (or forms);
- specifications and a description of the survey data management system, including the type of software to be used for the development of the system;
- survey data dictionary, including codes, terminology and definition of all variables;
- SOPs for data collection, validation, analysis, use and archiving (at both central and cluster levels);
- SOPs for setting up the data management system (at both central and cluster levels), software version control, release of software updates, maintenance of data and IT code backups;

Fig. 16.5

The life cycle of survey data

- SOPs for data transfer during and after survey operations;
- specifications for data and form storage;
- data sharing plan;
- list of all equipment (e.g. laptops and tablets) to be used for data generation; and
- process and steps to lock the survey database from further editing i.e. data freezing.

The rest of this section provides recommended content for the components of the DMP that have not been covered elsewhere in this chapter.

Data confidentiality, beneficence and non-maleficence

Access to digital data files, including backups, that allow an individual to be identified should be strictly controlled by the data manager. Analytical datasets, all analyses and published reports must never contain the names or other personal information of surveyed individuals.

All survey staff handling data (both on paper and digitally) should respect the confidentiality of the collected information (**Chapter 11**). All paper forms and registers that allow an individual to be identified should be stored securely (i.e. in a locked room or cupboard) at the central DMU, with access controlled by the survey data manager. For the full list of survey documents, and guidance about their archiving and destruction after completion of the survey, see the World Health Organization (WHO) publication "Good practices guidance handbook for national TB surveys" *(9)*.

Also, TB prevalence survey operations among the general population must follow the principles of beneficence and non-maleficence. This means that the correct person is appropriately treated if they are identified as having TB or other illnesses, and that people without TB are not treated for TB. This requires correctly identifying individuals (e.g. by using names and other personal identifiers) and assigning data and results (CXR and laboratory results) to them.

Data security

The datasets used in the survey should be stored securely, with appropriate access controls to ensure that only authorized survey staff can enter, view, edit or delete data. The location of the files will depend on the infrastructure in place in the field and at the central DMU, which could range from stand-alone computers to networks with secure file servers operated by dedicated IT staff (sometimes extending to hosting on remote data centres). The data manager should ensure that data files are held securely. The survey data management system should be password protected. Staff access to the system must be appropriate to the roles each person has within the survey.

The following requirements should be satisfied:

- People should only use the survey data management system when logged in with their own account (username and password). They must not share their account details with others or provide access to another person after logging into the system using their account details.
- Editing of records should only be possible when a user is logged in with the necessary rights for read or write access. The name of the user should be displayed on the data entry screen throughout the data entry session. If the name displayed on the screen is not that of the person entering the data, then that individual should log off, then log on again under their own name before continuing.
- Passwords should be changed at regular, pre-established intervals.
- When someone leaves a workstation or tablet, that person should log out from the system. Failing this, automatic logout should be set to occur after idle periods.
- An audit log of all transactions should be captured by the system and should be retrievable at any time by authorized system administrators.

System security

The data manager should ensure that computers used for the survey have effective and up-to-date antivirus programs and firewalls, and are protected physically from risks such as theft, power breaks or power surges. All data entered in the data management system should be encrypted to protect from misuse if the computer or server is stolen or corrupted.

Data backup

Automatic daily online backup is recommended, to ensure that data are saved at another storage facility or in the cloud (provided data are encrypted and this does not violate local regulations). These backups should be configured to take place in the evening (e.g. 9 pm), when most survey data activities have been completed. Clear SOPs of how to use the backup files and where they are located should be developed and accessible to authorized personnel.

Data transfer

Secure data transfer channels – with data encryption and access control – should be established so that data from cluster sites, laboratories and central CXR readers can reach the central survey data management system. Local regulations should be adhered to (e.g. personal and sensitive information uploaded to a cloud platform). Data transfer agreements between relevant parties transferring data should be set up and signed (e.g. between the national TB laboratory and the organization managing the survey).

A dashboard showing progress of daily uploads of the survey records from each cluster must be built on

the central server, to monitor data synchronization. The central survey data manager should contact the field data manager if the data transfer is behind schedule.

For web-based data management systems that support connection to the central server, the team leader and field data manager should ensure that data synchronization to the central server is conducted every day during survey operations. This is particularly important for central CXR reading because daily upload of CXR images allows timely reading of CXRs at the central level, while the survey team is still at the cluster site.

Data sharing

A clear data sharing plan should be developed and agreed among all relevant stakeholders. Data sharing is a vital component of data management in research studies, including prevalence surveys. Participant data collected during these surveys should be shared and safeguarded through an appropriate public repository, provided that the data are adequately anonymized. These data can be used further in systematic reviews to aggregate reported results with other survey results. Some peer-reviewed journals require data to be freely accessible for readers to ensure transparency and reproducibility.

Data archiving

After completion of field operations, all essential documents and datasets should be stored safely for at least 5 years and according to agreed SOPs *(10)*. There should be a clear procedure for when and how the survey materials will be archived or destroyed, always ensuring that confidentiality is not violated.

The final consolidated survey dataset should be archived (fully anonymized) and safeguarded. A general data repository (e.g. Dryad *(11)* or Figshare *(12)*) can be used; alternatively, an institutional data repository can be used, provided it is compliant with WHO policy (e.g. it issues a declaration of interest) *(10)*.

Storage of paper documents (if relevant)

All paper forms and registers should be stored in one or more locked rooms, with survey data managers responsible for holding the keys. Only the project investigators should have access to the survey datasets and documents.

16.3 Data collection

This section describes the process and content of data collection during field operations, according to the typical flow of data at a cluster site or at other locations.

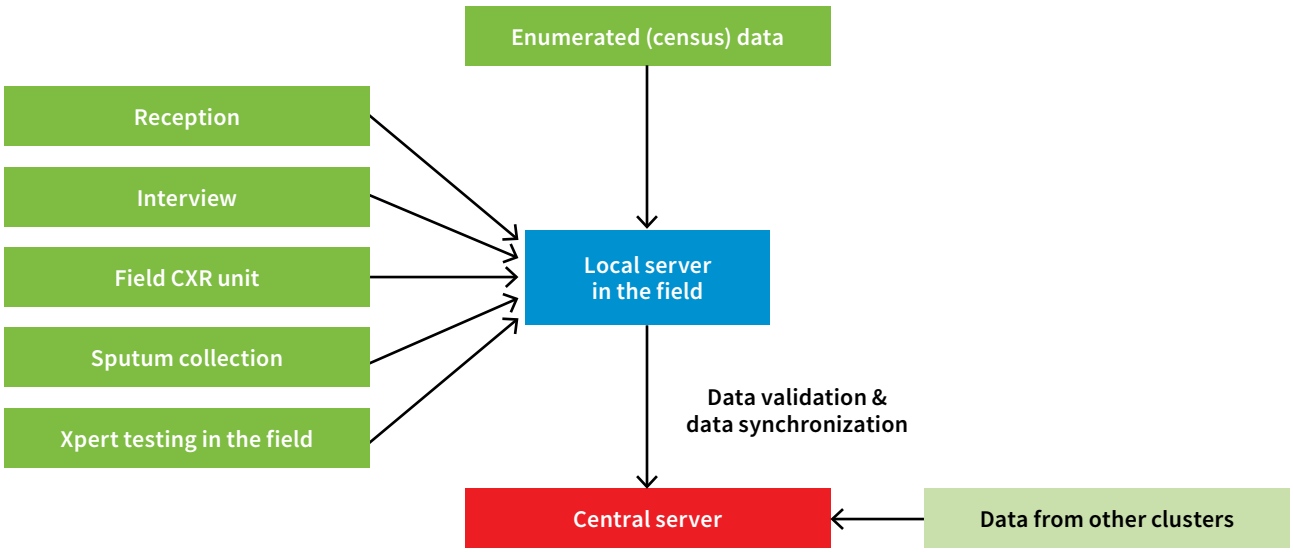
16.3.1 Data collection in the field

Fig. 16.6 presents the typical flow of data at a cluster site, from the enumeration step of collecting enumeration data from each household in the sampled cluster, registration of participants at the cluster site, symptom screening and interview, to CXR and sputum collection. Other stations could be added to the data flow according to the survey protocol. All data are stored on a local server in the field. Data are checked and cleaned at the end of each day of cluster operations, then uploaded to the central server according to an agreed schedule and when internet connections are available. Having a local server and a LAN at the cluster site means that operations can proceed even when there is limited, or no, internet connection.

For the purposes of this section, it is assumed that the data collection process is directly digital.

Fig. 16.6

Standard data flow at survey cluster sites



CXR: chest X-ray.

Enumeration (census)

Basic information about all enumerated people within a cluster, including those who do not satisfy survey eligibility criteria, are recorded in the enumeration (or household) register. A PIN is assigned to each enumerated person, then invitation cards are issued to those eligible to participate. Each card includes the individual's name and PIN (as a barcode).

Enumeration data are recorded using mobile devices (tablets or phones) during household visits. These data can be uploaded to the local server immediately or at fixed points during the day. Each day, the field data manager should verify the enumeration data using a built-in data validation tool. Enumeration data should be available within the local data system when participants report to the site to participate in cluster operations.

Some countries collect geographical coordinates of the households during the enumeration using GPS tools (**Box 16.5**).

Reception

When a person arrives at the cluster site, a receptionist scans the barcode on the person's invitation card to find their record in the system. The receptionist verifies the participant's identity and sociodemographic information collected during the enumeration, then prints additional barcodes with PINs and attaches them to the participant's survey card to be scanned at each survey station. The participant is then referred to the first station for the interview and symptom screening. The receptionist uses a dashboard to monitor the number of survey participants that are processed in real time.

Interview and symptom-screening station

The interviewer scans the barcode on the participant's survey card to retrieve the participant's record on their device screen, and to verify the name and demographic information. The interviewer enters the participant's responses to the interview questions directly into the data management system (for details, see **Chapter 6**). The field team leader can use a dashboard to monitor the number of the registered and interviewed participants, including those with symptoms, in real time. The interview can include both a screening interview and an in-depth interview, depending on the objectives of the survey. In some surveys, these interview stations are separated. Careful consideration should be given to only collecting data during interviews that are linked to specific survey objectives in terms of the analysis and use of the data. All participants are then referred to the CXR station for further screening.

CXR station

The staff member at the CXR station scans the barcode on the participant's survey card to retrieve the participant's record on their device screen, and to verify the name and demographic information before the radiographer takes the CXR. These are usually digital X-rays and can now include computer-aided detection (CAD) to potentially improve the standardization and quality of readings (see **Chapter 7** and **Box 5.5** in **Chapter 5)**.

Decision-making based on interview and CXR screening results

The data management system should include algorithms to guide participant flow in accordance with the survey protocol. For example, the eligibility of a participant for sputum collection (based on either the interview or CXR screening results) should be automatically populated in the data management system. The field team leader should then review those results and either confirm or overrule them. Depending on the team leader's final decision, the participant is either referred to the sputum specimen collection station or completes their participation and exits the survey. Both the automated decision and the decision made by the team leader should be saved in the system.

Sputum specimen collection station

The laboratory technician scans the barcode on the participant's survey card to retrieve the participant's record on their device screen, and to verify the name and demographic information before collecting the sputum specimens (the number of specimens collected will depend on the survey protocol). The system should warn the technician if, based on results from the previous screening steps, the participant is not eligible to provide a sputum sample. Data relevant to sputum specimen collection should be entered directly into the system while the participant is still at the station.

Some paper forms and registers could be used at this station (e.g. a referral form that accompanies sputum specimens to the central laboratory and a sputum specimen dispatch register). These documents are usually kept at the cluster site, with a copy sent to the laboratory. The sputum specimen dispatch register could include information such as the time of sputum specimen collection, time of transportation to the laboratory and temperature in the specimen container during transit.

Field laboratory using Xpert Ultra

Testing with Xpert Ultra preferably should be done as close to the cluster site as possible, so that if action needs to be taken and care provided, this can be done promptly. In the field, the laboratory technician from the field team is responsible for testing the specimens and reporting positive Xpert Ultra results to the field team leader, who will undertake appropriate action to collect further samples for liquid culture if diagnostic Option 1 is used (**Chapter 3**).

The laboratory technician scans the specimen barcode to retrieve the participant's record from the system, if applicable. Additional barcode stickers

BOX 16.5
USE OF GPS IN NATIONAL TB PREVALENCE SURVEYS

Devices for collecting geographical coordinates (latitude and longitude) are widely available, including in many smartphones. Recording household geographical coordinates during the enumeration can be beneficial for many reasons. First, follow-up visits (e.g. in the case of a positive laboratory result or an abnormal CXR) are pivotal in most national TB prevalence surveys because they enable access to the households for further clinical examination, if needed, and are useful in ensuring that a person is correctly referred for TB treatment.

Second, a system for randomly revisiting households can be put in place to monitor the performance of field teams. Third, such recording could support follow-up activities based on subsequent findings from the prevalence survey (e.g. treatment outcomes and investigations of household contacts).

In many countries and especially in informal settlements, there is no reliable postal address system that can identify the location of people's houses; GPS coordinates fill that gap. A "Track Back" or "Go To" function is present on most handheld navigation devices, and can be used to return to the location of the household.

Collected GPS data can be plotted on a map (see **Fig. B16.5.1**). Depending on the sampling strategy, this gives survey managers the opportunity to monitor whether all households in a cluster have been enumerated and to see whether the entire selected area was covered (i.e. no areas were missed).

However, GPS coordinates also enable the identification of participants. Therefore, clear rules on the confidentiality and use of these data must be well defined in advance of their collection in the protocol.

Household latitude and longitude can enable spatial analyses using geographical information systems (GIS). For example, investigating geographical clustering of TB cases, the association between prevalent TB and the distance to the nearest diagnostic centre or population density, or the association between health care seeking behaviour and the distance to the nearest clinic.

Fig. B16.5.1

Google Earth images overlaid by GPS data collected by field teams to monitor household distribution in two different clusters in the national TB prevalence survey of Zambia, 2013–2014

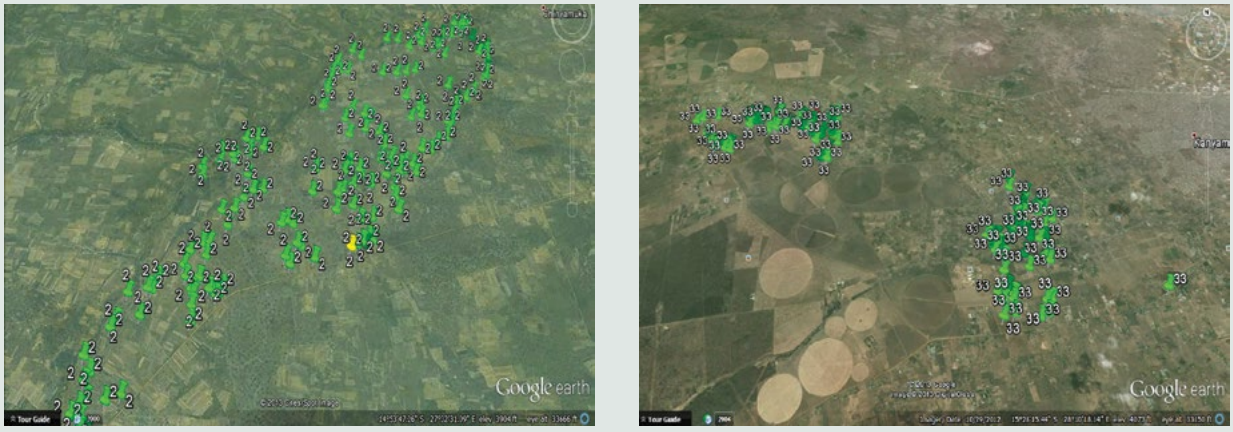


Photo credit: National TB Programme, Zambia (reproduced with permission).
GPS: global positioning system; TB: tuberculosis.

accompanying the Xpert test request form should be stuck onto the Xpert logbook in the field laboratory and onto the testing cartridge. The Xpert testing procedures in the field must comply with the SOP, and should be performed by trained, certified and experienced technicians. The Xpert test results are saved by the system at the GeneXpert platform and backed up on the test form and Xpert register, as required by the protocol. The Xpert machines should be interoperable with the survey data management system, so that results are transferred directly into the survey database.

The Xpert laboratory can also have a specimen collection dashboard to monitor the number of specimens submitted and tested.

Box 16.6 provides examples of automatic capture of field CXR and Xpert results.

Survey exit station

The responsible person scans the barcode on the participant's survey card to retrieve the participant's record on their device screen, and to verify that the participant underwent all necessary procedures according to the study protocol. A confirmation of survey exit is then recorded in the system.

Additional stations

Some surveys may have additional activities or stations at the survey site; for example, HIV counselling and testing, and substudies for TB risk factors and comorbidities (**Chapter 10**). These activities or stations should be included in the cluster flow, and the modules for data collection should be added to the survey data management system.

Field data manager station

A field data manager should have a separate station with a device such as a laptop connected to both local (i.e. LAN) and central servers. The field data manager monitors in real time the cluster dashboard that summarizes information from all field stations, and runs a data validation routine at least once a day. The system should identify and provide a list of data problems that need to be addressed promptly while the team is in the field, especially if this involves contacting survey participants. The field data manager ensures that data are transferred to the central data management system according to the agreed schedule.

16.3.2 Data collection in other locations

Depending on the survey case definition, and laboratory and CXR investigations in each survey protocol, data are generated in locations outside cluster operations. Such data need to be collected and consolidated into the single survey database.

BOX 16.6
EXAMPLES OF AUTOMATIC CAPTURE OF FIELD CXR AND XPERT RESULTS FROM NATIONAL TB PREVALENCE SURVEYS OF ESWATINI AND MOZAMBIQUE, 2018–2019

During the field operations of the fully digital surveys in Eswatini and Mozambique, different stations were connected to the field servers using LANs. Android tablets were used for data collection at cluster sites, using the ODK platform. The medical officer used a laptop with Microsoft Windows®, and had password-protected access to the whole data management system using a restricted profile.

The data management systems for both surveys included the automatic digital capture of CAD scores for CXR (CAD4TB, Delft) and, using an application programming interface (API), the results of Xpert testing at the field sites were entered directly into the survey database. CXR results (both human readings and CAD scores), together with the symptom-screening results, were included in an automated algorithm to decide whether a participant was eligible to provide a sputum sample. Reliable real-time acquisition of these results allowed for a smooth flow of participants at cluster sites, and the CXR images were automatically uploaded to a cloud server.

Xpert field testing results, including repeat results from the central laboratories, were linked directly to each sample collected with the data management system. A culture eligibility algorithm automatically identified, in real time, participants who were eligible to submit additional samples for culture.

Laboratory test results on sputum specimens collected from eligible survey participants

For survey participants who are eligible according to the survey screening approach, specimens are collected in the field and sent to survey laboratories for diagnostic investigations (**Chapter 8**), such as additional Xpert testing, culture testing or drug susceptibility testing. In addition, the quality of each collected specimen and the reasons why a specimen was not collected should be documented. Data are collected either directly into the survey data management system and the corresponding data entry form for diagnostic investigations, or they are captured in LIMS and then merged (generally with the use of the PIN) with the survey database and transferred into that database.

Table 16.4

The first five lines of the data dictionary for the household register from the national TB prevalence survey of Myanmar, 2017–2018

#	PROMPT	FIELD NAME IN THE DATABASE	VARIABLE TYPE	FORMAT
1	Cluster number	ClusterHR_ID	NUMBER	###
2	Household number	HR_ID	NUMBER	###
3	Date	DateHR	DATE	DD-MM-YYYY
4	Region/State:	RegState	COMBO	Sorted alphabetically
5	District:	District	UPPERCASE	
	… etc.			

TB: tuberculosis.

Central CXR reading

Depending on the survey protocol and CXR investigations (**Chapter 7**), a repeat reading of CXRs of survey participants could take place at a central location. This is done either for quality control of the field reading or because the central CXR reading is used during the imputation analysis of a survey case status (see **Chapters 4** and **17**). Data from this central reading are collected either directly into the survey data management system and the corresponding data entry form for CXR investigations, or they are captured in a separate information management system and then merged (generally with the use of the PIN) with the survey database and transferred into that database.

16.4 Ensuring data quality

This section describes the procedures and processes used to ensure that survey data are accurate, reliable, precise and complete. The various procedures and processes are presented in terms of whether they should be done before field operations (as part of preparation and planning) or during and after field operations.

16.4.1 Before field operations

Development of a data dictionary

A data dictionary describes all the variables included in the survey database, along with encoded category values (e.g. 0=no and 1=yes, 9=missing), validation rules and screen prompts (**Table 16.4**). The data dictionary provides a link between the data entry screens and the variable names in the database. It helps both system developers and data analysts to make sense of the database.

The data dictionary should be developed and maintained in a file format that allows tracking of changes. Data dictionaries need strict version control and should be kept up to date by the data manager as the data management system evolves. This is particularly important at the time of data validation, cleaning and analysis.

Use of a unique personal identification number

A unique PIN is key to linking data on a particular person that are generated and recorded at multiple places and multiple times. A PIN is often created using a combination of cluster number, household number within the cluster and individual number within the household.

According to **Fig. 16.7**, the PIN for the third (3) enumerated person from household 136 of cluster 9 would be 0913603. The number for each component should be zero-padded (i.e. 09 rather than 9) and include enough digits to allow complete enumerations of all units. For example, if there are more than 99 clusters, then cluster number 9 should be encoded as 009.

Once each cluster has been assigned a unique number, staff at a cluster can allocate household and individual numbers independently, without the need for any central level control and without fear of creating duplicate PINs. During the enumeration, PINs should be assigned to everyone in a household, regardless of whether they are eligible to take part in the survey or not.

Additional use of a serial number

In addition to the PIN, some surveys have also allocated a serial number (SN) to participants, sequentially as participants arrive at the reception station. Although not strictly necessary, SNs have been useful for managing the flow of participants and later for investigating problems such as mismatched PINs.

The SN is usually composed of the individual sequential arrival number at the cluster. For example, the 86th person to arrive at the reception will have an SN of 086.

Fig. 16.7

Example of the composition of a 7-digit PIN

	CLUSTER NUMBER	HOUSEHOLD NUMBER WITHIN THE CLUSTER	INDIVIDUAL NUMBER WITHIN THE HOUSEHOLD
PIN	09	136	03

PIN: personal identification number.

Use of a sputum specimen sample number

A system to generate sample identifiers (IDs) for sputum specimen samples is required because eligible participants provide multiple sputum specimens (e.g. a spot and a morning sample). The different samples need to be linked with the participant's PIN.

Laboratories also create separate laboratory sample IDs when processing samples; for example, for culture tubes when using a mycobacterial growth indicator tube (MGIT™). Therefore, it is crucial that the laboratory IDs are linked with the PIN within the LIMS and the data management system.

Use of barcodes, barcode printers and barcode scanners

PINs should never be written manually on paper documents or entered manually in data entry screens because the chances of error are high, especially when people are busy, as is often the case during survey operations. Instead, PINs should be printed as scannable codes (e.g. onto stickers) and read using scanners. This can be done using QR codes or, more often, using barcodes (see **Figs. 16.8** and **16.9**). Using barcode labels and scanners reduces transcription errors; it also helps to ensure accurate linkage of data generated for each survey participant over time and across locations.

Using barcode technologies requires advance planning. Depending on the availability of barcode printers, barcodes could be printed during the enumeration household visits, preprinted before the enumeration according to the previsit listing of individuals (if available) or printed at reception. Labels for eligible individuals should be used on invitation cards and on all paper forms and registers as participants move through the cluster operation. Barcoded labels could also be used to encode on sputum specimen collection containers (see **Box 16.7**).

Both approaches for when to print barcode labels – printing at reception and preprinting – have advantages and disadvantages, as shown in **Table 16.5**.

Many surveys have found it useful to give each participant a bracelet or lanyard with their PIN barcode (**Fig. 16.10**). Bracelets should only be used if this practice is acceptable to local communities. The bracelet or lanyard helps to track participants as they move around different cluster stations; it also helps to ensure data are recorded for the right person.

An example of the use of barcodes in the Lesotho survey is described in **Box 16.7**.

Linking data from multiple sources

The final consolidated survey dataset must be checked regularly for duplicate records on the same individuals

Fig. 16.8

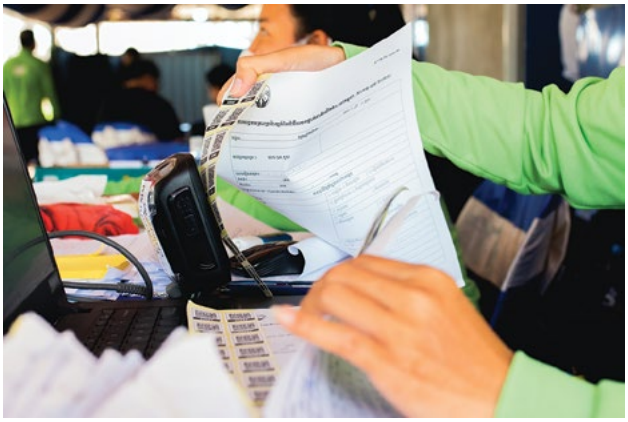
Barcode and scanner used to register a participant's invitation card for the national TB prevalence survey of Eswatini, 2018–2019

Photo credit: Eveline Klinkenberg.
TB: tuberculosis.

Fig. 16.9

Scanning preprinted barcodes a) used to register a participant's tracking sheet and b) an interviewer scanning a barcode with his tablet computer to bring up the questionnaire during the national TB prevalence survey of Cambodia, 2023–2024

a)



b)

Photo credit: WHO/Tytaart.
TB: tuberculosis.

Table 16.5

Advantages and disadvantages of barcode printing approaches

BARCODE PRINTING APPROACHES	ADVANTAGES	DISADVANTAGES
Printing barcode labels during enumeration (or during reception on arrival of participants)	• Reduces the number of stickers (stickers are only printed for those eligible to take part). • On-the-spot printing.	• Need mobile printing equipment for the enumerators (and reception), adding to the cost and training needs.
Preprinting barcode labels	• Avoids having to use and troubleshoot the equipment while at households during enumeration (or reception).	• Risk of mixing up the stickers. • Having to print stickers for all eligible household members who may not be available during the enumeration visit.

Fig. 16.10

Using paper bracelets with barcodes during the national TB prevalence survey of Nepal, 2018–2019

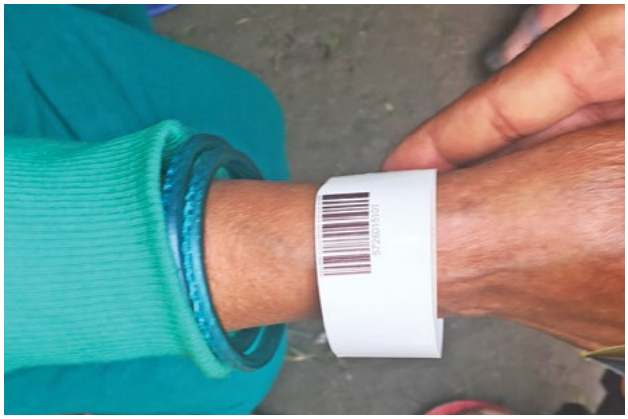


Photo credit: National TB Programme, Nepal.
TB: tuberculosis.

after merging data from all clusters, central laboratory test results and central CXR readings. There are various ways in which multiple records for the same individual could be generated; for example, problems with the merging process (e.g. related to unstable internet data transfers and multiple attempts at merging records) or with PINs (e.g. if a field site used the wrong cluster number that also corresponds to another cluster, or if the incorrect PIN was scanned from a different person).

Design and functionality of data entry screens

Data entry screens should mirror any paper versions (if used) and follow recommendations on good data form design *(13–15)*. Long questionnaires should be broken down into clearly labelled and numbered sections, both on paper and on screen. Data entry screens should be easy to use and navigate. Data should be saved automatically while a form is being filled in, and data should be validated in real time. To aid accurate data capture, it is important to:

- include "other", "no response" or "not applicable" options for all questions, so that missing data can be correctly identified;
- use skip patterns to avoid fields that do not require data entry, with an automatically assigned value of "not applicable" in the skipped fields;
- avoid free text fields and instead use coded options (e.g. check boxes or drop-down lists);
- allow enough space between questions on the screen to avoid data entry errors; and
- make the cursor move automatically from one question to the next.

Data entry screens should be designed with validation and consistency checks at the time of data entry to avoid common problems such as:

- duplicate records;
- invalid data types (dates, numbers);
- missing data; and
- numbers outside plausible ranges (e.g. age <15 and >110 years).

Data entry screens must be thoroughly tested and piloted to ensure that they function correctly and are easy to use.

16.4.2 During and post field operations

Data validation

Data validation is a continuous process, carried out both during and after data entry. The development and use of data validation code should be embedded into the survey data management system, so that it can be easily run (e.g. from a menu or a button) daily in all locations where data are collected (the field, laboratories and central CXR unit) and at the DMU, to identify and fix problems with the data.

The code should identify:

- duplicate records;
- unmatched or unlinked records;
- inconsistent PIN and SN (if used);
- protocol violations, such as a person who is not eligible for providing sputum but from whom sputum was collected, a person who is eligible but from whom no sputum was collected or a person who provided a spot sample but no morning sample;
- logically inconsistent values (e.g. a person is recorded as being male and pregnant);

BOX 16.7
THE USE OF BARCODES IN THE NATIONAL TB PREVALENCE SURVEY OF LESOTHO, 2019

Lesotho had three field teams and each team comprised nine people: three research assistants each with a tablet computer, a medical officer to interpret the CXR with a laptop computer, an IT officer with a laptop computer (local server), a receptionist with a barcode printer and scanner, and a laboratory technician, HIV counsellor and field team leader each with a tablet computer. Enumeration data were collected using tablets; all tablets had SIM cards with internet connectivity. Once enumeration of a household was complete, data were sent directly to the central server. If connectivity was poor, the enumeration continued in offline mode but as soon as the connection was restored, data were synchronized with the central server. A dashboard at the central server showed the number of people enumerated in each cluster and those eligible to participate. Once the target number was reached, the enumeration stopped. All eligible people were given an invitation card with a preprinted barcoded PIN (**Fig. B16.7.1**).

At the survey site, the IT officer or data manager downloaded all the enumeration data onto the local server daily, to avoid dependency on possibly unreliable internet connections during survey operations. When a participant arrived at the reception station, the IT officer scanned the barcode on the invitation card to retrieve the participant's record for verification. The IT officer then printed 10 barcoded PIN stickers (with the same PIN as on the invitation card) and attached it to the paper tracking form (**Fig. B16.7.2**). These stickers were for use with the consent form, CXR register, specimen containers, sputum register and HIV register as required (**Fig. B16.7.3**).

In addition to the PIN, Lesotho used a second identification number, the SN, to track participants' flow through the field operation. This SN was assigned at reception and linked to the PIN in the database but only the PIN was scanned at subsequent stations.

After providing consent, the participant was then guided to the first station where one of the field team staff scanned the person's barcode on the invitation card and opened the symptom-screening questionnaire on the tablet. The barcode on the invitation card was also scanned when the participant visited each of the different field stations.

The data at the local server were synchronized with the central server in real time if the internet allowed. Several automatic reports were built into the system to monitor data quality and inconsistencies; the feedback from the central DMU to the field team was shared in real time via messaging apps. The reports were accessible by field team leaders and IT officers in the field.

Fig. B16.7.1

An invitation card with a preprinted barcode used in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

Fig. B16.7.2

Barcodes being printed at reception after scanning the invitation card in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

Fig. B16.7.3

Barcodes placed on sputum specimen containers in the national TB prevalence survey of Lesotho, 2019

Photo credit: WHO/Irwin Law.
TB: tuberculosis.

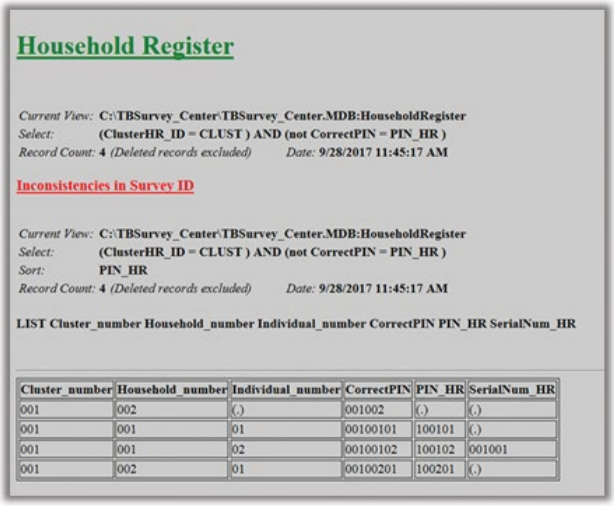
- missing values and incomplete records; and
- invalid dates and numbers, such as age outside plausible ranges or invalid codes for categorical data.

The code should produce a report that can easily be interpreted; for example, a list of all problematic participant records, sorted by PIN. Listing should be organized by type of error, such as duplicated records and unmatched records (by dataset), as shown in **Fig. 16.11a–b**.

All corrections in the database should be documented properly by the data managers in a data correction log. A mechanism such as an automated audit log should be in place to document changes in the database, keeping a record of past and new values where data are corrected, together with dates when the changes were made.

Fig. 16.11a

Example of the data validation output (errors in creating PIN according to cluster, household and individual number) from the national TB prevalence survey of Myanmar, 2017–2018



Household Register

Current View: C:\TBSurvey_Center\TBSurvey_Center.MDB:HouseholdRegister
Select: (ClusterHR_ID = CLUST) AND (not CorrectPIN = PIN_HR)
Record Count: 4 *(Deleted records excluded)* *Date:* 9/28/2017 11:45:17 AM

Inconsistencies in Survey ID

Current View: C:\TBSurvey_Center\TBSurvey_Center.MDB:HouseholdRegister
Select: (ClusterHR_ID = CLUST) AND (not CorrectPIN = PIN_HR)
Sort: PIN_HR
Record Count: 4 *(Deleted records excluded)* *Date:* 9/28/2017 11:45:17 AM

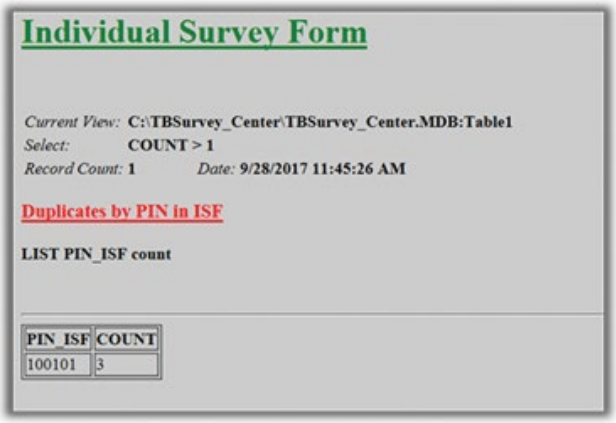
LIST Cluster_number Household_number Individual_number CorrectPIN PIN_HR SerialNum_HR

Cluster_number	Household_number	Individual_number	CorrectPIN	PIN_HR	SerialNum_HR
001	002	(.)	001002	(.)	(.)
001	001	01	00100101	100101	(.)
001	001	02	00100102	100102	001001
001	002	01	00100201	100201	(.)

Source: National TB programme of Myanmar (reproduced with permission).

Fig. 16.11b

Example of the data validation output showing multiple records for PIN=100101 from the national TB prevalence survey of Myanmar, 2017–2018



Individual Survey Form

Current View: C:\TBSurvey_Center\TBSurvey_Center.MDB:Table1
Select: COUNT > 1
Record Count: 1 *Date:* 9/28/2017 11:45:26 AM

Duplicates by PIN in ISF

LIST PIN_ISF count

PIN_ISF	COUNT
100101	3

Source: National TB programme of Myanmar (reproduced with permission).
PIN: personal identification number; TB: tuberculosis.

Validation of positive laboratory and CXR results

Changes in the relatively small number of survey cases identified (the numerator) can have a significant impact on the estimate of prevalence in contrast to changes in the large number of survey participants (the denominator). Therefore, the following validation checks are recommended to ensure that all participants with at least one positive laboratory test result are accurately captured in the survey data management system:

- All participants with positive laboratory results or a CXR reading suggestive of TB should be identified and selected from the survey database. These records should be cross-checked against the primary data sources (e.g. laboratory registers and CXR image readings), and any inconsistencies must be corrected by the DMU.
- Records with any incoherent values (e.g. screen negative but sputum positive) should be re-examined.

Dashboard for data visualization

A dashboard that shows the status of survey operations (e.g. **Fig. 16.12**) allows the field team leader and survey data manager to review activities at each survey station, and to ensure consistency. For example, the number of CXRs to be taken should correspond with the number of CXRs actually taken; similarly, the number of participants eligible for sputum collection should correspond to the number of people registered at the laboratory station. If these numbers do not match, the source of error should be identified and fixed as soon as possible.

Fig. 16.12

A dashboard to track survey flow of the national TB prevalence survey of Eswatini, 2018–2019

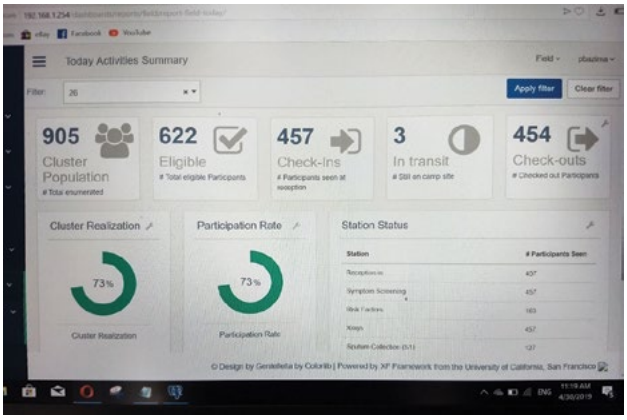


Photo credit: Eveline Klinkenberg.
TB: tuberculosis.
The real-time dashboard shows the total number of people enumerated in the cluster, the number eligible to be invited, the number who attended, the number currently (in transit) being screened, and the number who completed all field activities and left the site.

This approach both simplifies and expedites data cleaning and preparation of the data for analysis.

Monitoring and supervision of data collection

Monitoring and supervision of data collection at all cluster sites should take place regularly. At least weekly calls between the field and central data managers are recommended, to discuss any issues or complications and to provide feedback to the field staff. Regular monitoring of the performance of data collection, while ensuring the confidentiality of survey participants, includes:

- checking the consistency and completeness of field data, laboratory results and central CXR readings, using scripted data validation tools at the DMU level;
- monitoring survey performance through weekly progress reports; and
- monitoring data transfer activities.

Monitoring and supervision should also be done through in-person field visits. Such visits are critical for adherence to the SOPs and good data management practices. The main objective of field visits is to see how well data management processes are implemented and problems are solved. Dashboards and automatically generated reports are useful to assess the performance of field teams before and during such visits. The survey data manager and survey coordinator should visit field teams in each cluster at the beginning of survey operations, and as needed during those operations. **Chapter 14** provides a list of key monitoring indicators.

16.5 Data analysis and use

This section describes the various analyses and uses of survey data to guide actions, both during and after field operations. Uses include the monitoring or progress of field operations, the provision of care to survey participants, and the analysis of survey data to measure the epidemiological burden of TB.

16.5.1 During field operations

Cluster register

The field data managers should maintain a register that monitors and facilitates the various data management activities that are required to take place in each cluster, according to the DMP and survey protocol. Although data from these cluster registers are not used in the final consolidated survey database, they are important tools that ensure the quality and completeness of that database. Such registers contain cluster information on:

- whether and when the expected operations were performed and completed;
- the field staff working in the cluster for all data management activities;
- the planned and actual dates of data transfers;
- the planned and actual dates of support supervision and monitoring visits from the central level; and
- data management issues, including data collection and linkage errors, glitches in the system and equipment failure.

It is recommended to facilitate use of these cluster register (ideally digital) data incorporated with digital dashboards as part of the data management system.

Survey progress reports

Progress reports that monitor cluster operations at both the cluster and DMU levels should be generated automatically from the survey data management system, at different frequencies. The survey data manager at central DMU should produce a report frequently (e.g. weekly), to summarize progress in data management processes and cluster operations, to document the quality of data, and to describe problems and suggested solutions. In addition to information on field operations, weekly progress reports should include information on laboratory processes and central CXR reading performance. A template for such a report can be based on the indicators shown in **Chapter 14**. Progress reports are a basis for discussion and decisions by the survey coordinator and the various survey committees (e.g. steering, technical and managerial), and for technical recommendations by other stakeholders.

An example of a progress report in the field would be a report produced daily to allow discussion within the field team for real-time monitoring of progress, and for identifying and resolving any issues (**Fig. 16.13**).

Daily cluster-level reports could include the number of:

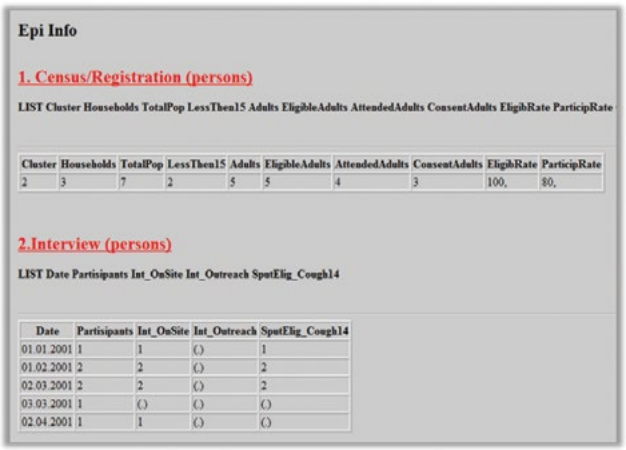
- household members enumerated;
- people who attended the survey site;
- interviewed participants;
- participants:
  - with symptoms;
  - with CXR done;
  - with abnormal CXR;
  - eligible for sputum collection;
  - from whom sputum specimens were collected; and
- sputum samples that have not yet been collected (e.g. morning samples).

Provision of care based on positive laboratory results

All survey participants diagnosed with TB disease in programmatic terms must be identified accurately and have care offered to them, according to national TB guidelines (see **Chapter 9**). In most countries, diagnosis of TB disease is based on a single positive laboratory test result of a single sputum specimen. The definition for a survey participant to be classified as a "survey case" is usually stricter than a TB disease diagnosis in programmatic terms (see **Chapter 4**). In both cases, provision of care must be ensured. Other diagnoses that are not TB

Fig. 16.13

A cluster-level progress report from the national TB prevalence survey of Myanmar 2017–2018



Epi Info

1. Census/Registration (persons)

LIST Cluster Households TotalPop LessThen15 Adults EligibleAdults AttendedAdults ConsentAdults EligibRate ParticipRate

Cluster	Households	TotalPop	LessThen15	Adults	EligibleAdults	AttendedAdults	ConsentAdults	EligibRate	ParticipRate
2	3	7	2	5	5	4	3	100,	80,

2.Interview (persons)

LIST Date Partisipants Int_OnSite Int_Outreach SputElig_Cough14

Date	Partisipants	Int_OnSite	Int_Outreach	SputElig_Cough14
01.01.2001	1	1	()	1
01.02.2001	2	2	()	2
02.03.2001	2	2	()	2
03.03.2001	1	()	()	()
02.04.2001	1	1	()	()

Source: National TB programme of Myanmar (reproduced with permission).
TB: tuberculosis.

may also be identified during the survey, and these participants must also be referred for further management. It is recommended to add a "referred" variable to the central survey database to record when a participant is referred to health services based on laboratory or CXR results either during or after cluster operations.

16.5.2 After field operations

Data analysis and report writing

Specialized statistical software is required for the analysis of TB prevalence survey data. The DMP must be designed in such a way that it produces a final consolidated survey database that is easily accessible for analysis by the statistical software. This can be done either through directly reading the database (e.g. via Open Database Connectivity connections) into the statistical software, or through data export and import routines.

Interim data analysis reports are also recommended, with a focus on monitoring progress with data collection and data validation. The survey DMP should include templates for both the interim and final analysis reports. **Chapter 17** has information on the final data analysis and report content, and **Chapter 20** on possible uses of survey results.

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CHAPTER 17

Final analysis and estimation of prevalence

Cluster sample surveys are difficult to analyse for several reasons, including the need to properly account for the data's clustered feature. To ensure a robust interpretation of the results of a tuberculosis (TB) prevalence survey, it is important to investigate potential sources of error and bias – one major source of potential bias is missing data. Individual-level analyses are preferable to clustered-level analyses, in part because they enable missing value imputation. A statistician must supervise the development of an analysis plan, the analysis itself and the interpretation of the results.

This chapter covers three major topics:

- core survey data, including interview, chest X-ray (CXR) screening, TB symptom screening, Xpert® MTB/RIF Ultra (Xpert Ultra) and culture results, and health care seeking behaviour; describing and understanding these data, and assessing their completeness and internal consistency;
- cluster-level analysis to estimate TB prevalence; and
- individual-level analysis to estimate TB prevalence, using a logistic regression model that accounts for clustering, missing value imputation, and the fact that survey participation varies by cluster, sex and age group.

This chapter also provides a set of recommended table shells for tabulation and cross-tabulation of core survey data.

17.1 Overview

Estimating the point prevalence of TB disease (e.g. as a proportion) from a nationwide prevalence survey is more complex than counting the number of TB cases and dividing it by the total number of eligible survey participants. Instead, because of the clustered sampling approach used in these surveys (see **Chapter 5**), the calculation of TB point prevalence, and the uncertainty surrounding this estimate, must take into consideration the clustered design. Failure to do so will almost certainly understate the uncertainty surrounding the point estimate (i.e. its standard error) and may also affect the point estimate itself.

As with all epidemiological studies, surveys never go exactly according to plan; hence, potential sources of error or bias are introduced in the results. A common deviation from the protocol is one associated with assumptions made to calculate the sample size; for example, if either the observed prevalence is lower than anticipated or the between-cluster variability is greater than anticipated (giving a larger design effect), the prevalence estimate will be less precise than was intended. A potential source of bias is the inaccurate population representation in terms of probability proportional to size of district (e.g. the use of out-of-date census data). Another potential source of bias is the representativeness of the sample of people who actually participate in the survey, compared with those eligible to do so; for example, imagine that people who do not participate are at a higher or lower risk of having TB disease than those who do. Such shortcomings associated with these surveys must be accounted for and corrected, when appropriate, in the analysis.

This chapter is structured and presented in such a way as to illustrate how the World Health Organization's (WHO's) Global Task Force on TB Impact Measurement suggests an analysis report of a prevalence survey should be set out if it is to provide a comprehensive and transparent description of survey data related to the primary objective of estimating the prevalence of TB. The first part of the survey report (see **Section 17.2**) describes the data and assesses their completeness and internal consistency. Apart from providing an overview and understanding of the "core data" (i.e. the data that all TB prevalence surveys must collect), this part also identifies potential biases due to deviations from the sampling frame or missing data. The second part of the report (see **Section 17.3**) defines the outcomes analysed and describes the methods used to estimate point prevalence, accounting for both the sampling frame and for missing data. The final part of the report (see **Section 17.4**) summarizes results and presents concluding remarks about the survey and its findings, putting it within context both nationally and internationally.

It might seem attractive to use estimates of prevalence and duration of TB disease drawn from these surveys to derive incidence *(1, 2)*. However, unbiased duration measurements can only be estimated through specific projects and not through these surveys. If TB patients identified during the survey are interviewed about the duration of their symptoms, then the measured average duration obtained from the surveyed individuals will not represent the average duration of other patients in the same country who were not included in the survey. The reason is that the natural history of

the disease has been affected by the survey investigations (i.e. most individuals with prevalent TB were not diagnosed with TB before the survey), resulting in an average duration of disease shorter than the duration of disease in other patients in the country.

17.2 Description and assessment of the completeness and internal consistency of the core data

Sections 17.2.1–17.2.5 describe how to assess the completeness and internal consistency of the core data, as might be done in an analytical report. This analysis assumes that there are three strata (or geographical areas) in the survey; in reality, if there are any strata, the number will differ by country.

Initially, for the report it is important to describe the number of strata and clusters, and the number of clusters within each stratum. It should be possible to classify all surveyed individuals by stratum, cluster, age and sex, and all should have a unique personal individual identification (ID) number.

Of the total number of households identified in the clusters, it is recommended to describe the number and percentage of households that agreed to provide information on household membership, including age and sex of household members. Differences across strata in the number and percentage of households agreeing to or refusing to provide household information can also be assessed. Analyses should then be restricted to households that agreed to provide information on household composition.

The total number of individuals invited to participate in the survey in each cluster is expected to be close to the target cluster size, but there will be some variation around this target number (see **Chapter 5**). This number includes all eligible individuals aged 15 years and older who were listed on the household census, whether they were present on the day of the census and whether they agreed to participate in the survey. Only enumerated people can participate in the survey.

Table 17.1 shows individuals in the survey by eligibility status (and the reason for their ineligibility; e.g. non-resident of the household); both overall and by sex, age group and stratum.

For households that have been enumerated, **Table 17.2** shows the breakdown of eligible individuals according to whether they were not present on the day of the census and did not participate in the survey, present but did not consent, or present and consented to at least the CXR or interview during the survey. The number and percentage of individuals are shown by sex, age group, stratum and cluster among eligible individuals.

Table 17.1

Breakdown of all individuals identified by the survey team into eligible and ineligible (by reason for ineligibility); overall and by sex, age group and stratum

		INELIGIBLE[a]						ELIGIBLE		TOTAL (ALL)
		REASON 1		REASON 2		REASON 3				
		n[b]	%[c]	n[b]	%[c]	n[b]	%[c]	n[d]	%[c]	n[e]
Sex[e]	Male									
	Female									
Age (years)	0–4									
	5–14									
	15–24									
	25–34									
	35–44									
	45–54									
	55–64									
	≥65									
Stratum[f]	Stratum 1									
	Stratum 2									
	Stratum 3									
Total										

[a] Reasons for ineligibility are spelt out in the survey protocol and typically include those aged below 15 years, and those not resident in the household (depending on country definition).

[b] Number of participants with reason for ineligibility.

[c] Percentage of all individuals enumerated in census.

[d] Refers to N_1 in **Fig. 17.1**.

[e] Refers to N in **Fig. 17.1**.

[f] Restricted to individuals who are "age-eligible" (i.e. aged ≥15 years).

Table 17.2

Breakdown of eligible individuals, n (%), into non-participants and participants (present and consented to one or both of CXR and interview); overall and by sex, age group and stratum

		NON-PARTICIPANTS[a]		PARTICIPANTS (PRESENT AND CONSENTED TO ONE OR BOTH OF CXR AND INTERVIEW)		TOTAL (ELIGIBLE)
		n	%[b]	n[c]	%[b]	n[d]
Sex	Male					
	Female					
Age (years)	15–24					
	25–34					
	35–44					
	45–54					
	55–64					
	≥65					
Stratum	Stratum 1					
	Stratum 2					
	Stratum 3					
Cluster	Cluster 1					
	Cluster 2					
	Cluster 3…[e]					
Total						

CXR: chest X-ray.

This table may be reproduced separately for males and females to explore whether patterns (e.g. by age group) are different for males and females.

[a] Includes individuals who were not present on the day of the survey, or those who were present but did not consent to CXR and interview.

[b] % of total eligible.

[c] Refers to N_2 in **Fig. 17.1**.

[d] Refers to N_1 in **Fig. 17.1**.

[e] Plus additional clusters.

Additional socioeconomic indicators (e.g. occupation and education) could also be presented.

Fig. 17.1 shows the number of individuals who were enumerated and who participated in the various stages of the survey using the case definition from Option 1 (see **Chapter 4**). A similar flowchart could be adapted for the case definition from Option 2.

Fig. 17.2 is a simple way to visually inspect whether there are age and sex differences between the two populations that are being compared. Two population comparisons are recommended here for TB prevalence surveys that give useful insight into the success (or not) of the survey sampling design: country versus eligible survey populations and eligible versus survey participant populations.

17.2.1 Interview data

The number and percentage of individuals who were screened for TB symptoms and also had a CXR, among those eligible, are presented in **Table 17.3**.

Among those eligible, the percentage of individuals with a CXR is presented overall, and by sex, age group, stratum and cluster in **Table 17.3**. That table also includes the overall number and percentage of individuals with a symptom screen among individuals eligible for an interview, and the number and percentage of individuals with a symptom screen by sex, age group, stratum and cluster.

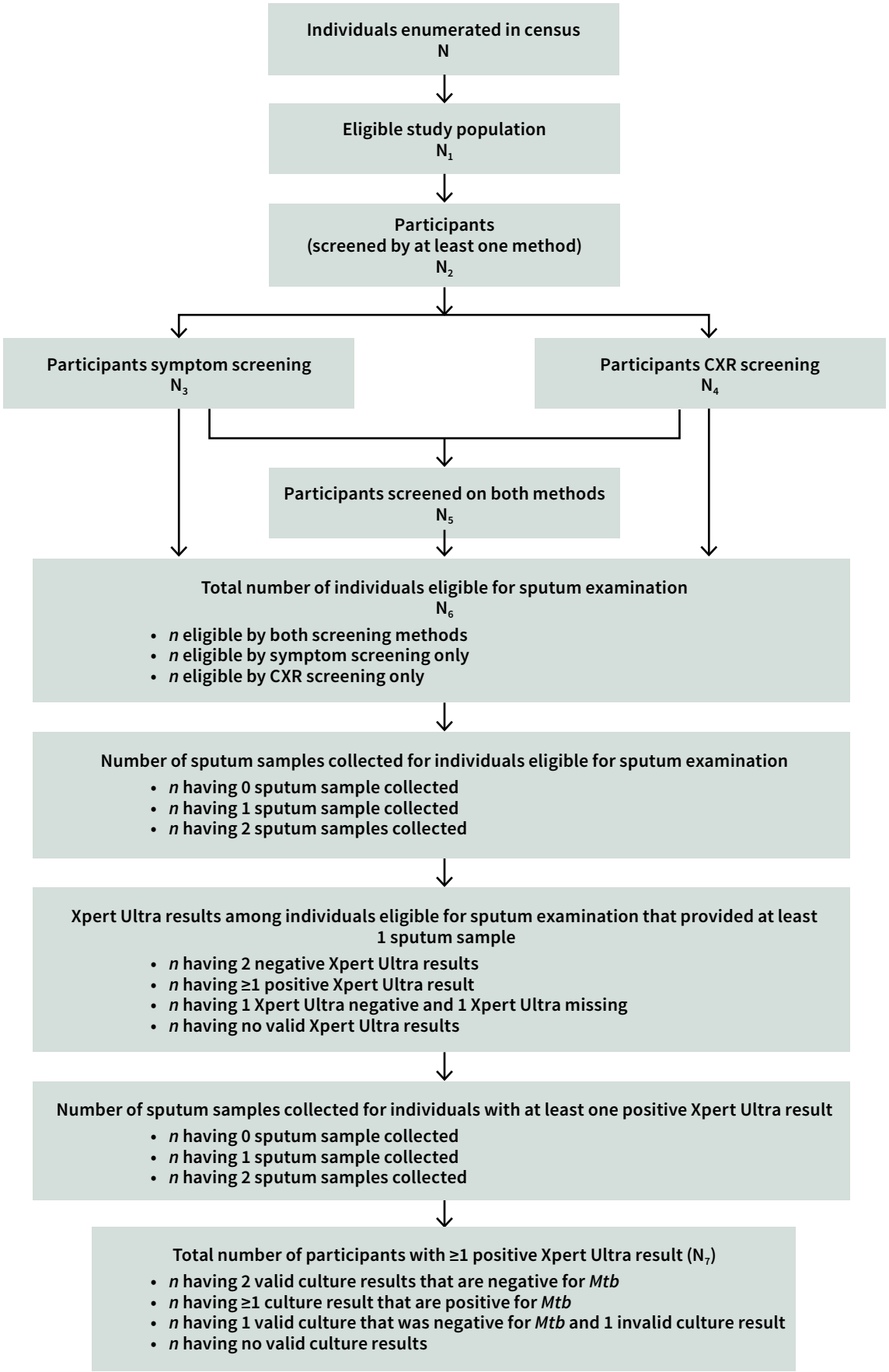
17.2.2 CXR screening and quality assurance

Among all participants who had X-rays taken, **Table 17.4** shows the number and percentage of individuals with CXR reading results that were classified as normal, abnormal and unknown by the field reader, both overall and by sex, age group, stratum and cluster.

Of the total number of CXRs read in the field, **Table 17.5** shows the number and percentage of CXRs that were re-read at central level or had a missing result. Cross-tabulation of the field CXR result with the central CXR result can show the overall percentage of agreement in CXR results between the results from the field reading and the central reading (see **Table 17.5**). More importantly, it shows how many individuals were assessed as *not* eligible for sputum examination based on the field CXR reading, but who *were* eligible for sputum examination according to the central reading of the CXR. This gives information about how many TB cases might have been missed by the survey.

Fig. 17.1

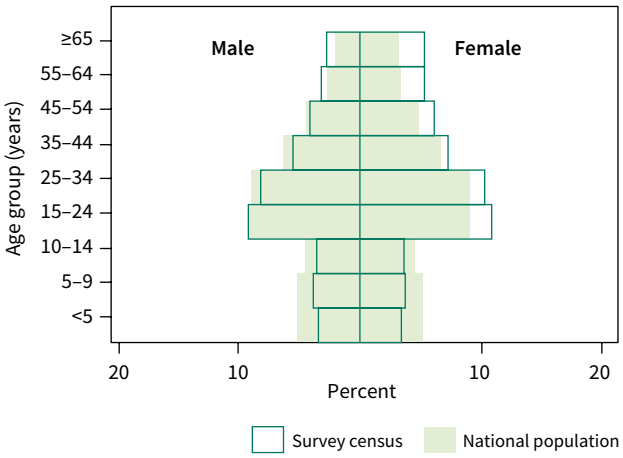
Schematic diagram of numbers of participants screened for TB in the prevalence survey, according to the survey protocol (Option 1)



CXR: chest X-ray; *Mtb*: *Mycobacterium tuberculosis*; TB: tuberculosis.

Fig. 17.2

Distribution by age and sex of the national population[a] compared with the distribution by age and sex of the enumerated population from the national TB prevalence survey of South Africa, 2018–2019 *(3)*



[a] Source: Data from the South Africa national census 2011 extrapolated to 2018.

Table 17.3

Coverage by CXR and symptom screening

		NUMBER ELIGIBLE	CXR SCREENING		SYMPTOM SCREENING	
		N_a	n[b]	%[c]	n[d]	%[c]
Sex	Male					
	Female					
Age (years)	15–24					
	25–34					
	35–44					
	45–54					
	55–64					
	≥65					
Stratum	Stratum 1					
	Stratum 2					
	Stratum 3					
Cluster	Cluster 1					
	Cluster 2					
	Cluster 3…[e]					
Total						

CXR: chest X-ray.

[a] Number eligible (N_1 in **Fig. 17.1**).

[b] Number with outcome (N_4 in **Fig. 17.1**).

[c] % of total eligible.

[d] Number with outcome (N_3 in **Fig. 17.1**).

[e] Plus additional clusters.

Table 17.4

Field CXR reading

		NORMAL[a]		ABNORMAL[a]		UNKNOWN[b]		TOTAL (OF THOSE WITH A CXR)
		N	%	n	%	n	%	n[c]
Sex	Male							
	Female							
Age (years)	15–24							
	25–34							
	35–44							
	45–54							
	55–64							
	≥65							
Stratum	Stratum 1							
	Stratum 2							
	Stratum 3							
Cluster	Cluster 1							
	Cluster 2							
	Cluster 3…[d]							
Total								

CXR: chest X-ray.

[a] For definitions of normal and abnormal field CXR readings, see **Chapter 7**.

[b] Unknown may include results that are inconclusive owing to poor CXR image, indeterminate or missing.

[c] Refers to N_4 in **Fig. 17.1**.

[d] Plus additional clusters.

Table 17.5

Comparison between field and central reading of CXR

CXR, CENTRAL READER	CXR, FIELD READER						TOTAL
	NORMAL[a]		ABNORMAL[a]		UNKNOWN[b]		
	n	%	n	%	n	%	n
Normal[a]							
Abnormal consistent with TB[a]							
Abnormal inconsistent with TB[a]							
Unknown[b]							
CXR not read							
Total							

CXR: chest X-ray; TB: tuberculosis.

[a] For definitions, see **Chapter 7**.

[b] Unknown may include results that are inconclusive owing to poor CXR technique, indeterminate or missing.

If computer-aided detection (CAD) is used, then the CXR interpretation is dependent on the use cases of CAD (**Chapter 7**). **Table 17.6** shows CXR results if CAD is used. The final sputum eligibility is then determined according to the use of CAD, alone or in combination with human reading (**Chapter 7**).

When human reading is done after or in parallel to CAD, a cross-tabulation to describe the difference between CAD reading and human reading may be presented.

Table 17.6

CAD CXR results

		BELOW THRESHOLD[a]		ABOVE THRESHOLD[a]		UNKNOWN[b]		TOTAL (OF THOSE WITH A CXR)
		n	%	n	%	n	%	n[c]
Sex	Male							
	Female							
Age (years)	15–24							
	25–34							
	35–44							
	45–54							
	55–64							
	≥65							
Stratum	Stratum 1							
	Stratum 2							
	Stratum 3							
Cluster	Cluster 1							
	Cluster 2							
	Cluster 3…[d]							
Total								

CAD: computer-aided detection; CXR: chest X-ray.

[a] For more information on CAD threshold and results, see **Chapter 7**.

[b] Unknown may include results that are inconclusive owing to poor CXR technique, indeterminate or missing.

[c] Refers to N_4 in **Fig. 17.1**.

[d] Plus additional clusters.

17.2.3 TB symptom screening

Table 17.7 shows the percentage of individuals with reported TB symptoms (the exact number and type of symptom are not specified here because the number of symptoms that are enquired about may vary by country protocol) and the percentage of individuals who are sputum-eligible based on TB symptoms. The number and percentage of individuals with TB symptoms by sex, age group, stratum and cluster are shown, as well as the number and percentage of individuals found to have any TB symptom, and the number and percentage of individuals eligible for sputum examination based on TB symptoms.

17.2.4 Laboratory results

The content and tables presented in this section are based on the use of Xpert Ultra and culture. However, the table shells given could be adapted in the context of the use of other WHO-recommended rapid diagnostic tests that might emerge in the future to diagnose TB.

Valid Xpert Ultra results (provided as a semiquantitative categorization of the bacillary load) are reported as negative, trace, very low, low, medium or high. Culture results are reported as negative, positive for *Mycobacterium tuberculosis (Mtb)*, positive for non-tuberculous mycobacteria (NTM), contaminated or not available. Results are cross-tabulated by the following: eligibility for sputum examination according to field CXR reading, eligibility for sputum examination according to reported symptoms, eligibility for sputum examination according to either CXR or reported symptoms, or eligible for sputum examination based on CXR exemption.

Table 17.8a presents Xpert Ultra results for each of the two sputum samples, by semiquantitative Xpert result, and **Table 17.8b** presents combined Xpert Ultra results among individuals eligible for sputum examination. These tables are for the Option 1 case definition (**Chapter 4**). Xpert Ultra results that are not available (**Table 17.8a**) include invalid result, error and no result.

Table 17.9a presents culture results for each of the two sputum samples separately, among individuals who were eligible for sputum examination, and **Table 17.9b** presents combined culture results among individuals eligible for sputum examination. These tables are for the Option 2 case definition (**Chapter 4**).

Table 17.10 presents culture results among individuals with at least one positive Xpert Ultra result, using the Option 1 case definition (**Chapter 4**).

Table 17.7

Current TB symptoms and eligibility for sputum examination based on TB symptoms

		N[a]	SYMPTOM 1		SYMPTOM 2		SYMPTOM 3…[c]		ANY SYMPTOM		SPUTUM-ELIGIBLE BASED ON TB SYMPTOMS	
			n[b]	%[c]	n[b]	%[c]	n[b]	%[c]	n[b]	%[d]	n[e]	%[f]
Sex	Male											
	Female											
Age (years)	15–24											
	25–34											
	35–44											
	45–54											
	55–64											
	≥65											
Stratum	Stratum 1											
	Stratum 2											
	Stratum 3											
Cluster	Cluster 1											
	Cluster 2											
	Cluster 3…[g]											
Total												

TB: tuberculosis.

[a] Number with interview data on TB symptoms (N_3 in **Fig. 17.1**).

[b] Number with symptoms.

[c] Plus additional symptoms.

[d] Percentage with symptoms over total number of those with interview data on TB symptoms.

[e] Number eligible for sputum examination based on TB symptoms.

[f] Percentage eligible for sputum examination based on TB symptoms over total number of those with interview data on TB symptoms.

[g] Plus additional clusters.

Option 1 case definition

Table 17.8a

Xpert Ultra results by screening method

	SAMPLE 1 RESULT														SAMPLE 2 RESULT													
	NEGATIVE		TRACE		VERY LOW		LOW		MEDIUM		HIGH		NOT AVAILABLE[a]		NEGATIVE		TRACE		VERY LOW		LOW		MEDIUM		HIGH		NOT AVAILABLE[a]	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Eligible for sputum examination according to CXR only[b]																												
No																												
Yes																												
Unknown																												
Eligible for sputum examination according to symptoms only[c]																												
No																												
Yes																												
Unknown																												
Eligible for sputum examination according to CXR and symptoms																												
No																												
Yes																												
Unknown																												
Eligible based on CXR exemption (e.g. no CXR done, no reported symptoms), if applicable																												
No																												
Yes																												
Total																												

CXR: chest X-ray.

[a] Xpert Ultra invalid result, error or no result; n represents the number in the respective group and % represents the percentage over total eligible for sputum examination.

[b] This includes those who are symptom negative (or symptom result not available if CXR exemption category is not used).

[c] This includes those who are CXR negative (or CXR result not available if CXR exemption category is not used).

Table 17.8b

Combined Xpert Ultra results from the two samples among individuals eligible for sputum examination (total = N_6 in Fig. 17.1)

SAMPLE 1 RESULT	SAMPLE 2 RESULT						
	NEGATIVE	TRACE	VERY LOW	LOW	MEDIUM	HIGH	NOT AVAILABLE
Negative							
Trace							
Very low							
Low							
Medium							
High							
Not available							

Option 2 case definition

Table 17.9a

Culture results by screening method

	SAMPLE 1 RESULT										SAMPLE 2 RESULT									
	NEGATIVE		POSITIVE		NTM		CONTAMI-NATED		NOT AVAILABLE[a]		NEGATIVE		POSITIVE		NTM		CONTAMI-NATED		NOT AVAILABLE[a]	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Eligible for sputum examination according to CXR only[b]																				
No																				
Yes																				
Unknown																				
Eligible for sputum examination according to symptoms[c]																				
No																				
Yes																				
Unknown																				
Eligible for sputum examination according to CXR or symptoms																				
No																				
Yes																				
Eligible based on CXR exemption (e.g. no CXR done, no reported symptoms), if applicable																				
No																				
Yes																				
Total																				

CXR: chest X-ray; NTM: non-tuberculous mycobacteria.

[a] Culture test not done, result missing; n represents the number in the respective group and % represents the percentage over total eligible for sputum examination.

[b] This includes those who are symptom negative (or symptom result not available if CXR exemption category is not used).

[b] This includes those who are CXR negative (or CXR result not available if CXR exemption category is not used).

Table 17.9b

Combined culture results among individuals eligible for sputum examination (total = N_6 in Fig. 17.1)

SAMPLE 1 RESULT	SAMPLE 2 RESULT				
	NEGATIVE	POSITIVE FOR *Mtb*	NTM	CONTAMINATED	NOT AVAILABLE
Negative					
Positive for *Mtb*					
NTM					
Contaminated					
Not available					

Mtb: *Mycobacterium tuberculosis*; NTM: non-tuberculous mycobacteria.

Table 17.10

Culture results among individuals with at least one positive Xpert Ultra result using the Option 1 case definition (total = N_7 in Fig. 17.1)

SAMPLE 1 RESULT	SAMPLE 2 RESULT				
	NEGATIVE	POSITIVE FOR *Mtb*	NTM	CONTAMINATED	NOT AVAILABLE
Negative					
Positive for *Mtb*					
NTM					
Contaminated					
Not available					

Mtb: *Mycobacterium tuberculosis*; NTM: non-tuberculous mycobacteria.

Fig. 17.3 and Fig. 17.4 present the final classification of the survey TB case status of screen-positive individuals according to the case definitions presented in Chapter 4, using Option 1 (primary case definitions) and Option 2, respectively. It is highly recommended to populate each cell of the case definition algorithm presented in Chapter 4 according to the survey findings, to describe and understand the distribution of TB test results and symptoms, and the different survey case definition patterns.

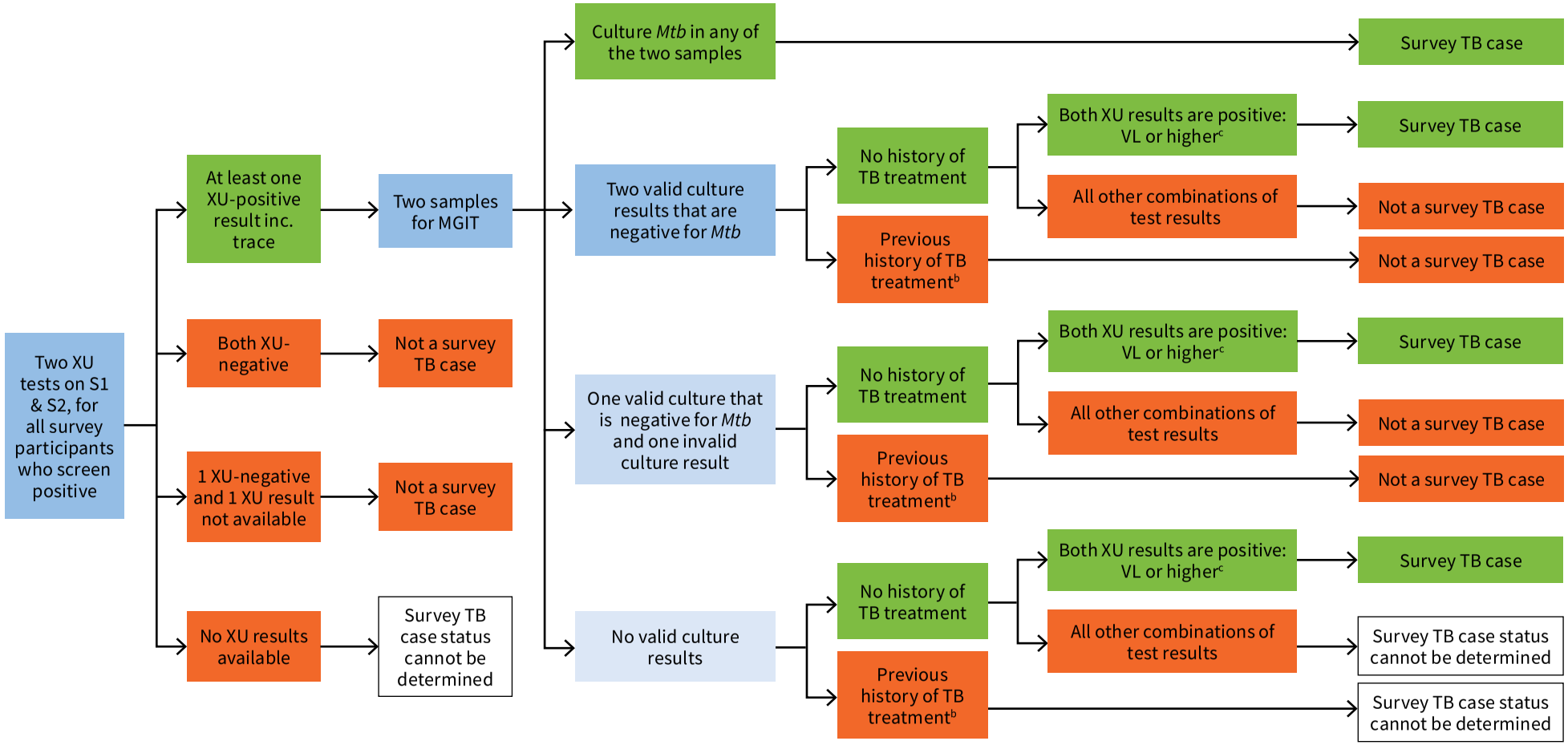
Additional material and figures from future national TB prevalence surveys showing the final classification of survey TB case status using either Option 1 or Option 2 will be published on the WHO website once results are available.

Table 17.11 presents the final classification of survey participants as survey TB case, not a survey TB case and participants for whom TB status could not be determined, disaggregated by age, sex, stratum and cluster.

Finally, Table 17.12 presents self-reported HIV status and HIV status for those tested during the survey among all survey participants, individuals who were eligible for sputum examination and among survey TB cases.

Fig. 17.3

Option 1 (primary case definitions, for primary analysis): classification of the survey TB case status of screen-positive individuals[a]



MGIT: mycobacteria growth indicator tube; *Mtb: Mycobacterium tuberculosis*; N: culture negative; NTM: non-tuberculous mycobacteria; S: sample; TB: tuberculosis; VL: very low; XU: Xpert Ultra.

[a] Two Xpert Ultra tests for all screen-positive individuals, followed by two confirmatory tests using liquid culture for all individuals with at least one Xpert-positive result.

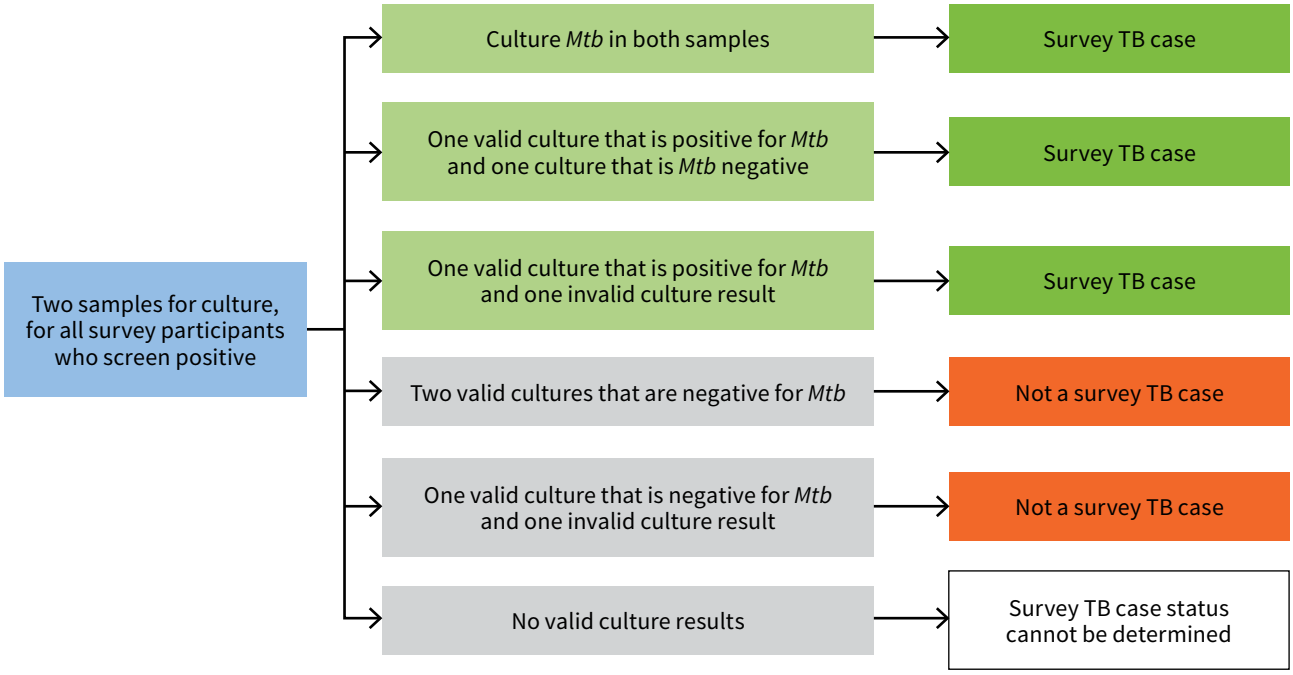
[b] Previous history of TB within the past 5 years. If a person had TB more than 5 years before the survey, that person should be included in the box for "no history of TB treatment".

[c] Xpert Ultra provides a semiquantitative categorization of the bacillary load. From highest to lowest, the categories are high, medium, low, very low and trace. These categories correlate with the sputum bacillary load of *Mtb*. There is no semiquantitative category when the test result is negative.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results that are negative for *Mtb*:** N or NTM.
- **Invalid culture results:** the result is missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).
- **Valid Xpert Ultra results:** Xpert positive (including trace), Xpert negative.

Fig. 17.4

Option 2: classification of the survey TB case status of screen-positive individuals[a]



Mtb: Mycobacterium tuberculosis; N: culture negative; NTM: non-tuberculous mycobacteria; TB: tuberculosis.

[a] Option 2: Two tests using liquid culture for all screen-positive individuals.

- **Negative for *Mtb*:** either N/N, N/NTM, NTM/N or NTM/NTM.
- **Valid culture results negative for *Mtb*:** N or NTM.
- **Invalid culture results:** missing, contaminated (with no acid-fast bacilli) or non-interpretable (i.e. culture grown but no identification; this rarely happens).

Table 17.11

Classifying survey participants as survey TB case, not a survey TB case and survey participants for whom TB status could not be determined

		SURVEY CASE		NOT A SURVEY CASE		TB STATUS COULD NOT BE DETERMINED		TOTAL
		n[a]	%[a]	n	%	n	%	
Sex	Male							
	Female							
Age (years)	15–24							
	25–34							
	35–44							
	45–54							
	55–64							
	≥65							
Stratum	Stratum 1							
	Stratum 2							
	Stratum 3							
Cluster	Cluster 1							
	Cluster 2							
	Cluster 3…[b]							
Total								

TB: tuberculosis.

[a] n represents the number in the respective group and % represents the percentage over total eligible for sputum examination.

[b] Plus additional clusters.

Table 17.12

HIV testing results among survey participants

	ALL SURVEY PARTICIPANTS		ELIGIBLE FOR SPUTUM EXAMINATION		SURVEY TB CASE	
	n	%	n	%	n	%
Self-reported HIV status						
Negative						
Positive						
Unknown						
HIV status tested during the survey						
No						
Yes						
Unknown						
HIV test result among those tested during the survey						
Negative						
Positive						
Unknown						
Combined final HIV status[a]						
Negative						
Positive						
Unknown						

HIV: human immunodeficiency virus; TB: tuberculosis.

[a] This is a combination of self-reported HIV status and HIV test status.

17.2.5 Do variations in TB notification rates between subpopulations of interest reflect true differences in TB disease burden?

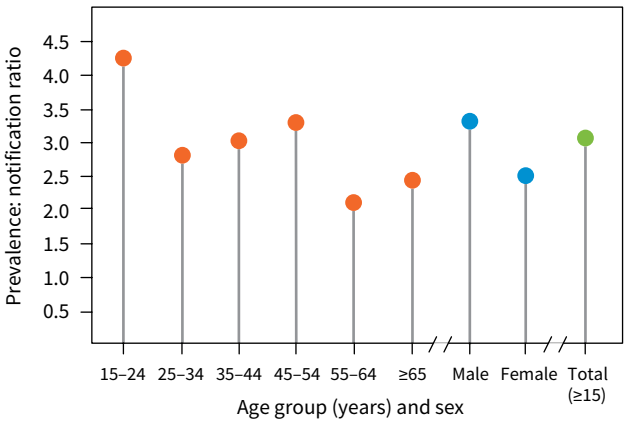
It is often observed that TB case notification rates are higher among men than among women, or higher in certain geographical areas. To interpret such differences in TB case notifications, it is recommended to compute ratios of measured prevalence over notification rates specific to subpopulations of interest and to compare those ratios. An example of prevalence to notifications ratios is shown in **Fig. 17.5**.

As an example, if notification rates among men are higher than notification rates among women, a concern may be that women are less able than men to access health services. However, if the ratio of prevalent over notified cases is similar among men and women, sex differences in TB notification rates may be interpreted as reflecting actual sex differences in disease burden. In this example, the survey results would not provide evidence to support the hypothesis that, on average, women have less access to health services than men.

On the other hand, whenever a large difference between the prevalence to notifications ratio is observed between subpopulations of interest, systematic differences in screening and diagnostic algorithms

Fig. 17.5

Ratio of TB prevalence to notifications[a] by age and by sex, from the national TB prevalence survey of the Philippines, 2016 *(4)*



TB: tuberculosis.

[a] Notification rates were estimated using smear-positive pulmonary TB notifications (2016) obtained from the National TB Control Programme, and population estimates from the UN Population Division (2015 revision).

or notification of TB may be suspected. Such differences should be investigated and addressed through changes in relevant policies for TB control, to improve overall TB control performance.

In general, prevalence surveys are not powered to detect statistical differences in prevalence between subpopulations. The proposed approach to computing ratios of prevalence to notification rates is not aimed at showing statistical evidence of differences in prevalence between subpopulations; instead, it is aimed at comparing patterns in notifications to patterns in prevalence, to identify potential weaknesses in policies for case-finding and reporting.

17.3 Estimation of pulmonary TB prevalence: methods of analysis

This section presents the methods of analysing survey data, both at the cluster and individual levels, with the primary goal of estimating overall TB prevalence. For individual-level analyses in particular, one recommended logistic regression model is presented to account for the cluster sample survey design, and to correct for the bias due to missing data and for differentials in participation in the survey by age, sex and cluster. All analyses for examples shown in this chapter were undertaken using Stata *(5)*; however, the analyses could be done using other statistical software such as R *(6)*.

17.3.1 Outcomes analysed

Definitions of who is a survey TB case and who is not a survey TB case can be found in **Chapter 4**. All survey participants are classified into one of three categories based on the observed data: survey TB case = yes, survey TB case = no, and survey TB case = status cannot be determined.

17.3.2 Cluster-level analyses

The use of a cluster sample survey design means that if an individual-level analysis is done without taking account of the clustering, then the confidence interval for the value of true TB prevalence will be too narrow. A simple solution to account for the clustering is to aggregate the individual-level data to the level of the cluster, so that the cluster (rather than the individual) becomes the unit of analysis.

This "simple solution" is recommended if the number of clusters is less than 30. TB prevalence surveys typically include 50 or more clusters; hence, strictly speaking, a cluster-level analysis is not essential. Nevertheless, this method is recommended as the first step in the analysis because it is simple and transparent, and because it requires a careful description of the variation in cluster-level TB prevalence. This is an important feature of the data that should be described clearly and summarized in a graph.

For a cluster-level analysis, TB prevalence among survey participants is calculated separately for each cluster, and the average cluster-level prevalence $\bar{p}$ is calculated as:

$$\bar{p} = \frac{1}{c}\sum_{i} p_i$$

where c is the number of clusters and p_i are the cluster-specific TB prevalence values for each of the clusters, for $i = 1,.., c$. An approximate 95% confidence interval is calculated based on the observed between-cluster variation.

Specifically:

- the standard deviation (SD) of the cluster-level prevalences is calculated;
- the standard error (SE) of the mean across clusters is calculated as $^{SD}/_{\sqrt{c}}$, where c is the number of clusters; and
- an approximate 95% confidence interval is calculated as the mean prevalence across clusters, plus or minus 1.96 times the SE of the mean.

A histogram should also be plotted to indicate the distribution of cluster-level TB prevalence (**Fig. 17.6**).

17.3.3 Individual-level analyses

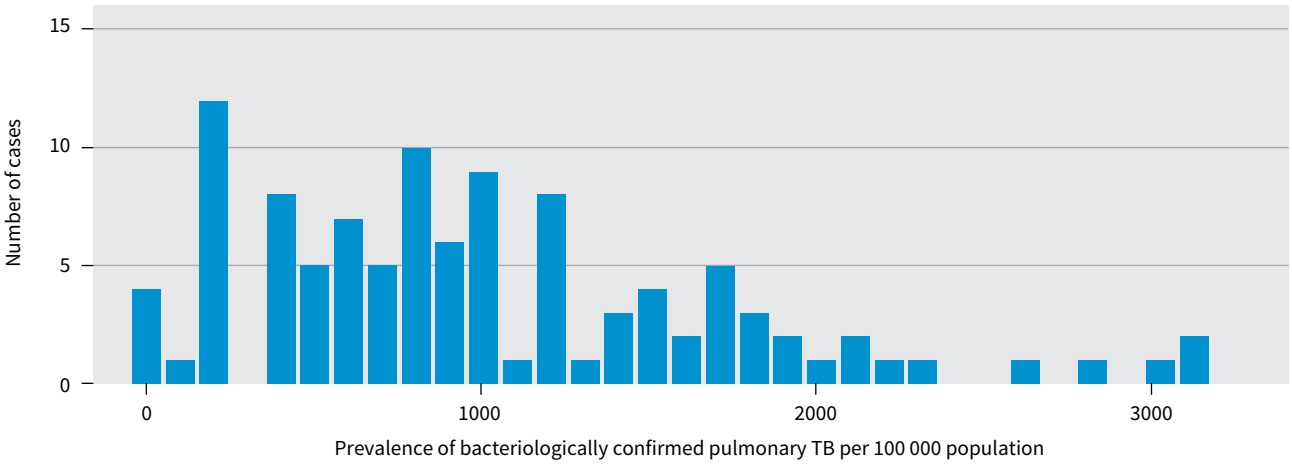
In addition to using cluster-level estimates and combining them to estimate the population prevalence, individual-level analyses should be performed *(7)*. The most crucial characteristic of the latter is that they take clustering of individuals into consideration. Other advantages are that they facilitate adjustment of the estimation of TB prevalence according to the effects of other important participant characteristics, such as age and sex, and allow an investigation of the extent to which the bias introduced by the incompleteness of the data can be corrected *(8)*.

Individual-level analyses are performed using **logistic regression with robust SEs based on observed between-cluster variability**. This approach is possible because the outcome is binary (a participant either is or is not a survey TB case); it accounts efficiently for the clustering of individuals and allows handling of missing data by imputation techniques *(9)*.

The recommended analysis should use logistic regression with robust SEs with missing value imputation (for individuals eligible for sputum examination), and inverse probability weighting (applied to all survey participants). Missing value imputation is used for individuals eligible for sputum examination for whom survey TB case status could not be determined based on the available results for screening and diagnostic tests. Inverse probability weighting is then used to correct for differentials in participation in the survey (among individuals who were eligible to participate in the survey) by age, sex and cluster. Through the combination of imputation of missing data and the use of

Fig. 17.6

Cluster variation of the number of bacteriologically confirmed pulmonary TB cases, from the national TB prevalence survey of the Philippines, 2016 *(4)*



weights, the analysis aims to represent the whole of the survey eligible population (=N_1 in **Fig. 17.1**), but the weights are applied only to survey participants (=N_5 in **Fig. 17.1**).

When performing the analysis, this guidance recommends using a step-by-step approach, starting with a simple model on the complete case (model 1) data, followed by a second model complete case data and multiple imputations (model 2), and finally a third model using multiple imputations and inverse probability weighting (model 3) (**Fig. 17.7**). This makes it possible to assess the effect of the different statistical techniques on the point estimates and its SE. However, only the model combining multiple imputations and inverse probability weighting will be retained as the final model to provide a valid estimate of TB prevalence.

Fig. 17.7

Statistical approaches and steps for the estimation of TB prevalence

	Enumerated	Model 1	Model 2	Model 3
Eligible	Non-eligible[a]			
Participants	Non-participants[b]	*Ignored*	*Ignored*	*Accounted for by IPW*
	Not eligible for sputum examination	CC	CC	CC
	Eligible for sputum examination		MI	MI

CC: complete case analysis; IPW: inverse probability weighting; MI: multiple imputation; TB: tuberculosis.

[a] Children (≤15 years) and non-residents (≤2 weeks in household).

[b] Those who did not participate in cluster operations.

17.3.4 Missing value imputation

Why is missing value imputation necessary?

There will always be missing outcome data in TB prevalence surveys. What matters here are the missing data that make it impossible to classify a participant who was eligible to provide sputum samples as either a survey TB case or not a survey TB case (**Chapter 4**).

A prevalence estimate that uses only individuals with complete data on prevalent TB will be biased except under the strong assumption that those with full information are a random subset of the eligible study population. Methods that incorporate missing value imputation are unbiased under a weaker assumption (see below); thus, imputation is valuable both for obtaining a more valid estimate of TB prevalence and in assessing the bias of simpler approaches. However, it should always be possible to collect virtually complete data during the household census on a few key individual characteristics that are risk factors for pulmonary TB; in particular, an individual's age or birth year, sex and history of TB treatment. The stratum and cluster for all eligible individuals is always known.

Multiple imputation of missing data is not a good substitute for collecting the data in the first place. It is essential to keep to a minimum missing data on outcome variables (symptom screening, CXR, and Xpert Ultra and culture results) and key explanatory variables (individual characteristics known to be risk factors for TB). Hence, even though it is possible to reduce the harmful impact of missing data during the analysis, all of the following are essential: community sensitization, repeat visits and tracing of missed individuals, and minimizing procedural and laboratory errors (e.g. CXR machines not working, not obtaining sputum samples from participants who were eligible for sputum examination, Xpert Ultra testing machines not working, and

much higher or lower than expected culture contamination rates).

Important concepts for missing value imputation

Three key types of missing data are distinguished in the literature, and these need to be understood to take proper account of missing data in the analysis *(9–11)*. The three types are missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR). These are explained in this section, in the context of data being missing for the primary outcome variable of prevalent TB, yes or no, among survey participants who were eligible to provide sputum samples for diagnostic testing.

MCAR

MCAR occurs when the probability that an individual has missing data on prevalent TB is NOT related to either the value of the outcome (i.e. survey TB case yes or no) or an individual characteristic that is a risk factor for the outcome (e.g. age, sex, stratum, cluster or TB symptoms). Among participants who were eligible to provide sputum samples but who did not provide two sputum samples, it is probable that missing data are not MCAR because missing data are more likely to happen for individuals with a relatively lower probability of having TB who find it more difficult to provide a sputum sample (e.g. individuals without TB symptoms). However, among participants who were eligible to have sputum taken and provided two sputum samples for Xpert Ultra testing (Option 1), it may be reasonable to assume that Xpert Ultra test results are MCAR if the only reason for missing test results is invalid test results or that samples were provided but not tested because they were lost.

MAR

MAR occurs when the probability that an individual has missing data for the outcome variable of survey TB case (yes or no) **is** related to individual characteristics such as age, sex, stratum, TB symptoms and CXR reading. However, **within** groups of individuals who are the same for age, sex, stratum, TB symptoms and CXR reading, the probability of data being missing on the outcome variable is **not** associated with its value (i.e. survey TB case yes or no). Missing value imputation is implemented with the assumption that MAR is true.

For Option 2 (2 sputum samples collected for culture testing, among all sputum-eligible participants), the observed prevalence of TB – stratified on at least an individual's age, sex, stratum, TB symptoms and CXR reading – is used to predict survey TB case (yes or no) for individuals for whom data are missing.

For Option 1 (2 sputum samples collected for Xpert Ultra testing, and a further 2 sputum samples collected for culture testing among participants with at least 1 positive Xpert Ultra test result), imputation of missing data should be done in two steps: first, imputing missing data on culture-positive status (positive or negative) among individuals with at least one positive Xpert Ultra test result; and second, imputing survey TB case (yes or no) among sputum-eligible participants with no valid results from the Xpert Ultra test. In this way, an unbiased estimate of true pulmonary TB prevalence in the population can be obtained.

MNAR

MNAR occurs when the probability of an individual having missing data on the outcome variable (i.e. survey TB case yes or no) differs between individuals who have TB and those who do not have TB, even when individuals have been stratified on known risk factors for TB (e.g. urban or rural area of residence, age and sex). In this situation, it is not possible to "correct" the estimate of TB prevalence simply by using missing value imputation based on the patterns in the observed data; instead, a sensitivity analysis is required.

The observed data themselves cannot distinguish between MCAR, MAR and MNAR. In practice, the aim is to impute data in a way that makes the MAR assumption plausible. Where possible, it is useful to collect information (e.g. the reason for not providing sputum samples, not having at least one valid Xpert Ultra test result, or not having at least one valid culture result) to make a more informed assessment of the plausibility of the MAR assumption.

Describing and understanding the patterns of missing values

Before undertaking missing value imputation, the first step of the analysis should always be to describe and understand the patterns of missing values on survey TB case status among individuals eligible for sputum examination. This summary should be done both overall and by individual risk factors for prevalent TB; for example, age group, sex, stratum (area of residence), previous or current TB treatment, TB symptoms and CXR reading. Some of these summaries are covered by the tables in previous sections of this chapter. They are mentioned again here because it is essential to understand the extent of, and patterns of, missing data.

For Option 1, it is important to summarize the patterns of missing data in two steps. Step 1 is a summary of missing culture results among participants with at least one positive result from the Xpert Ultra; this can be done using **Tables 17.13a** and **17.13b**. Step 2 is a summary of missing Xpert Ultra test results among participants who were eligible to provide sputum samples; this can be done using **Tables 17.14a** and **17.14b**.

Table 17.13a

Culture results and missing culture results among participants with at least one positive Xpert Ultra result (Option 1, Step 1 of multiple imputation)

		NO VALID CULTURE RESULTS (MISSING CULTURE RESULTS)		ONE VALID CULTURE RESULT THAT IS NEGATIVE FOR *Mtb* AND ONE INVALID CULTURE RESULT		TWO VALID CULTURE RESULTS THAT ARE NEGATIVE FOR *Mtb*		CULTURE POSITIVE FOR *Mtb* IN ANY OF THE TWO SAMPLES	
		n	%	n	%	n	%	n	%
Sex	Male								
	Female								
Age (years)	15–24								
	25–34								
	35–44								
	45–54								
	55–64								
	≥65								
Stratum	Stratum 1								
	Stratum 2								
	Stratum 3								
Cluster	Cluster 1								
	Cluster 2								
	Cluster 3…[a]								
Xpert Ultra results[b]	Trace								
	Very low								
	Low								
	Medium								
	High								
	Not available								
History of TB treatment	No								
	Yes, previous[c]								
	Yes, current								
Total									

Mtb: *Mycobacterium tuberculosis*; TB: tuberculosis.

[a] Plus additional clusters.

[b] This is the highest category of Xpert Ultra test results across 2 samples.

[c] Make note of the number of people with a history of TB treatment within the past 5 years. This information is important when defining who is and is not a survey case (see **Chapter 4**).

Table 17.13b

Participant characteristics by survey TB case status among participants with at least one positive Xpert Ultra result (Option 1, Step 1 of multiple imputation)

		NOT A SURVEY TB CASE		SURVEY TB CASE		SURVEY TB CASE STATUS CANNOT BE DETERMINED	
		n	%	n	%	n	%
Sex	Male						
	Female						
Age (years)	15–24						
	25–34						
	35–44						
	45–54						
	55–64						
	≥65						
Stratum	Stratum 1						
	Stratum 2						
	Stratum 3						
Cluster	Cluster 1						
	Cluster 2						
	Cluster 3…[a]						
Xpert Ultra results[b]	Trace						
	Very low						
	Low						
	Medium						
	High						
	Not available						
History of TB treatment	No						
	Yes, previous[c]						
	Yes, current						
Total							

TB: tuberculosis.

[a] Plus additional clusters.

[b] This is the highest category of Xpert Ultra test results across 2 samples.

[c] Make note of the number of people with a history of TB treatment within the past 5 years. This information is important when defining who is and is not a survey case (see **Chapter 4**).

Table 17.14a

Xpert Ultra results and missing Xpert Ultra results among participants who were eligible to provide sputum samples (Option 1, Step 2 of multiple imputation)

		NO XPERT ULTRA RESULTS AVAILABLE (MISSING XPERT ULTRA RESULTS)		ONE XPERT ULTRA NEGATIVE AND ONE NOT AVAILABLE		BOTH XPERT ULTRA NEGATIVE		AT LEAST ONE XPERT ULTRA POSITIVE RESULT (INCLUDING TRACE)	
		n	%	n	%	n	%	n	%
Sex	Male								
	Female								
Age (years)	15–24								
	25–34								
	35–44								
	45–54								
	55–64								
	≥65								
Stratum	Stratum 1								
	Stratum 2								
	Stratum 3								
Cluster	Cluster 1								
	Cluster 2								
	Cluster 3…[a]								
History of TB treatment	No								
	Yes, previous[b]								
	Yes, current								
Any TB symptoms	No								
	Yes								
Eligible for sputum sample collection based on TB symptoms	No								
	Yes								
CXR result	Normal								
	Abnormal								
Total									

CXR: chest X-ray; TB: tuberculosis.

[a] Plus additional clusters.

[b] Make note of the number of people with a history of TB treatment within the past 5 years. This information is important when defining who is and is not a survey case (see **Chapter 4**).

Table 17.14b

Participant characteristics by survey TB case status among participants who were eligible to provide sputum samples (Option 1, Step 2 of multiple imputation)

		NOT A SURVEY TB CASE		SURVEY TB CASE		SURVEY TB CASE STATUS CANNOT BE DETERMINED	
		n	%	n	%	n	%
Sex	Male						
	Female						
Age (years)	15–24						
	25–34						
	35–44						
	45–54						
	55–64						
	≥65						
Stratum	Stratum 1						
	Stratum 2						
	Stratum 3						
Cluster	Cluster 1						
	Cluster 2						
	Cluster 3…[a]						
History of TB treatment	No						
	Yes, previous[b]						
	Yes, current						
Any TB symptoms	No						
	Yes						
Eligible for sputum examination based on TB symptoms	No						
	Yes						
CXR result	Normal						
	Abnormal						
Total							

CXR: chest X-ray; TB: tuberculosis.

[a] Plus additional clusters.

[b] Make note of the number of people with a history of TB treatment within the past 5 years. This information is important when defining who is and is not a survey case (see **Chapter 4**).

Implementation of multiple missing value imputation

The imputation process will be done on the primary outcome – that is, survey TB case (yes or no) – and missing data on other variables will not be imputed. This primary outcome could be defined using either the Option 1 or Option 2 classification of who is a survey TB case (as defined in **Chapter 4**). The process for implementing multiple missing value imputation depends on whether Option 1 or Option 2 is chosen for case definition. For both, imputation of missing data is done only among individuals who are eligible to provide sputum samples for diagnostic testing for TB. **Box 17.1** explains how missing values are imputed.

The process of creating the imputed datasets can be implemented in Stata using the *mi* suite of commands for multiple imputation, and in other statistical packages (e.g. R using the *mice* package). The *mi* impute command in Stata does not allow for correlation among individuals in the same cluster; however, because TB symptoms, the CXR reading, an individual's previous history of TB treatment and an individual's HIV status are included as variables in the imputation model, at least part of the correlation among individuals in the same cluster will be explained by the model. Including cluster as an explanatory variable in the imputation model is not recommended, given the low number of TB cases in proportion to the number of clusters.

The overall point prevalence of TB and its 95% confidence interval is calculated for each imputed dataset using logistic regression with robust SEs (to account for the clustered sampling design).

BOX 17.1
MULTIPLE MISSING VALUE IMPUTATION

If the survey uses Option 1 for the classification of who is a survey TB case, imputation of the missing data is done in two steps among sputum-eligible participants whose prevalent TB status could not be determined owing to missing Xpert Ultra or culture test results.

Step 1

The first step is to impute missing data on survey TB case (yes or no) among individuals who had at least one positive Xpert Ultra test result but survey TB case status could not be determined (**Table 4.1**, **Fig. 17.3**). Using the data on individuals for whom survey TB case status could be determined, a logistic regression model is used to impute the missing data on survey TB status, creating M_1 datasets that each include all the individuals with at least one positive Xpert Ultra test result and in which all of them are classified as survey TB case = yes, or survey TB case = no. The imputation model should include variables that are predictors of survey TB case status (yes or no) among the individuals with at least one positive Xpert Ultra test result; such variables are expected to include the semiquantitative category of the Xpert Ultra tests, and whether the individual has a previous history of TB treatment or is currently receiving treatment for TB. Each of these M_1 imputed datasets are then combined with a dataset that includes all the sputum-eligible individuals who were not eligible for culture testing, to create M_1 datasets that include all sputum-eligible individuals.

The rationale for choosing M_1, the number of imputed datasets at Step 1, could be based on the proportion of individuals with no valid culture results and the proportion of sputum-eligible individuals with no valid Xpert Ultra test results. For example, among the individuals with at least one positive Xpert Ultra test result, if 10% of individuals have no valid culture results and 5% of sputum-eligible individuals have no valid Xpert Ultra test results, then the total number of imputed datasets would be M_1 =10 x 5 = 50. This guidance recommends a maximum of 100 imputed datasets, so that if the calculated $M_1 > 100$, then $M_1 = 100$.

Step 2

For each of these M_1 datasets, the second step is to impute missing data on survey TB case (yes or no) for the sputum-eligible individuals who had no valid Xpert Ultra test results. Using the data on individuals who are already classified as survey TB case = no, or survey TB case = yes (i.e. all individuals who had ≥1 valid Xpert Ultra test result), a logistic regression model is used to impute the missing data on survey TB case status. The imputation model should include variables that are predictors of survey TB case status (yes or no); such variables are expected to include the observed data on CXR results, TB symptoms, previous history of TB treatment, HIV status, age, sex and stratum. Through this process, a single imputed dataset will be created for each one of the M_1 datasets that were generated in the first step.

Once Step 2 is complete, there will be a total of M_1 imputed datasets that each include all the sputum-eligible individuals and in which all of those individuals are classified as survey TB case = yes, or survey TB case = no. Each of these imputed datasets is then combined with a dataset that includes all the individuals who were not sputum-eligible, to create M_1 imputed datasets that include all survey participants.

Single-step process

If the survey uses Option 2 for classification of survey TB cases, imputation of the missing data is done in one step among sputum-eligible participants whose survey TB case status could not be determined because of a lack of valid culture test results. The process corresponds to the second step described above for Option 1 (i.e. the approach that was described for imputing missing data on prevalent TB among individuals with no valid Xpert Ultra test results).

Only the ***overall*** point prevalence of pulmonary TB and its 95% confidence interval is estimated; thus, there are no explanatory variables included in the model for this stage. Next, an average of the estimates of TB prevalence from each of the imputed datasets is calculated, with a 95% confidence interval that considers both:

- the variation in the estimate of point prevalence among imputed datasets; and
- sampling variation including the effect of the clustering in the survey design; in Stata this can be done using the (user-written) *mim* command or the *mi estimate* command.

In summary, if four requirements are met – that is, the percentage of individuals with missing data is not too high (e.g. 10–15% or less), data are MAR, appropriate imputation models are used and the data from the imputed datasets are combined in an appropriate way – then it is possible to obtain an unbiased estimate of TB prevalence in the eligible population. It is also possible to obtain a valid 95% confidence interval for the prevalence of TB, allowing for both the clustering in the survey design and the uncertainty introduced by the imputation. If any of the four requirements are not met, then multiple imputation cannot be relied upon to provide a valid estimate of the prevalence of TB. If the percentage of individuals with missing data is more than 15%, but there is confidence that the other requirements are met, then it remains useful to apply multiple imputation, but the interpretation of the results must be more cautious.

Multiple imputation combined with inverse probability weighting

It is possible to adjust for the missing data using only multiple imputation, and this is the most efficient approach, provided the imputation models are specified appropriately. However, the recommended approach is to use a combination of multiple imputation and inverse probability weighting (*11, 12).*

Individuals who participate in the survey can be divided into two groups:

- *eligible for sputum examination* – individuals with an abnormal CXR, positive on symptom screening or unable to undergo CXR screening (or any combination of these); and
- *ineligible for sputum examination* – individuals who had a normal CXR and were also negative on symptom screening.

Individuals who were ineligible for sputum examination are assumed not to have TB and are coded as survey TB case status = no. For those eligible for sputum examination, multiple imputation is used to fill in missing data on survey TB case status. This is implemented in the same way as described above in the section on implementation of multiple missing value imputation. For each imputed dataset, a point estimate for population TB prevalence and a 95% confidence interval for that prevalence is then calculated, using robust SEs and weights.

Weights are calculated for each combination of cluster, age group and sex by counting the number of:

- eligible individuals in each combination of cluster, age group and sex (*N*); and
- survey participants in each combination of cluster, age group and sex (*n*).

The weight for each individual is then equal to *N/n*, for the particular combination of cluster, age group and sex that they are in. Next, an average of the estimates of TB prevalence from each of the imputed datasets is calculated, together with a 95% confidence interval. In Stata, this can be done using the *mim* or the *mi estimate* command, and *svy* commands.

In cases where the cluster sizes vary (i.e. when the final cluster sizes differ from the targeted cluster size), additional weights can be applied to account for this difference, so that each cluster will have the same weight in the final analysis.

For this approach to give an unbiased estimate of TB prevalence, it is necessary for data to be MAR for the imputation for missing values on survey TB case status. Also, the method for weighting, explained above, assumes that non-participants have the same TB prevalence as participants after stratification by cluster, age group and sex.

Sensitivity analysis

Sensitivity analyses are useful for exploring the extent to which the estimate of TB prevalence varies with different assumptions about TB prevalence among individuals with missing data on survey TB case (yes or no). This guidance proposes two sensitivity analyses, but more could be performed depending on the survey context.

A first sensitivity analysis is based on the assumption that all the individuals with missing data on survey TB case status are NOT survey TB cases. This is an extreme assumption that is unlikely to be true, but it could provide a lower estimate of the true prevalence of TB.

A second sensitivity analysis is based on the assumption that all the survey participants who were eligible to provide two sputum samples for Xpert Ultra testing (Option 1) or culture testing (Option 2), but provided no sputum samples, are NOT survey TB cases.

17.4 Summary and conclusions

The report's concluding remarks should refer to the quality of the survey in terms of how many cases it is expected to have missed, the prevalence of TB disease in the country, and how the survey findings relate to,

and complement, existing knowledge about TB epidemiology and control in the region.

Summary remarks when reporting the results of a prevalence survey could include:

- the coverage of the survey population for CXR, interview and symptom screening;
- the percentage of abnormal CXRs missed by the field reader, or CAD, of the CXR when compared with the central CXR reading;
- missing data for Xpert Ultra and culture results;
- Xpert Ultra and culture results; and
- TB prevalence as measured according to each of the outcomes and its 95% confidence interval.

This chapter was updated in line with recent theoretical and practical guidance on best-practice methods for the analysis of TB prevalence surveys *(13)*.

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CHAPTER 18

Comparing results from repeat and previous surveys

18.1 Introduction

Conducting a repeat national tuberculosis (TB) prevalence survey in a country that has conducted similar surveys in the past can be used to assess time trends in the prevalence of TB disease and the burden of TB disease more broadly. Changes in TB prevalence are typically slow; for this reason, repeat national TB prevalence surveys should only be considered every 10 years or so.[1] Conducting a repeat survey also makes it possible to evaluate the impact of TB prevention and care interventions that have been implemented since the previous survey, and whether targets for reductions in TB disease burden have been reached.

The design and implementation of repeat surveys should benefit from lessons learned and data generated from previous surveys. For example, data from previous well-designed and well-conducted surveys can be used to inform the determination of sample size and the sampling design of repeat surveys. Similarly, valuable field experience and expertise that was gained during previous surveys can be used in optimizing the field operations of repeat surveys.

All design elements of a survey, including repeat surveys, should follow the guidance provided in earlier chapters.[2] If a country is interested in implementing a repeat prevalence survey using a specific design to detect a change in TB prevalence (a different approach from the one presented in **Chapter 5** and this chapter), additional materials are available in Chapter 9 of the previous edition of the handbook on TB prevalence surveys (referred to as the *Lime Book*) *(1)*.[3]

Over time, there is improvement in knowledge about the conduct of TB prevalence surveys, and available screening and diagnostic tools. Implementers of surveys should use the best tools available to them at the time of the survey, according to international standards. However, for the purpose of comparing repeat TB prevalence survey results with those from a previous survey to assess trends, results from both surveys need to be directly comparable. The production of results that are comparable can be achieved at the stage of either analysis or design of the repeat survey. At the outset, it is advisable to develop a concept note describing all data management and data analysis steps required to make results of repeat surveys comparable, ensuring that any change in TB prevalence detected is due to true changes in TB burden.

This chapter provides guidance on how to compare results from a repeat prevalence survey with those from a previous survey. **Section 18.2** highlights the importance of clearly describing and understanding key design elements of the surveys being compared. **Section 18.3** provides suggestions about how to produce survey datasets that are directly comparable and outlines one approach for comparing results from two surveys. **Section 18.4** presents illustrative examples from Viet Nam, the Philippines and Myanmar on the comparison of repeat survey results with those from an earlier survey, at the analysis stage. **Section 18.5** describes the example of the 2023–2024 prevalence survey in Cambodia, in which comparison with survey results from the past was anticipated and addressed at the stage of survey design.

18.2 Description and understanding of the key design elements of both surveys

To inform a fair, direct comparison of results from a repeat national TB prevalence survey and a previous survey, the key design elements of both surveys, and their similarities and differences, need to be clearly described and understood.

18.2.1 Sample size calculation, sampling design and eligibility criteria

The first key elements to describe and understand are sample size calculation, sampling design and the criteria used to determine eligibility to participate in the survey. **Table 18.1** shows the main elements that need to be compared and provides structure for describing them, for both a repeat survey and a previous survey.

18.2.2 Screening and diagnostic testing algorithm

The next key elements to describe and understand are the screening and diagnostic testing algorithms used in each survey.

It is financially and logistically reasonable for a country conducting a repeat survey to use the same X-ray technology for screening purposes that was used in the previous survey. This usually means that the relevant X-ray equipment would be available, and staff

[1] See **Table 1.1** in **Chapter 1**.

[2] In particular, that on screening, diagnostic algorithms, case definitions and sampling design provided in **Chapter 3**, **Chapter 4** and **Chapter 5**.

[3] This approach is more complex and its use has been very limited to date.

Table 18.1

Comparison of sample size calculation, sampling design and eligibility criteria used in a repeat and previous survey

	SURVEY 1 ("PREVIOUS" SURVEY)	SURVEY 2 ("REPEAT" SURVEY)
Sample size considerations		
Prior hypothesis on the true prevalence of TB		
Relative precision of TB prevalence estimate		
Design effect		
Coefficient of between-cluster variation *k*		
Participation rate		
Final sample size calculated		
Sampling design		
Sampling frame		
Sampling design (e.g. cluster random sampling)		
Strata		
Sampling unit (definition of a cluster)		
Number of clusters		
Cluster size		
Eligibility criteria		
Age		
Residency		

TB: tuberculosis.

would have already received training and acquired field experience. However, because of technological advances in digital imaging, and the possibility of using computer-aided diagnosis, digital methods have distinct advantages over conventional film-based systems. Thus, the use of digital imaging technology is now preferable, even if a conventional film-based system was used in the previous survey.

The same concept applies to laboratory methods used for diagnostic testing. This is probably the aspect of a survey for which it is most difficult to implement the same methods over time. Laboratory methods have evolved rapidly in recent years – for example, with the availability of rapid molecular tests endorsed by WHO since 2010 and their subsequent evolution and improvements in culture methods. An estimate of TB prevalence from a repeat survey that used a liquid sputum culture method for TB diagnosis cannot be directly compared with an estimate from a previous survey that used a solid sputum culture method, given the differences in sensitivity and specificity between these two culture methods. Similarly, Xpert® MTB/RIF Ultra (Xpert Ultra), a rapid test approved by WHO in 2017, is now recommended as the main diagnostic test in a survey (see Option 1 in **Chapter 3** and the associated case definitions in **Chapter 4**); it has a higher sensitivity than both smear microscopy and solid culture, which were relied upon in most surveys implemented up to 2016.

The use of both "old" and "new" methods in a repeat survey is one way to ensure the availability of directly comparable results, if the associated cost implications are acceptable. This was done in the third national TB prevalence survey implemented in Cambodia, in 2023–2024: Option 1 as described in **Chapter 3** was used, together with additional laboratory tests (solid culture) to allow for a direct comparison with the previous survey.[1]

Table 18.2 shows the main elements of screening and diagnostic testing algorithms that need to be compared and a structure for describing them, for both a repeat survey and a previous survey.

18.2.3 TB case definitions

The next key element to describe and understand is survey TB case definitions, since the estimate of TB prevalence is computed according to these definitions.

For example, an earlier survey might have used solid culture results (e.g. using Löwenstein-Jensen [LJ]) to define whether someone is a survey case or not, while a survey implemented using this guidance would use liquid culture results (e.g. mycobacterial growth indicator tube [MGIT™]). Given the difference in diagnostic performance between the two different types of culture test (with liquid culture being much more sensitive than solid culture), the estimates of prevalence from the two surveys cannot be directly compared. Adjustments are needed to account for what is known about the different sensitivity of the two culture methods; also, biases

[1] See also section 3.4 in **Chapter 3** for discussion of this approach.

Table 18.2

Comparison of the screening and diagnostic testing algorithms used in a repeat and previous survey

	SURVEY 1 ("PREVIOUS" SURVEY)	SURVEY 2 ("REPEAT" SURVEY)
Screening tools		
Symptom screening		
Chest X-ray		
Other		
Screening algorithm		
Laboratory methods used for diagnostic testing		
Xpert		
Culture		
Other		

Table 18.3

Comparison of the case definitions used in a repeat and previous survey, illustrated using the example of the first and second national surveys in Viet Nam

	SURVEY 1 (2006–2007)	SURVEY 2 (2017–2018)
Survey TB case definition	• Two or more positive smears; or • one positive smear plus an abnormal CXR consistent with TB; or • one positive smear plus a positive *Mtb* culture.	• Bacteriologically confirmed cases according to an expert panel decision based on Xpert MTB/RIF result, culture results, CXR findings and TB treatment history.

CXR: Chest X-ray; *Mtb*: *Mycobacterium tuberculosis*; TB: tuberculosis.

should be extensively considered and discussed.

Table 18.3 shows how survey case definitions can be compared for both a repeat survey and a previous survey, illustrated using the example of the 2006–2007 and 2017–2018 surveys in Viet Nam *(2–4)*. In these two surveys in Viet Nam, the case definition in the first survey used smear microscopy and solid culture test results whereas the second survey used Xpert MTB/RIF and culture (both LJ solid and MGIT[1]) results.

18.3 Making repeat survey datasets comparable and preparing for final analysis

If the design of two surveys is different, results cannot be directly compared.

The main recommendation when comparing results from two TB prevalence surveys is to make both survey datasets as comparable as possible in terms of the key design elements discussed in **Section 18.2**. In practice, this means that the final analysis of both datasets may be restricted to only a subset of eligible individuals and participants, and that a common definition (or one that is as similar as possible) is applied to establish which individuals screened positive and which individuals were a survey TB case.

A common definition for both surveys should be established for:

- **Eligibility criteria.** For example, it could be that in the first survey, all individuals aged 10 years and older were eligible to participate, whereas in the second, only individuals aged 15 years and older were eligible. For the comparison, there should be a common criterion related to age for eligible individuals (e.g. only individuals ≥15 years will be eligible to be included for the comparison of the TB prevalence estimates from the two surveys).
- **Survey cases.** This is probably the hardest thing to achieve when seeking to make a fair comparison of results from two different surveys. It is essential to spend time and effort thinking about how to choose a common survey TB case definition that can be applied to both surveys.

Table 18.4 provides a structure for describing the eligibility criteria and case definitions used in a repeat and previous survey, and a common case definition to be used for direct comparison of survey results.

18.3.1 A practical analytical guide for statistical comparison of results from a repeat survey and a previous survey

Once the common definitions to be used for direct comparison of survey results have been established, and once the necessary data management required to

[1] The final culture result was mostly the MGIT result, and the LJ result was only taken into account when the MGIT result was contaminated or unavailable.

Table 18.4

Description of key design elements of two surveys and a common definition to be used for comparison of results

	SURVEY 1 ("PREVIOUS" SURVEY)	SURVEY 2 ("REPEAT" SURVEY)	COMMON DEFINITION FOR THE COMPARISON BETWEEN SURVEYS
Eligibility criteria			
Criterion 1			
Criterion 2 …			
Definition of a positive screening			
Survey TB case definition			

TB: tuberculosis.

produce two final datasets based on these common definitions (one for each of the two surveys) has been completed, statistical analysis to compare results can be done.

The example below describes one possible method for comparing prevalence survey estimates. *Statistical advice should be sought when developing the analytical component of the survey protocol and a statistician should also do the analysis of survey data*.

The comparison could be done in three steps:

- Step 1: Combine the datasets from the two surveys, including the multiple imputations.
- Step 2: Create a binary variable *survey* that identifies the two surveys in the combined dataset with *survey=1* for the first survey and *survey=2* for the second survey.
- Step 3: Estimate the prevalence ratio (PR) by fitting a log-binomial model with survey status as the dependent variable and the variable *survey* created in Step 2 as the only independent variable, combined with multiple imputations and inverse probability weighting (see **Chapter 17**). The number of imputations should be the same for the two surveys being compared.

The Stata *glm* command, in addition to the *mim* and *svy* package, can be used to estimate the PR in Step 3 by specifying the *binomial* family and the *log* link.

An example of the code that could be used is:

```
xi:mim,: svy: glm survey_status i.survey,
family(binomial) link(log)
```

The PR is the exponential of the estimated coefficient of the variable survey.

In addition to the PR, the 95% confidence interval (CI) is estimated, and a *P*-value is provided to test the null hypothesis of a PR equal to 1. If the *P*-value is below 0.05, there is statistical evidence of a difference between the two surveys.

Assuming that Survey 1 is the reference category in the above model:

- a PR of less than 1 is in the direction of a lower estimated prevalence in the second survey as compared with the first survey; and
- a PR of more than 1 is in the direction of a higher estimated prevalence in the second survey as compared with the first survey.

It is important to consider the point estimate of the PR, its 95% CI and its related P-value to interpret the results correctly; the 95% CI provides a range of PR values that are compatible with the observed data.

Another option is to estimate the prevalence difference (PD) instead of the PR – the PD corresponds to the estimated difference in the two prevalence estimates – along with its corresponding 95% CI. To do this, the only change would be in Step 3, where it would be necessary to specify a link *identity* in the *glm* function in Stata.

An example of the Stata code that could be used to estimate the PD, assuming the imputations done at an earlier stage, is:

```
xi:mim,:svy: glm survey_status i.survey,
family(binomial) link(identity)
```

It is also possible to implement this in R using the *mice* package for the multiple imputations and the survey package specific to the survey design (function *svydesign*) before running the regression model (function *svyglm*).

An example of the R codes to estimate the PR, assuming the imputations done at an earlier stage, is:

```
design <- svydesign(id = ~cluster_num, strata
= ~strata_var, weights = ~weight_var, data =
survey_data_imputed)

model <- svyglm(survey_status ~ survey , family
= quasibinomial(link = "logit"), design = design)
```

18.4 Country examples of producing comparable survey datasets at the analysis stage

This section provides three country examples of how comparable survey datasets can be produced. These are for Viet Nam, the Philippines and Myanmar.

The tables and figures that are included are not examples that should be systematically reproduced for other countries; rather, they are intended as practical illustrations of how results from two surveys can be compared, which can guide comparison of results in other countries.

18.4.1 Example from Viet Nam

A first national TB prevalence survey was implemented in Viet Nam in 2006–2007 and a repeat survey followed in 2017–2018 *(2–4)*.

Comparison of the characteristics of eligible participants

Table 18.5 shows the characteristics of eligible participants and the proportion of those who screened positive in the two surveys in Viet Nam.[1] Statistical tests were also performed to explore statistical evidence of a difference in the distribution of these characteristics between the two surveys.

Comparison of laboratory test results used for TB diagnosis among individuals who screened positive

Fig. 18.1 summarizes the screening algorithm, diagnostic testing methods and survey TB case definition used in the two national TB prevalence surveys in Viet Nam. The populated example is useful for comparing the different definitions used and the corresponding number of individuals at each stage of the survey.

Table 18.6 shows the laboratory test results for participants who screened positive in the two surveys in Viet Nam. Statistical tests were also performed to com-

Table 18.5

Comparison of the characteristics of participants eligible for sputum collection in the first (2006–2007) and second (2017–2018) national TB prevalence surveys in Viet Nam

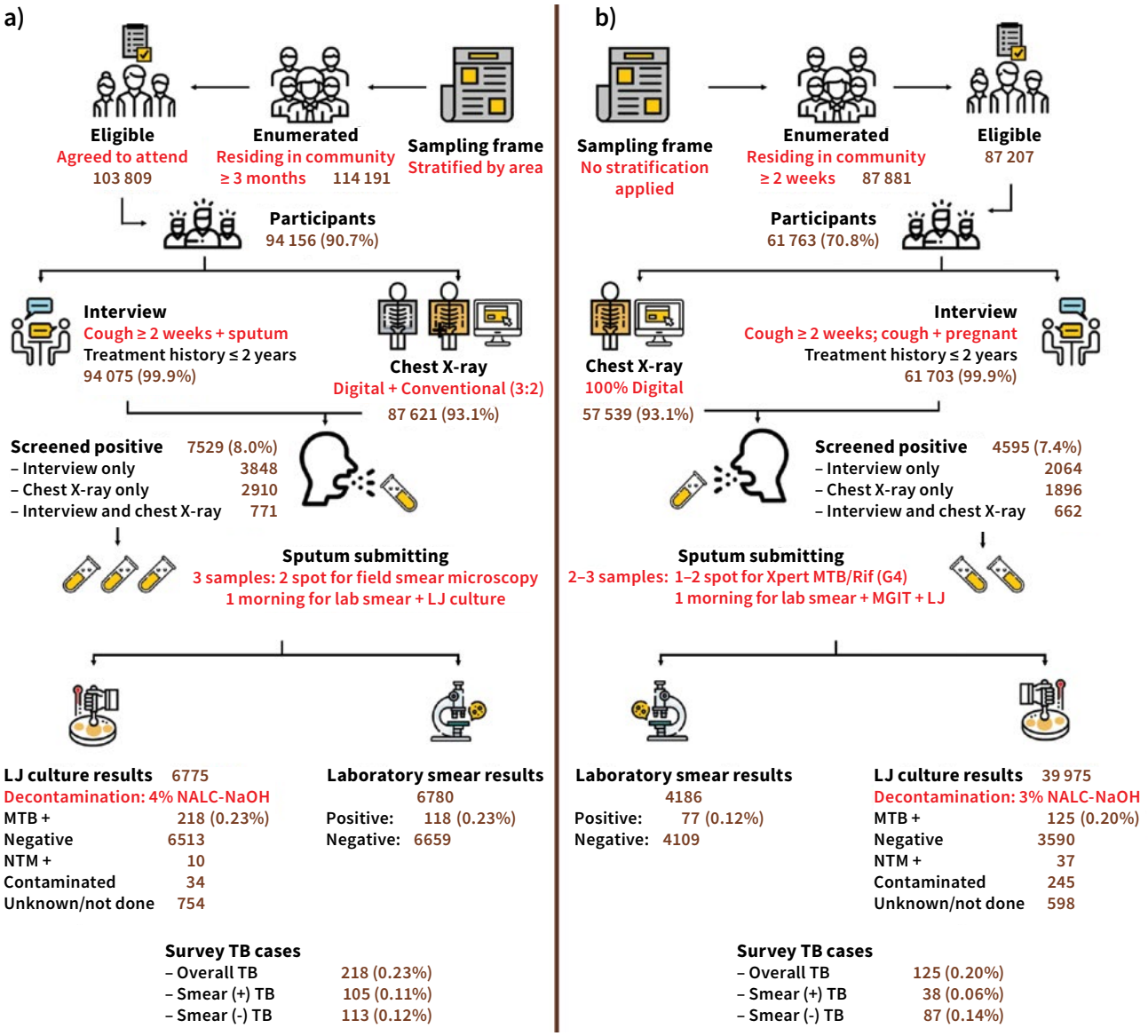
	FIRST SURVEY, 2006–2007			SECOND SURVEY, 2017–2018			*P*-VALUE
	PARTICIPANTS	SCREENED POSITIVE		PARTICIPANTS	SCREENED POSITIVE		
	n	*n*	%	*n*	*n*	%	
Sex							
Male	42 596	4 580	10.8	27 150	2 794	10.3	0.053
Female	51 560	2 949	5.7	34 613	1 801	5.2	0.001
Age (years)							
15–24	20 934	620	3.0	6 542	120	1.8	<0.001
25–34	18 681	950	5.1	10 191	349	3.4	<0.001
35–44	19 790	1 429	7.2	11 508	548	4.8	<0.001
45–54	16 285	1 587	9.8	13 289	1 056	8.0	<0.001
55–64	8 138	1 055	13.0	11 143	1 162	10.4	<0.001
≥65	10 328	1 888	18.3	9 090	1 360	15.0	<0.001
Area							
Urban	26 353	2 058	7.8	18 656	1 383	7.4	0.119
Remote	17 532	2 406	8.7	15 882	1 179	7.4	<0.001
Rural	40 271	3 065	7.6	27 225	2 033	7.5	0.489
Region							
North	45 669	3 913	8.6	25 575	1 849	7.2	<0.001
Central	14 646	1 062	7.3	13 525	1 195	8.8	<0.001
South	33 841	2 554	7.6	22 663	1 551	6.8	0.002
Total	**94 156**	**7 529**	**8.0**	**61 763**	**4 595**	**7.4**	**<0.001**

n: number; TB: tuberculosis.
Source: Nguyen et al. (2021) *(2)*.

[1] The table shows the data for people who screened positive (on either or both of symptoms and CXR). Tables for people who were only symptom-screen positive or only CXR-screen positive could also be produced.

Fig. 18.1

Summary results from the first (a) and second (b) national TB prevalence surveys in Viet Nam, 2006–2007 and 2017–2018



LJ: Löwenstein-Jensen; MTB: *Mycobacterium tuberculosis*; NALC: N-acetyl-l-cysteine; NaOH: sodium hydroxide; NTM: non-tuberculous mycobacteria; TB: tuberculosis.

Source: Nguyen et al. (2021) *(2)* (reproduced with permission).

pare the distribution of the results between the two surveys.

Common case definition used for survey comparisons

The first survey used sputum smear microscopy and LJ solid culture assays; the second survey used the molecular assay Xpert MTB/RIF and MGIT liquid culture. To ensure comparable laboratory results between the surveys, for the second survey, sputum smear microscopy and LJ solid culture on sputum samples were also conducted.

The case definition used for direct comparison of the two surveys was "culture-positive for *Mtb* using an LJ solid culture assay".

Comparison of survey TB cases

Table 18.7 shows the number and proportion of survey TB cases among participants who screened positive in the two surveys in Viet Nam. A statistical test was also performed to compare these two proportions between the two surveys.

Comparison of TB prevalence survey results

Once the design of the two surveys had been described in detail and compared, and a comparable survey TB

Table 18.6

Laboratory test results from the first (2006–2007) and second (2017–2018) national TB prevalence surveys in Viet Nam

	FIRST SURVEY, 2006–2007		SECOND SURVEY, 2017–2018		*P*-VALUE
	n PARTICIPANTS	% PARTICIPANTS	*n* PARTICIPANTS	% PARTICIPANTS	
Total	94 156	100	61 763	100	
Screened positive	7529	8.0	4595	7.4	<0.001
Direct smear microscopy					
Negative	6659	7.07	4109	6.65	0.001
Any positive	118	0.13	77	0.12	0.835
Scanty	35	0.04	36	0.06	0.056
1+	47	0.05	26	0.04	0.485
2+	21	0.02	7	0.01	0.114
3+	15	0.02	8	0.01	0.636
Not reported[a]	752	0.80	409	0.66	0.003
LJ culture					
Mtb	218	0.23	125	0.20	0.230
NTM	10	0.01	37	0.06	<0.001
No growth	6513	6.92	3590	5.81	<0.001
Contaminated	34	0.04	245	0.40	<0.001
Not reported[a]	754	0.08	598	0.97	<0.001

LJ: Löwenstein-Jensen; *Mtb: Mycobacterium tuberculosis*; *n*: number; NTM: non-tuberculous mycobacteria; TB: tuberculosis.

[a] Test result was unknown or no sample available.

Source: Nguyen et al. (2021) *(2)*.

Table 18.7

Number of survey TB cases in the first (2006–2007) and second (2017–2018) national TB prevalence surveys in Viet Nam

	FIRST SURVEY, 2006–2007		SECOND SURVEY, 2017–2018		*P*-VALUE
	n PARTICIPANTS	% PARTICIPANTS	*n* PARTICIPANTS	% PARTICIPANTS	
Total	94 156	–	61 763	–	
Screened positive	7 529	8.0	4 595	7.4	<0.001
Survey TB case (LJ culture-positive)	218	0.23	125	0.20	0.204

LJ: Löwenstein-Jensen; *n*: number; TB: tuberculosis.

Source: Nguyen et al. (2021) *(2)*.

case definition had been established, both surveys were re-analysed using the recommended methods described in **Chapter 17**. Two-step multiple imputation was not required because neither of these surveys used the new survey TB case definition (see **Chapter 4**).

Comparable estimates of TB prevalence from both surveys could then be computed. **Fig. 18.2** shows an example of how these comparisons can be presented for the two surveys undertaken in Viet Nam.

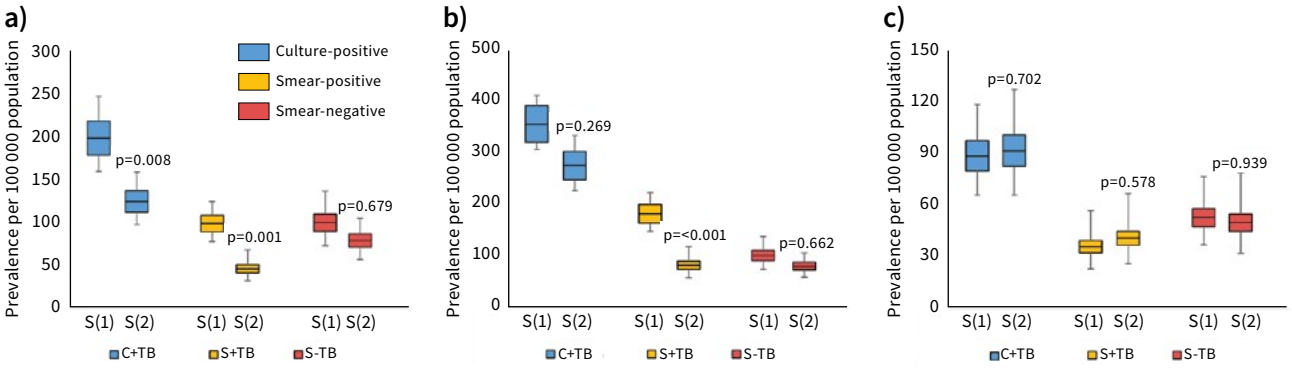
Results from the comparison of the prevalence of culture-positive TB (from diagnostic testing using solid culture) in the first and second national TB prevalence surveys in Viet Nam are shown in **Table 18.8**.

The adjusted prevalence of culture-positive TB declined by 37.1% (95% CI: 11.5–55.4%), from 199 (95% CI: 160–248) cases per 100 000 adults in 2006–2007 to 125 (95% CI: 98–159) cases per 100 000 adults in 2017–2018.

Fig. 18.2

Comparison of the prevalence (cases per 100 000 individuals aged ≥15 years) of culture-positive TB, smear-positive TB and smear-negative TB in the first (2006–2007) and second (2017–2018) national TB prevalence surveys in Viet Nam

(a) Overall prevalence; (b) prevalence among male participants; (c) prevalence among female participants. The tops and bottoms of the boxes indicate the standard errors of the prevalence; horizontal lines within boxes indicate the point estimates of the prevalence; error bars indicate 95% CIs.



CI: confidence interval; S(1): first TB prevalence survey (2006–2007); S(2): second TB prevalence survey (2017–2018); TB: tuberculosis.
Source: Nguyen et al. (2021) *(2)* (reproduced with permission).

Table 18.8

Comparison of the prevalence of culture-positive TB per 100 000 adults in the first (2006–2007) and second (2017–2018) national TB prevalence surveys in Viet Nam

CHARACTERISTIC	FIRST SURVEY, 2006–2007	SECOND SURVEY, 2017–2018	COMPARISON
	ADJUSTED POINT ESTIMATE (95% CI)	ADJUSTED POINT ESTIMATE (95% CI)	ADJUSTED % CHANGE (95% CI)
Overall	199 (160–248)	125 (98–159)	–37.1 (–55.4 to –11.5)
Sex			
Male	356 (307–412)	275 (226–334)	–18.0 (–42.2 to +16.3)
Female	89 (66–119)	92 (66–128)	+11.1 (–96.1 to +36.7)
Age (years)			
15–24	40 (21–76)	0	NA
25–34	102 (68–154)	77 (44–135)	+19.0 (–50.2 to +194.1)
35–44	224 (169–297)	143 (94–217)	–20.6 (–49.3 to +57.8)
45–54	304 (233–397)	209 (149–294)	–20.6 (–33.3 to +54.8)
55–64	353 (245–509)	344 (252–469)	+7.5 (–72.4 to +32.9)
≥65	597 (469–760)	346 (244–490)	–34.6 (–8.7 to +60.6)
Area			
Urban	202 (157–261)	232 (181–297)	+31.6 (–117.4 to +20.6)
Remote	178 (136–234)	160 (111–229)	–1.0 (–61.3 to +50.2)
Rural	243 (201–294)	150 (113–199)	–43.2 (–65.0 to –7.4)
Region			
North	212 (175–257)	146 (108–197)	–33.3 (–8.7 to +58.8)
Central	166 (110–252)	174 (118–256)	–4.8 (–100.0 to +54.3)
South	235 (192–288	209 (165–266)	+2.0 (–69.5 to +38.7)

CI: confidence interval; TB: tuberculosis
Source: Nguyen et al. (2021) *(2)*.

Table 18.9

Comparison of survey design and survey TB case definitions in the 2007 and 2016 surveys in the Philippines

	2007 SURVEY	2016 SURVEY
Census	Sampling frame restricted 30 000 sample size 73 clusters initially selected 3 strata 23 clusters excluded Final 50 clusters	Nationwide 51 000 sample size 108 clusters initially selected 4 strata 2 clusters excluded Final 106 clusters
Sample	Aged ≥10 years Participants: 22 867 Participation rate: 90%	Aged ≥15 years and resident of cluster for 2 weeks or more Participants: 46 689 Participation rate: 76%
Screening	Conventional CXR No symptom screening (but those aged ≥20 years interviewed)	Digital CXR Symptom screening: Cough ≥2 weeks Haemoptysis
Diagnosis	>1 laboratory 3 sputum specimens	6 laboratories 1–3 sputum specimens
Smear	1 x smear FM with mercury lamp	1 × smear FM with LED lamp
Culture	Different culture methods Concentrated LJ method Ogawa and pooled LJ method[a] (specimen 1, specimen 2, specimen 3) Contamination rate: 11%	1 × Ogawa culture (specimen 2) Contamination rate: 2–6%
Xpert MTB/RIF	N/A	1 Xpert MTB/RIF (s1)
Survey TB case definition	**Bacteriologically confirmed TB** • Sputum smear-positive and/or culture-positive TB **Smear-positive TB** • Two sputum smear-positive specimens, or one smear-positive specimen associated with a positive culture or CXR reading **Culture-positive TB** • At least one sputum culture-positive specimen	**Bacteriologically confirmed TB** • At least one positive sputum Xpert MTB/RIF and/or culture *Mtb* **Smear-positive TB** • Bacteriologically confirmed TB with a smear-positive specimen

CXR: chest X-ray; FM: fluorescence microscopy; LED: light-emitting diode; LJ: Löwenstein-Jensen; *Mtb: Mycobacterium tuberculosis*; *n*: number; N/A: not applicable; TB: tuberculosis.

[a] initially concentrated LJ culture was done for the first 37 participants then due to the heavy workload for the laboratory, the method was changed to direct Ogawa and pooled concentrated LJ.

18.4.2 Example from the Philippines

The TB prevalence surveys implemented in the Philippines in 2007 and 2016 provide another example of how survey results can be compared *(5, 6)*.

Table 18.9 provides a comparison of the survey designs and case definitions used in the two surveys.

To compare the results of the two surveys, the analysis was restricted to participants meeting the following criteria.

1. Eligibility to participate criteria:
   — 2007 survey: aged ≥15 years (*n*=19 341); and
   — 2016 survey: aged ≥15 years and residency status (*n*=61 467).
2. Participation defined by:
   — 2007 survey: had a CXR (*n*=17 226); and
   — 2016 survey: had an interview +/– CXR (*n*=46 689).
3. Screening outcomes defined by CXR result only (i.e. symptom screening excluded).
4. Survey TB cases are defined by Ogawa culture result only (i.e. LJ excluded). In the 2007 survey, the second sputum specimen result was used; where that result was missing or contaminated, the first specimen result was used instead.

These criteria were used to conduct a restricted analysis of TB prevalence in 2007 and 2016. The prevalence of culture-positive TB was 463 per 100 000 (95% CI: 333–592) in 2007; this increased to 512 per 100 000 (95% CI: 420–603) in 2016. Similarly, smear-positive, culture positive TB was 193 per 100 000 (95% CI: 117–269) in 2007, and 286 per 100 000 (95% CI: 223–349) in 2016 (**Fig. 18.3**).

Fig. 18.3

Adjusted TB prevalence estimates using the restricted analysis and the recommended methods to estimate TB prevalence in the 2007 and 2016 surveys in the Philippines

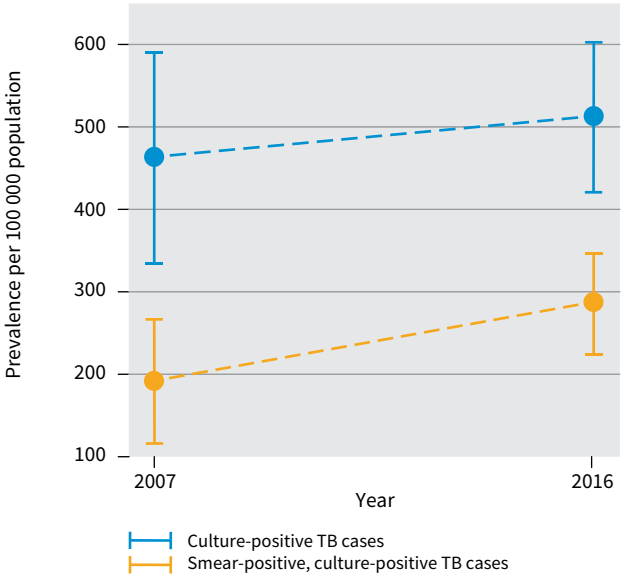
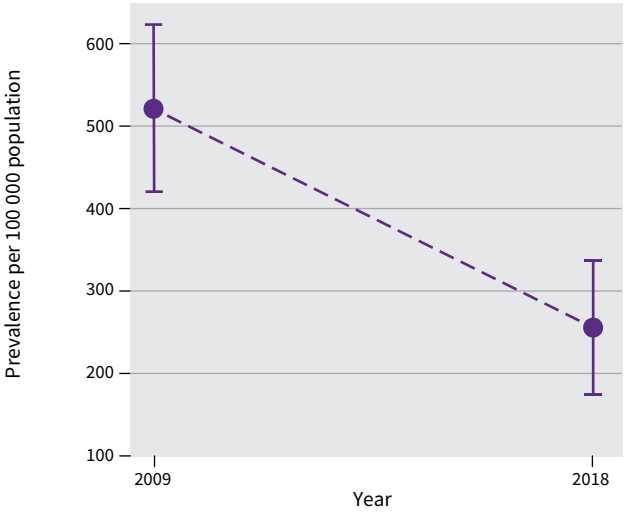


Fig. 18.4

Prevalence of bacteriologically confirmed pulmonary TB in adults (≥15 years) in the 2009–2010 and 2018 surveys in Myanmar



TB: tuberculosis.

18.4.3 Example from Myanmar

Myanmar's national TB programme (NTP) conducted a national TB prevalence survey in 2009–2010 and a repeat survey in 2018 *(7, 8)*. The first survey enumerated 57 607 adults (≥15 years) in 70 clusters, of whom 51 367 (89%) participated. The 2018 survey was implemented in 138 clusters selected from three strata (Yangon, region and state); 75 676 eligible adults were enumerated, of whom 66 480 (88%) participated. In both surveys, participants were screened by symptom questionnaire and CXR, as recommended in World Health Organization (WHO) guidance.

To compare changes in TB prevalence, the TB case definition for the 2018 survey was restricted to those with bacteriologically confirmed TB in the 70 clusters (selected randomly) in which culture testing was done for all individuals who screened positive (i.e. the same screening and testing algorithm as that used in the 2009–2010 survey).

In the 2018 survey, the prevalence of cases found to be culture positive using one specimen, as described above, was 256 (95% CI: 173–339) per 100 000 population. The reported prevalence in 2009–2010 was 520 (95% CI: 415–624) per 100 000 population (**Fig. 18.4**).

These findings showed a 51% reduction in the prevalence of culture-confirmed pulmonary TB. The average rate of decline in TB prevalence was 6.8% per year. Based on survey results, TB incidence was estimated to have fallen by 4.9% per year between 2009–2010 and 2018.

18.5 Planning for comparison of survey results at the stage of survey design: the example of Cambodia

A third national TB prevalence survey was implemented in Cambodia in 2023–2024, with the aim of assessing trends since the previous (second) survey in 2010–2011. The earlier survey used the previous WHO-recommended screening and diagnostic algorithm and associated case definitions. The 2023–2024 survey used the newly recommended screening and diagnostic algorithm (i.e. Option 1) that is described and explained in **Chapter 3** and the associated case definitions provided in **Chapter 4**. Although the survey had not been completed at the time of writing this chapter, it was the first example of a national survey that used the newly recommended algorithm (Option 1) and which also included additional diagnostic tests to enable direct comparisons with the previous survey.

18.5.1 National prevalence survey of 2010–2011 in Cambodia

The second national TB prevalence survey in Cambodia was implemented in 2010–2011 *(9–11)*. Briefly, there were 62 survey clusters in three strata (urban, rural and other), with a target cluster size of 640 individuals. The screening and diagnostic algorithm and associated case definition followed the WHO recommendations at that time. Culture was performed on two specimens (spot and morning) with direct preparation and using the solid media culture Ogawa.

A total of 68 087 individuals from 12 651 households

were enumerated in the survey census, of whom 40 423 (59%) were eligible and invited to participate. Of these, 37 417 (93%) did so. All participants were screened using CXR and an interview about symptoms. A total of 4780 participants (13%) were eligible for sputum examination, of whom 4612 (97%) submitted at least one sputum specimen and 4598 (96%) submitted two sputum specimens. A total of 314 bacteriologically confirmed pulmonary TB cases were identified. The prevalence of bacteriologically confirmed TB in participants aged 15 years and older was 831 (95% CI: 707–977) per 100 000 population.

18.5.2 National prevalence survey of 2023–2024 in Cambodia

The third national TB prevalence survey in Cambodia was implemented in 2023–2024. Briefly, a sample size of 44 520 eligible individuals aged 15 years and older was estimated to detect a 30% decline in culture-positive TB as compared to the 2010–2011 survey. There were a total 84 survey clusters in three strata (rural, urban other than Phnom Penh, Phnom Penh), with a target cluster size of 530 individuals. The screening and diagnostic algorithm used was Option 1 as described in **Chapter 3** i.e. screening using an interview about symptoms and CXR, two Xpert Ultra tests for anyone who screened positive, and confirmatory culture testing using liquid culture (MGIT) for all those with at least one positive Xpert Ultra result. The case definitions used were those provided in **Chapter 4**.

18.5.3 Use of solid-culture results to allow direct comparison of the two surveys

To enable comparison of TB prevalence estimates from the 2023–2024 survey with those of the 2010–2011 survey, the 2023–2024 survey included additional tests (compared with those defined in Option 1): solid culture (Ogawa media) for two additional samples (spot and morning), among individuals who screened positive and had at least one Xpert Ultra positive result.

Performing solid culture in the subgroup of those with an Xpert Ultra positive result would allow a direct comparison with the 2010–2011 survey, on the basis that Xpert Ultra testing is more sensitive than solid culture *(12)*. Therefore, it would pick up any individuals who would (with the exact same test sample) have a positive solid-culture result. In turn, the survey TB case definition in the 2023–2024 survey could be adapted to allow a fair comparison with the second (2010–2011) survey, and to provide a robust estimate of the true decline in TB prevalence between the second and the third surveys.

Results from the comparison of the two surveys were not available at the time of publication of this guidance; it will be added as supplementary online material once available.

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CHAPTER 19

Reporting and dissemination of survey findings

Once field operations from national tuberculosis (TB) prevalence surveys are completed, the focus shifts to finalizing the analysis, followed by reporting and disseminating the findings of the survey. Ideally, this is done through a survey report, which should be finalized soon after the completion of field operations. This is often a challenge for many survey teams. Prompt reporting and dissemination of results and their implications is critical to inform national policy and programmatic performance. It is also important to ensure survey integrity and transparency, particularly since it is most often public funds that support these activities.

This chapter outlines the main challenges associated with disseminating survey findings and provides guidance on reporting survey findings, including a suggested table of contents for the main survey report. Often, in addition to the main report (and often in advance of that report), a country will also have prepared summary reports and other summaries of key findings. This chapter also provides examples of dissemination of survey results, including presentation of the main survey results at different forums, at subnational, national and international level, and a list of publications related to national prevalence surveys since 2007.

19.1 Overview

A survey is not complete until the survey findings have been officially published. The minimum reporting and dissemination of survey findings includes:

- a main survey report (**Fig. 19.1**);
- a summary presentation for stakeholders; and
- at least one publication in a peer-reviewed journal.

Box 19.1 presents a suggested table of contents for the main survey report. Some sections – notably the introduction, objectives, methodology and annexes – can be written while the field operations are ongoing, since their content is largely based on the survey protocol. A minimum set of tables and figures to be prepared and included in the survey report is presented in **Chapter 17**. In addition to the main report, an option is to prepare a summary report that includes only the survey objectives, highlights of survey results and the main implications of the findings, with a limited number of key figures and tables.

Published reports of completed surveys can be used as templates, to speed up writing of the main survey report. **Box 19.2** provides an example of the experience of report writing and dissemination of survey findings from the survey in Ghana.

19.2 Main challenges associated with disseminating survey findings

One of the main challenges for surveys conducted since 2007 has been the long delay in disseminating survey findings and, in particular, in producing a main survey report *(3, 4, 5)* (**Fig. 19.2**).

Major challenges in report writing centred around finances, human resources and time management, for example:

- funding to hire people to write a survey report was limited or inadequate;
- the availability of dedicated human resources to write the report was not considered (e.g. contracts were not extended or staff left the survey for other employment after field operations were completed); and
- the time allowed for cleaning the data and analysing the results was inadequate or these tasks took longer than anticipated.

Other reasons given for delays in reporting and other observations about reporting and dissemination from the commissioned assessment are detailed in **Box 19.3**.

19.3 General guidance and best-practice examples

The following list offers general guidance for survey teams to address key challenges with the complete and timely reporting and dissemination of survey findings:

- A survey report is a key deliverable of any TB prevalence survey. Therefore, report writing is an integral part of the survey; as such, it should be planned accordingly (with sufficient human resources and funding). This includes identifying a report writing team during the survey, and assigning roles and responsibilities for report writing.
- Reporting and dissemination of survey findings should be an integral part of the survey budget and protocol, with a dedicated budget line for relevant activities, including a budget for staff time.

Fig. 19.1

Examples of national TB prevalence survey reports for (top left to bottom right) Bangladesh, 2015–2016; Ethiopia, 2010–2011; Indonesia, 2013–2014; Nepal, 2018–2019, Nigeria, 2012 and Zambia, 2013–2014

- Once field and laboratory operations are complete, staff should be available to conduct report writing before they move on to other duties; it is important to have people with sufficient dedicated time to complete analysis and report writing. At a minimum, the survey coordinator and data manager should be kept in position until the data are clean, and the analysis and reporting are complete. Staff are likely to be required for at least 6–12 months after field operations.
- Donors should ensure that the report is a specific deliverable of the grant agreement.
- Report writing should start (at least in part) during survey implementation (e.g. writing the introduction, objectives, methodology and other relevant sections). Publication of the survey protocol in a peer-reviewed journal can also contribute to the development and publication of the main report.
- Following the survey, a series of workshops should be organized during which data analysis can be conducted and report sections written. Such an approach could ensure timely reporting, ownership by the team and a budget to conduct these activities. WHO has organized workshops in the past for several countries, to facilitate the data analysis of surveys in a standardized manner and allow countries to share their experiences.
- The rich data generated from a TB prevalence survey could be used for academic accreditation of certain individuals from the survey team or other stakeholders. This can ensure that the analysis and write-up of results is timely and apt; for example:

BOX 19.1
SUGGESTED TABLE OF CONTENTS FOR THE MAIN SURVEY REPORT

Foreword
Acknowledgements
List of tables and figures
Acronyms
Executive summary

Introduction

- Background of TB in the country
- Justification for undertaking a prevalence survey
- Results of previous survey (if applicable)

Objectives

- Primary and secondary survey objectives

Methodology

- Survey management and organization
- Setting
- Sampling frame
- Sample size
- Sampling strategy
- Inclusion and exclusion criteria
- Procedures
- Laboratory management
- Data management, including data analysis plan
- Case definitions
- Ethical considerations
- Linkage to care
- Quality assurance procedures

Results

- Census
- Participation
- Screening
- Chest X-ray results (field and central reading)
- Laboratory results
- Previous TB history
- Survey cases
- Prevalence estimation
- Health care seeking behaviour
- HIV and other comorbidities
- Assessment of TB risk factors (optional)
- Clinical management
- Extrapolated TB prevalence in the general population, including all forms of TB

Discussion

- Trend of TB burden (in case of repeat survey)
- Programmatic implications
- Recommendations
- Strengths and limitations of the survey

References

Annexes

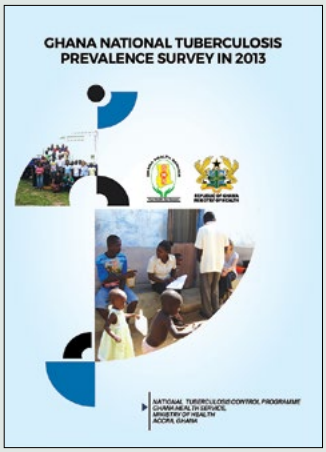
- Questionnaires
- List of all survey members, steering committee members and technical partners
- Funding breakdown
- Ethics committee approval
- Survey photos

BOX 19.2
COUNTRY EXPERIENCE OF DISSEMINATING FINDINGS FROM THE NATIONAL TB PREVALENCE SURVEY IN GHANA, 2013–2014

A lack of dedicated staff to write the main survey report delayed the release of the survey results until 2017, 3 years after completion of fieldwork in 2014. It was not until a dedicated person was employed by the national TB programme (NTP) that writing could start. However, even before the release of the main report, survey results had already been used to revise the burden estimates and inform the national TB strategic plan for 2014–2020. The main report presented survey findings in the sections that are suggested in the second edition of the World Health Organization (WHO) national TB prevalence survey guidance *(1)*. The report also presented the extrapolated TB prevalence among the general population (all forms of TB in the general population, including in children) by combining the survey and routine surveillance data. The report was disseminated as a workshop presentation, a hardcopy report and a publication in a peer-reviewed journal. A dissemination workshop for in-country stakeholders was held in March 2015, followed by a presentation of preliminary results at the Union World Conference on Lung Health in December 2015. After the report was finalized, 300 copies of the main survey report were printed and distributed to key stakeholders nationally (**Fig. B19.2.1**). An article on the main survey results was published in a peer-reviewed journal in 2020 *(2)*. Despite the delay in the public dissemination of survey results, the NTP did use the survey results to inform programmatic policy and decision-making.

Fig. B19.2.1

Main survey report of the national TB prevalence survey of Ghana, 2013–2014



BOX 19.3

ASSESSMENT OF NINE NATIONAL TB PREVALENCE SURVEYS CONDUCTED BETWEEN 2009 AND 2014: KEY FINDINGS ON SURVEY REPORTING AND DISSEMINATION OF RESULTS *(5)*

The development and execution of a detailed communication strategy should be built into all surveys. Such a strategy should include plans for report writing and wide dissemination, for identifying local advocates, and funds should be provided to facilitate more rapid generation of reports and dissemination of results to a broader audience. At present, most surveys lack a communication plan and many have experienced delays in publishing the final reports. These delays may lead to missed opportunities for advocacy, fundraising and use of findings by the broader TB community. Furthermore, these reports provide an important permanent record of key survey methods and findings. The use of a more standardized survey format could contribute to more rapid generation of reports, as is done in the Demographic and Health Surveys Program, where publication of comprehensive final reports typically occurs within 8–12 months of completion of data collection. As part of the survey process, a detailed plan should be developed that includes:

- details of the key recipients of the findings;
- the key survey messages conveyed to each group of recipients or different audiences; and
- when, where and how such communication should be operationalized.

The plan should be completed jointly with local stakeholders and advocacy groups, with expert consultation as needed. **The initial survey budget should include adequate funds to ensure that the communication plans are developed and executed, including writing of the final reports and dissemination activities.** Reasons for delays in analysis and reporting included:

- time for completion of quality control activities and resolution of discrepancies (analysis);
- delays in data cleaning and analysis (analysis);
- concerns over data quality (both reporting and analysis);
- lack of funding for writing and printing (reporting);
- staff turnover (both reporting and analysis);
- lack of skilled staff (both reporting and analysis);
- low priority for busy NTP managers (both reporting and analysis);
- factors such as political considerations (release of results); and
- other national priorities or emerging health emergencies (both reporting and analysis).

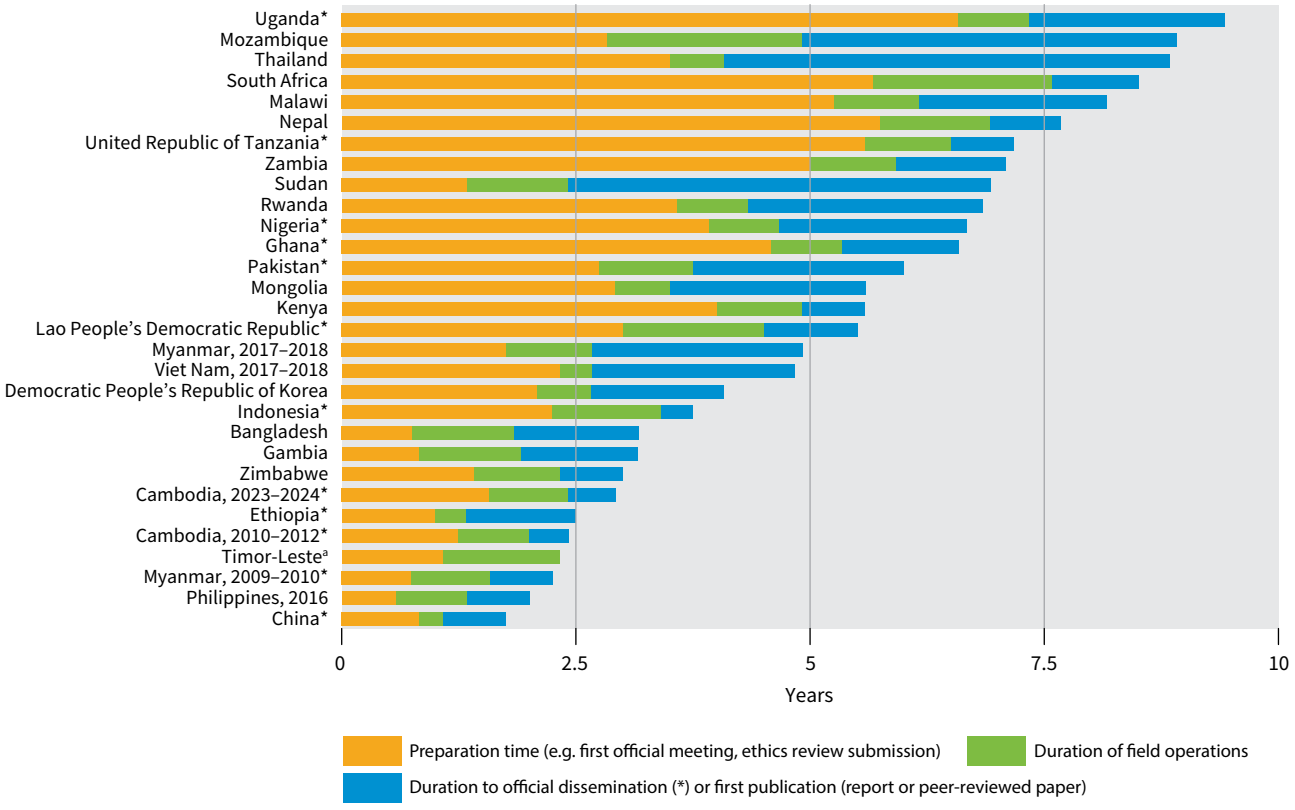
Within countries, data are not always systematically analysed, and secondary survey objectives and results (e.g. household socioeconomic-related information) are often left out of the final reports.

Also, there is often insufficient emphasis on advocacy and communication of the results. Most surveys lacked communication plans, and countries were not always prepared to deal with the implications of unexpected results (e.g. if the TB burden was higher or lower than expected).

Few, if any, of the NTPs appeared to have specifically developed a communication plan for the survey findings; this would include proactively identifying the groups with which they would communicate, the message, the timing and the modalities of communication, and reservation of funding for these activities.

Fig. 19.2

Approximate time taken (in years) for 30 national TB prevalence surveys to be completed: from survey preparation and field operations to official dissemination or first publication



[a] Results from the survey completed in Timor-Leste in 2023 are not yet published.

— both surveys in Viet Nam were part of the PhDs of NTP staff who were field team leaders in the survey (**Box 19.4**);
— in Zambia, in-depth analysis of survey findings was done by the survey coordinator as part of that person's post-doctorate studies, resulting in several published papers on health care seeking behaviour and non-tuberculous mycobacteria; and
— various institutions around the globe have requested data from the survey in South Africa for use in PhD projects (e.g. on use of chest X-ray images to evaluate computer-aided detection software and on subclinical – also known as asymptomatic – TB).

19.4 Approaches for disseminating survey findings

Dissemination of findings should be an integral part of a survey. When the main survey results are available, a series of dissemination meetings should be held according to a predefined plan. The first meeting should be a national consultation with key TB stakeholders, to receive guidance on further analysis and interpret the findings. South Africa held such a national consultation (**Box 19.5**), during which the main survey findings were presented and discussed. Another means of disseminating survey findings to the general public that has been used by some countries is leaflets summarizing survey results (**Fig. 19.3**).

Following a national consultation, survey findings should also be disseminated to lower administrative levels. This could be done as part of regular meetings (e.g. at regional or provincial level). Such opportunities can be used to further discuss the disaggregated results and lessons learned from the survey.

Finally, survey findings should be disseminated at the international level. This could be done with presentations and posters at international conferences, along with publications in peer-reviewed journals.

19.5 Publication of findings from past surveys

The minimum reporting and dissemination of survey findings includes a comprehensive survey report (electronic and printed copy), a summary presentation for stakeholders and at least one article in a peer-reviewed

BOX 19.4
DISSEMINATION OF TB PREVALENCE SURVEY FINDINGS IN VIET NAM, AS PART OF PHD THESES

A best-practice example for the dissemination of TB prevalence survey findings is that of Viet Nam. Both the first (2006–2007) and second (2017–2018) surveys led to the publication of PhD theses, including six articles in peer-reviewed journals *(6–11)* from the first survey and four articles from the second *(12–14, 29)*. Both PhD candidates were staff of the NTP's core team, and both served as field team leaders during their respective survey. Making a TB prevalence survey part of a PhD trajectory can serve several purposes:

- It raises the chance that the survey results will be published in peer-reviewed journals, because this is not only in the interests of the country and the technical assistance agency, but also in the personal interest of the PhD candidate.
- It increases the likelihood of timely publication of results. PhD trajectories typically take 3–4 years. If the trajectory includes writing of the survey protocol and field operations, timely publication of the results can be expected.
- It increases the chance that the survey quality is high, because the data collected form the basis of the PhD thesis.
- It ensures that there is one central person at the country level keeping oversight of everything that needs to happen after field operations have ended.
- It builds the capacity of in-country staff in conducting high-quality research.

The first PhD *(15)* was developed when the methodology for conducting and analysing TB prevalence surveys to estimate the burden of TB was still in development. The PhD also included health care seeking behaviour *(11)* as a theme, and a methodological paper on how to measure socioeconomic status by collecting data on only a small set of household indicators *(10)*. In addition to publications on TB burden *(9)* and screening *(7)*, a unique opportunity to conduct a concurrent tuberculin survey to estimate the prevalence of infection was undertaken *(8)*.

The second PhD *(16)* put more emphasis on how to measure bacteriologically confirmed TB, and used a relatively new analytical approach to conduct an in-depth analysis of the potential factors associated with the high male-to-female ratio in TB prevalence in Viet Nam *(13, 14, 29)*. This analysis was possible because additional data had been collected from a small part of the survey population using a nested case–control approach. This survey was also one of the first to examine the discordance between results of Xpert MTB/RIF assays and liquid culture in a survey context *(12)*.

journal. **Table 19.1** presents all reports and publications from countries that have completed a national TB prevalence survey, with respective references.

WHO has published a book to summarize the wealth of information available and to provide a structured summary – including objective, methods and key results – of the 25 national TB prevalence surveys conducted from 2007 to 2016 *(3)*. Papers summarizing findings from surveys in Asia *(20)* and Africa *(21)* have also been published.

Several overarching initiatives have combined the data from surveys in multiple countries to increase learning and synthesize lessons around TB screening *(22)*, sex differences in TB burden *(23)*, subclinical TB (also known as asymptomatic TB) *(24, 25)*, TB and comorbidities *(26, 27)*, and TB and household socio-economic status *(28)*.

BOX 19.5
DISSEMINATION OF FINDINGS FROM THE NATIONAL TB PREVALENCE SURVEY IN SOUTH AFRICA, 2018–2019

South Africa prepared both a short *(17)* and a long survey report (**Fig. B19.5.1**). Since the survey was the first of its kind for the country, there was a keen interest in the survey findings from all sectors. The short report was released two years after completion of the field survey activities (partly due to COVID-19 disruptions). This short report contained all pertinent results and recommendations from the survey and a limited number of figures and tables. It was uploaded to the official website of the Department of Health;[1] also, to enable wider dissemination, it was also uploaded to the websites of the three organizations primarily involved in the survey activities.

Fig. B19.5.1

Short and long survey reports of the national TB prevalence survey of South Africa, 2018–2019

In February 2021, South Africa hosted a virtual event at which the then Minister of Health, Dr Zweli Mkhize, officially released the national TB prevalence survey findings. The event was hosted virtually because of restrictions on travel and gatherings due to the coronavirus (COVID-19) pandemic. The event presented the survey's key findings, including the burden of TB disease, the impact of the COVID-19 pandemic on the prevalence of TB, and interventions to ensure continuity of care. The short survey report was publicly released just before the event. A panel of experts, including the survey's principal investigators from the South African Medical Research Council (SAMRC), the Human Sciences Research Council (HSRC) and the National Institute for Communicable Diseases (NICD), were present to support the minister in responding to questions about the survey from the attendees. A member of WHO (South Africa) was also invited to be part of the panel. The target audience for this webinar included the following:

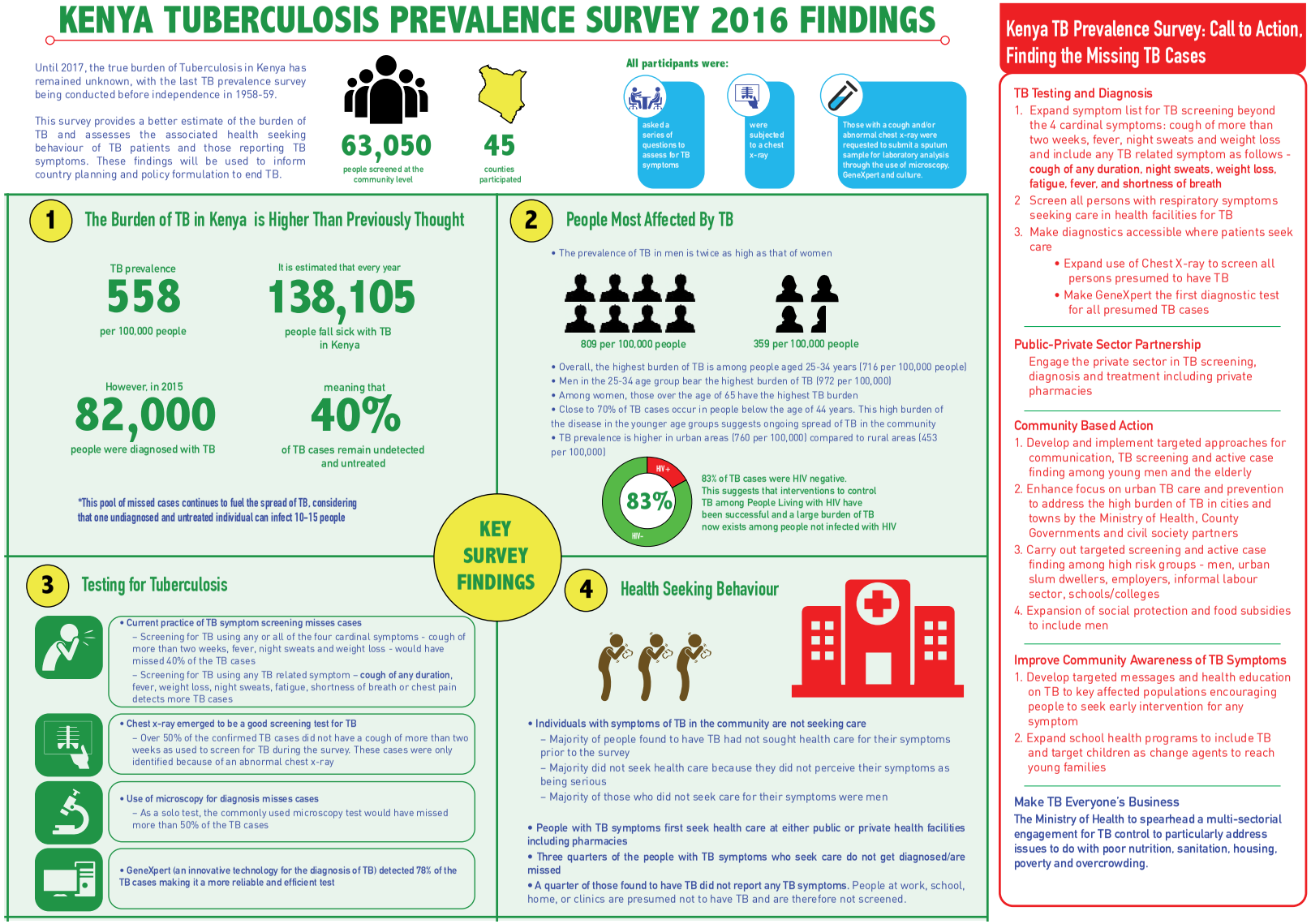
- national and provincial health department delegations;
- staff from HSRC, SAMRC, NICD and the National Health Laboratory Service;
- researchers from various research and educational institutions in the country;
- technical partners: University Research Co (URC), TB/HIV Care, Isibani Development Partners, Aquity Innovations NPC, Interactive Research and Development, and OHS Care;
- representatives from civil society organizations;
- health care workers;
- technical agencies: WHO and the Joint United Nations Programme on HIV/AIDS (UNAIDS);
- funding agencies: the United States Agency for International Development, Bill & Melinda Gates Foundation, and Global Fund to Fight AIDS, Tuberculosis and Malaria;
- South African National AIDS Council;
- members of the media; and
- members of the public.

The long report contained much more detail, additional analysis, more tables and figures, and was released three years after completion of survey activities. After both the reports were released, researchers, health workers, partners, civil society, media and other government departments engaged the survey team further on the findings contained in the reports. Following the official release of survey results, a journal article with the key findings from the survey was published in early 2021 *(18)*, and a more extensive article was published in 2022 *(19)*.

[1] The long report has not been uploaded to the website and is thus not publicly available.

Fig. 19.3

Leaflet summarizing the main findings from the national TB prevalence survey of Kenya, 2016



Source: National TB programme of Kenya, (reproduced with permission).

Table 19.1

Publications of findings from national TB prevalence surveys conducted using WHO-recommended methods since the first edition of the WHO guidance for national TB prevalence surveys, 2007[a]

COUNTRY	YEAR OF SURVEY(S)	PUBLICATIONS
Viet Nam	2006–2007; 2017–2018	*(6–16, 29, 30)*
Bangladesh	2007; 2015–2016	*(31, 32)*
Philippines	2007; 2016	*(33–36)*
Myanmar	2009–2010; 2017–2018	*(37–39)*
China	2010	*(40, 41)*
Cambodia	2010–2011	*(42–44)*
Ethiopia	2010–2011	*(45, 46)*
Lao People's Democratic Republic	2010–2011	*(47, 48)*
Pakistan	2010–2011	*(49, 50)*
Gambia	2012	*(51, 52)*
Nigeria	2012	*(53)*
Rwanda	2012	*(54, 55)*
Thailand	2012	*(56)*
United Republic of Tanzania	2012	*(57–60)*
Ghana	2013–2014	*(2, 61, 62)*
Indonesia	2013–2014	*(63)*
Malawi	2013–2014	*(64)*
Sudan	2013–2014	*(65)*
Zambia	2013–2014	*(66–73)*
Zimbabwe	2014	*(74–76)*
Mongolia	2014–2015	*(77)*
Uganda	2014–2015	*(78, 79)*
Democratic People's Republic of Korea	2015–2016	*(80)*
Kenya	2015–2016	*(81–84)*
Namibia	2018	*(85)*
Eswatini	2018–2019	*(86)*
Mozambique	2018–2019	*(87)*
Nepal	2018–2019	*(88)*
South Africa	2018–2019	*(17–19, 89, 90)*
Lesotho[b]	2019	*(91)*
India	2019–2020	*(92–94)*

TB: tuberculosis; WHO: World Health Organization.

[a] known publications as of May 2024.

[b] In accordance with the data access policy of the journal, Plos One, the survey team of Lesotho stored their data in an online data repository called Dryad: https://doi.org/10.5061/dryad.905qfttnq.

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CHAPTER 20

Use of survey results

As explained in **Chapter 1**, the main purpose of a national tuberculosis (TB) prevalence survey is to measure the burden of TB disease in the population at a given point in time, in countries where disease notification and vital registration systems cannot yet be relied upon and the burden of TB is estimated to be at a level that makes a survey feasible in terms of costs and logistics.[1] Repeat surveys (usually conducted after an interval of about 10 years) allow assessment of trends and progress towards targets for reductions in TB disease burden. Survey data also provide important insights that can help national TB programmes (NTPs) to identify ways to improve TB diagnosis and treatment, and to quantify and correct any underreporting of people diagnosed with TB through national disease surveillance systems *(1–4)*. In combination, survey results can be used for advocacy, resource mobilization, planning, policy development and programmatic action.

Beyond the national level, survey results have been essential for global and regional assessments of the burden of TB disease and progress towards globally agreed targets for reductions in this burden for many years. For example, results from national TB prevalence surveys in 17 countries were used to assess whether the 2015 targets for reductions in TB incidence, prevalence and mortality set in the World Health Organization (WHO) Stop TB Strategy and the United Nations (UN) Millennium Development Goals (MDGs) had been met *(5)*. In the 2024 edition of WHO's global TB report, survey results were the main source of data used to produce estimates of TB incidence for 29 countries that collectively accounted for 66% of the estimated global number of incident TB cases *(6)*, and for the associated assessment of progress towards the 2025 milestones of the WHO End TB Strategy (2016–2035) *(7)*. More repeat surveys will be needed between 2025 and 2030, to ensure robust assessment of trends in disease burden in the periods 2015–2025 and 2015–2030 and, in turn, assessment of the extent to which the 2025 milestones and 2030 targets of the End TB Strategy are achieved.

Collectively, survey results can also shed new light on TB epidemiology and related efforts to reduce the burden of TB disease. A recent example is the considerable proportion of people found to have bacteriologically confirmed pulmonary TB in a survey but who did not report or recognize symptoms during the survey screening process (this condition is now referred to as asymptomatic TB) *(8, 9)*.

This chapter covers three major topics: use of survey results for estimation of TB disease burden, other key results that can be generated from survey data and how they can be used, and country examples that illustrate how a range of survey results have been used in practice.

Section 20.1, which shows how survey results have been used for estimation of TB disease burden, includes:

- estimates of the national prevalence of bacteriologically confirmed pulmonary TB among people aged 15 years and older;
- estimates of the prevalence of TB disease for people of all ages and with all forms of TB, and how these have improved the precision and accuracy of the estimated level of TB prevalence compared with pre-survey estimates;
- assessment of national trends in disease burden; and
- estimates of the distribution of TB disease by age and sex.

Section 20.2 illustrates other key results that can be generated from survey data and how they can be used. Such results include evidence about case-detection and reporting gaps and how these vary by age and sex, the symptomatic status of people with TB disease in the community, the health care seeking behaviour of people with TB disease, the prevalence of HIV among people with TB, access to care according to HIV status and underreporting of people diagnosed with TB.

Section 20.3 showcases country examples that illustrate how a range of survey results have been used in practice, from seven countries: Cambodia, Ethiopia, Ghana, Myanmar, the Philippines, South Africa and Viet Nam. More detailed syntheses of survey results and how these have been used are available elsewhere *(1–3)*.

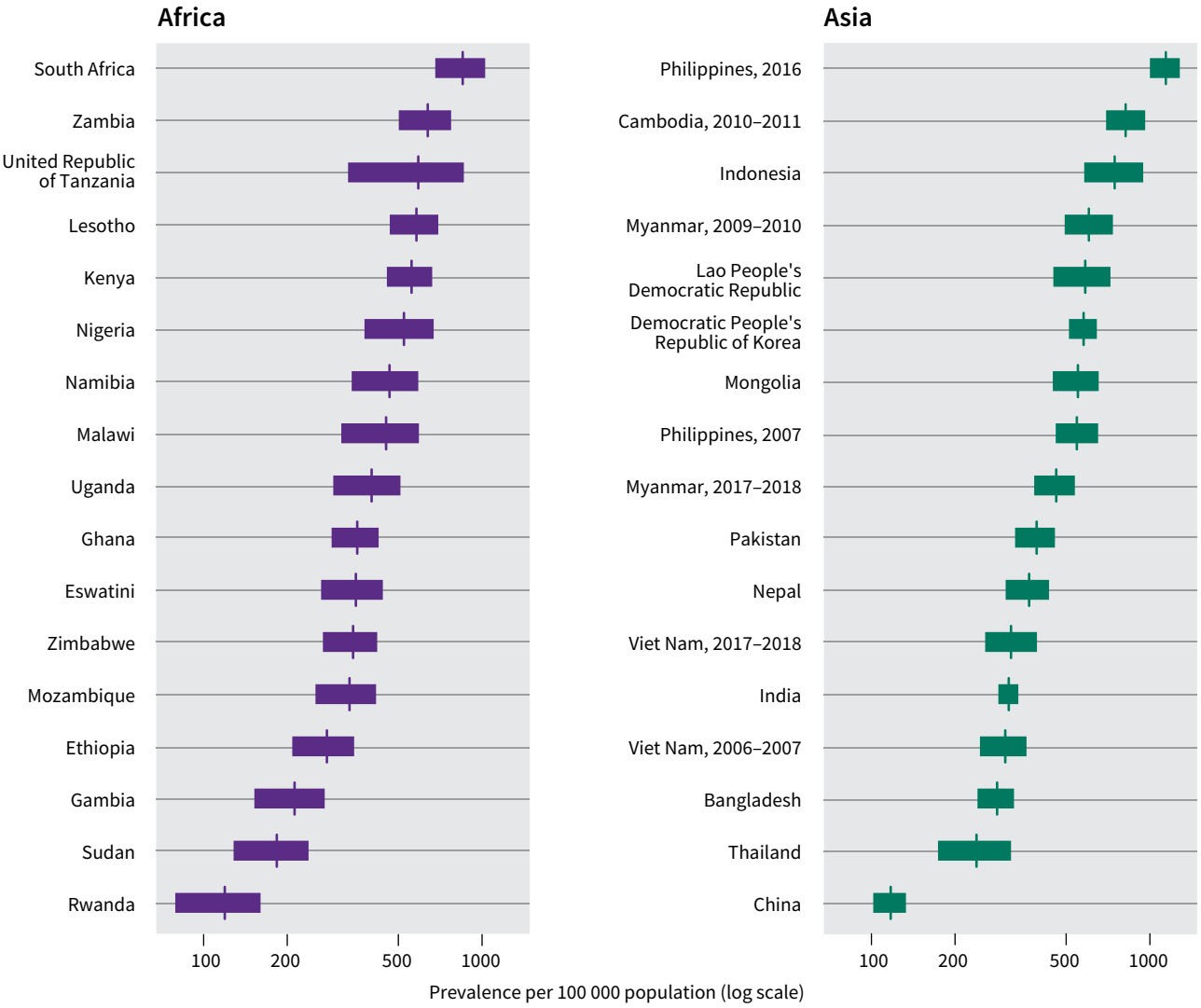
20.1 Estimates of TB disease burden

Surveys provide national estimates of the prevalence of TB disease that are often more accurate and precise than those available in the absence of a survey. They also provide evidence of how the burden of TB disease is distributed by age and sex.

[1] This is an estimated prevalence of bacteriologically confirmed pulmonary TB among those aged 15 years and older of 250 per 100 000 population in the last survey, or an estimated incidence of 150 per 100 000 population (all ages, all forms of TB). See **Table 1.1** in **Chapter 1**.

Fig. 20.1

Estimates of the prevalence of bacteriologically confirmed pulmonary TB (≥15 years) in surveys implemented, 2007–2021[a]



TB: tuberculosis.

[a] The measured prevalence of bacteriologically confirmed pulmonary TB was higher in the 2017 survey in Viet Nam compared with 2007. However, this was due to more diagnostic testing with more sensitive methods. When results based on the same method were compared, prevalence was estimated to have fallen between 2007 and 2017 (see also **Section 20.3** below). At the time this guidance was published, results from surveys in Cambodia (2023–2024) and Timor-Leste (2022–2023) were being finalized.

20.1.1 National estimates of the prevalence of TB disease

National surveys completed between 2007 and 2021 have shown that the estimated prevalence of bacteriologically confirmed pulmonary TB per 100 000 population aged 15 years and over was high in many countries, but there was also considerable variation (**Fig. 20.1**). In African countries, prevalence ranged from 119 (95% confidence interval [CI]: 79–160) per 100 000 population in Rwanda (2012) to 852 (95% CI: 679–1026) per 100 000 population in South Africa (in 2017). In Asian countries, prevalence ranged from 119 (95% CI: 103–135) per 100 000 population in China (2010) to 1159 (95% CI: 1016–1301) per 100 000 population in the Philippines (2016).

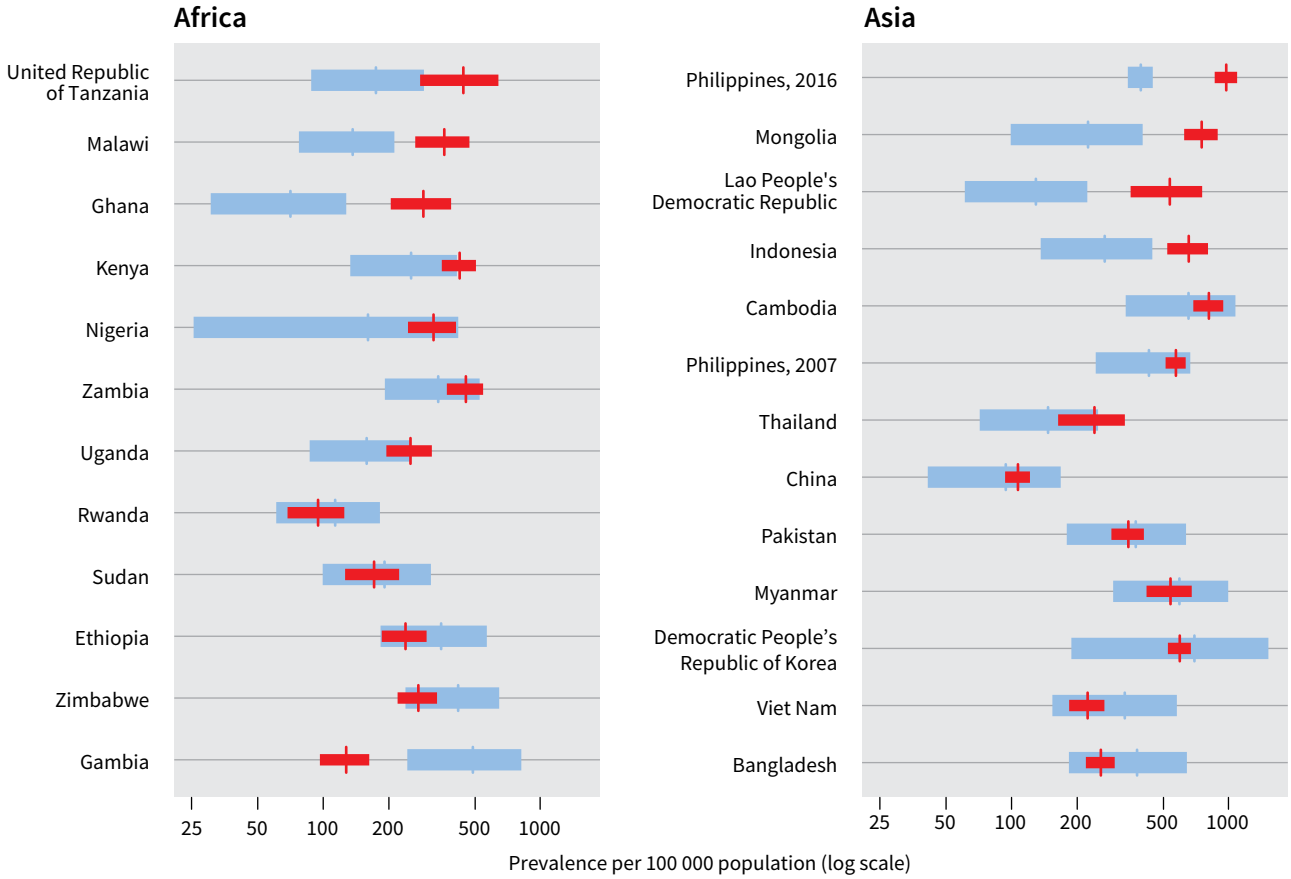
20.1.2 Improved precision and accuracy of national estimates of TB disease burden

Survey results can be used to produce estimates of the national prevalence of TB disease among all age groups, and for all forms of TB. These estimates are more accurate and precise (i.e. with narrower uncertainty intervals) than pre-survey estimates (**Fig. 20.2**).[1] Best estimates of TB prevalence based on survey results were higher than pre-survey estimates in 15 countries (most noticeably in Ghana, Indonesia, the Lao People's Democratic Republic, Malawi, Mongolia, the Philippines [2016] and the United Republic of Tanzania) and lower

[1] Estimates are not shown for later surveys, because WHO stopped publishing estimates of TB prevalence in 2016.

Fig. 20.2

Comparison of prevalence estimates (all ages, all forms of TB) (blue) from 25 surveys compared with pre-survey estimates (red), for national TB prevalence surveys implemented, 2007–2016[a]



TB: tuberculosis.

[a] Countries are listed in decreasing order according to the before–after difference.

in 10 countries (most noticeably in Ethiopia, the Gambia and Zimbabwe).

National estimates of TB prevalence (for all ages and all forms of TB) can be used to estimate TB incidence in the year of the survey.[1] For example, in the 2024 edition of WHO's global TB report, data from 31 prevalence surveys were used as a key input to estimates of TB incidence in the period 2010–2023 for 29 countries, which collectively accounted for 66% of the global number of incident cases in 2023 *(6)*.

20.1.3 Trends in TB disease burden at national level

When new survey data become available, it is possible to use those data alongside other sources of data (e.g. previous national TB prevalence surveys and time series of TB case notifications) to assess and update time series of estimates of TB disease burden.

Since 2016, the focus has been on using prevalence survey data to produce estimates of TB incidence, because this is the main indicator (alongside the number of deaths caused by TB) for which milestones and targets for reductions in TB disease burden have been set in the WHO End TB Strategy and the UN Sustainable Development Goals (SDGs) *(11)*.[2]

Examples of estimates of trends in TB incidence before and after a survey was implemented are shown for four countries in **Fig. 20.3**: Lesotho, Myanmar, South Africa and Viet Nam.

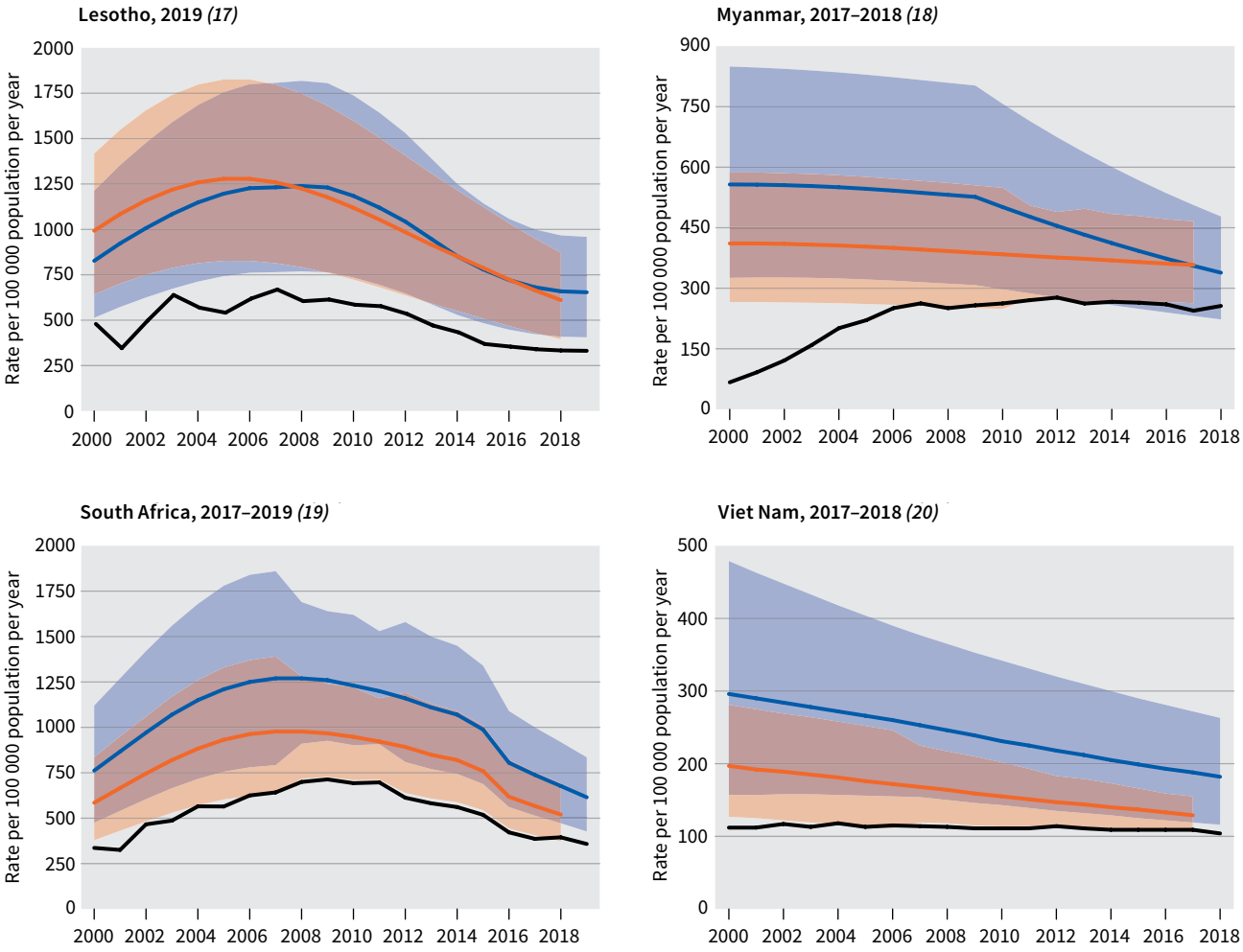
Updated estimates of TB disease burden are a crucial input to national TB epidemiological and programme reviews, the development of national strategic plans (including to inform the prioritization of programmatic activities), and associated advocacy and resource mobilization efforts (from both domestic and international donor sources of funding) *(12–16)*. Country examples are provided in **Section 20.3**.

[1] Methods used to estimate TB incidence using results from prevalence surveys are described elsewhere *(10)*.

[2] The target related to TB in the SDGs is to "end the epidemic" (this is part of Target 3.3). The indicator for assessment of progress is the TB incidence rate (new cases per 100 000 population per year).

Fig. 20.3

Estimated trends in TB incidence before (orange) and after (blue) a national TB prevalence survey was conducted in Lesotho, Myanmar, South Africa and Viet Nam. For comparison, the **black** solid line shows the case notification rate.



TB: tuberculosis.

20.1.4 The distribution of TB disease burden by age

Surveys provide reliable evidence about how the burden of TB disease is distributed by age and sex.

Results from 34 surveys implemented between 2007 and 2021 are shown in **Fig. 20.4** and **Fig. 20.5**. In Asian countries, cases were generally concentrated in older age groups (**Fig. 20.4**), but the pattern was more mixed in African countries (**Fig. 20.5**).

As transmission declines, more incident cases arise from old (remote) rather than recent infection. Therefore, a pattern in which prevalence increases with age suggests that transmission is falling. It is encouraging that prevalence surveys indicated that transmission is potentially declining in many Asian countries and in several African countries (e.g. Ghana, Lesotho, Malawi, Mozambique, Rwanda and the United Republic of Tanzania). Elsewhere, surveys suggested considerable community transmission; peaks in many African countries in the age groups 35–44 or 45–54 years also reflect the impact of the HIV epidemic.

20.1.5 The distribution of TB disease burden by sex

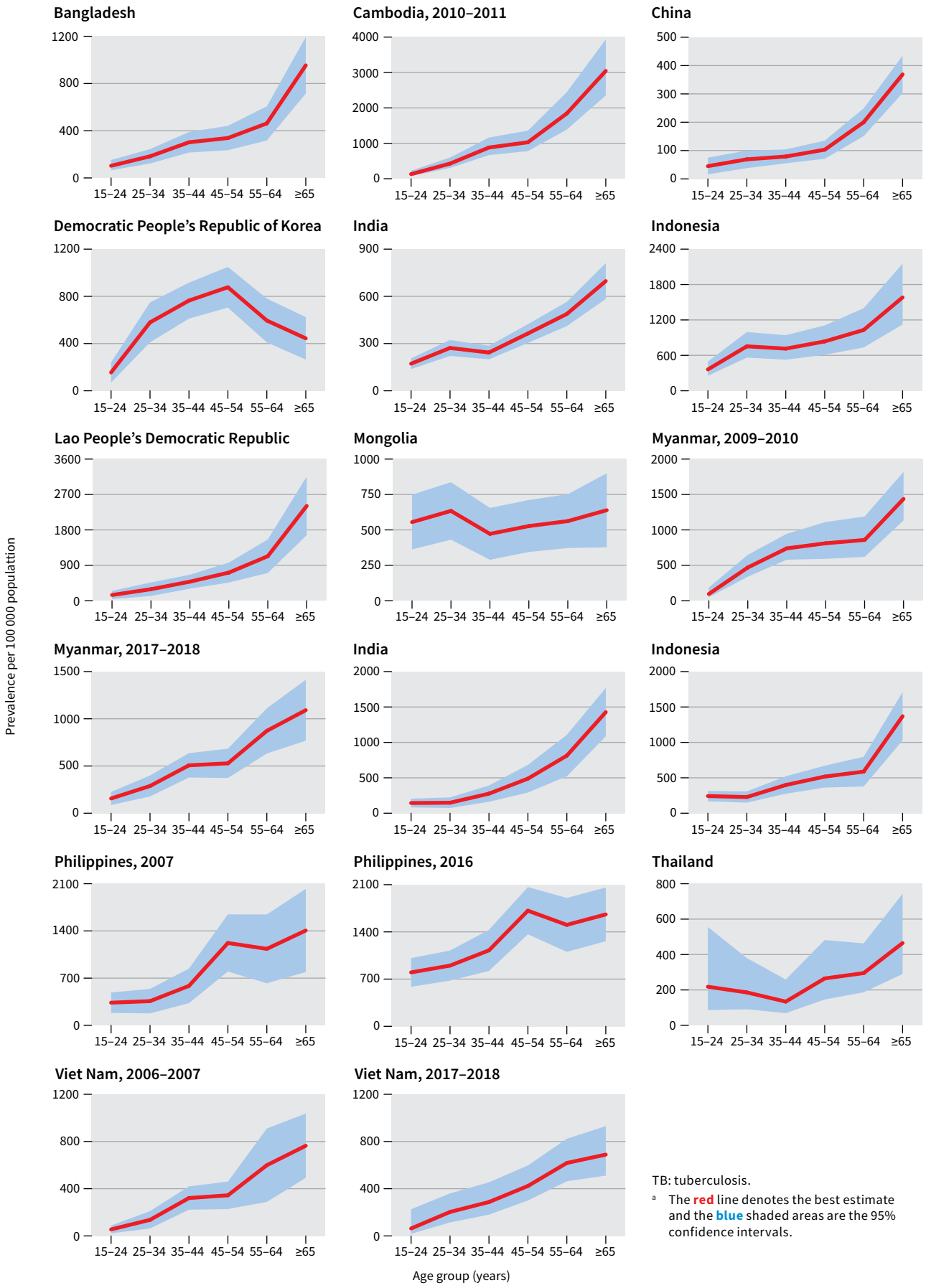
A striking finding across all surveys implemented in recent years was the much higher burden of TB disease in men than in women (**Fig. 20.6**). The male to female (M:F) ratio of bacteriologically confirmed pulmonary cases in surveys completed in 2007–2021 ranged from 1.2 (in Ethiopia) to 4.5 (in Viet Nam); in most countries it was in the range 2–4. These findings mean that men typically account for about 66–75% of the burden of TB disease in adults.[1]

The higher prevalence of risk factors in men than in

[1] A systematic review by Horton et al. *(21)* also concluded that TB prevalence is significantly higher among men than women in low- and middle-income countries, with strong evidence that men are disadvantaged in seeking and accessing TB care in many settings.

Fig. 20.4

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for national TB prevalence surveys implemented in Asian countries, 2007–2021[a]

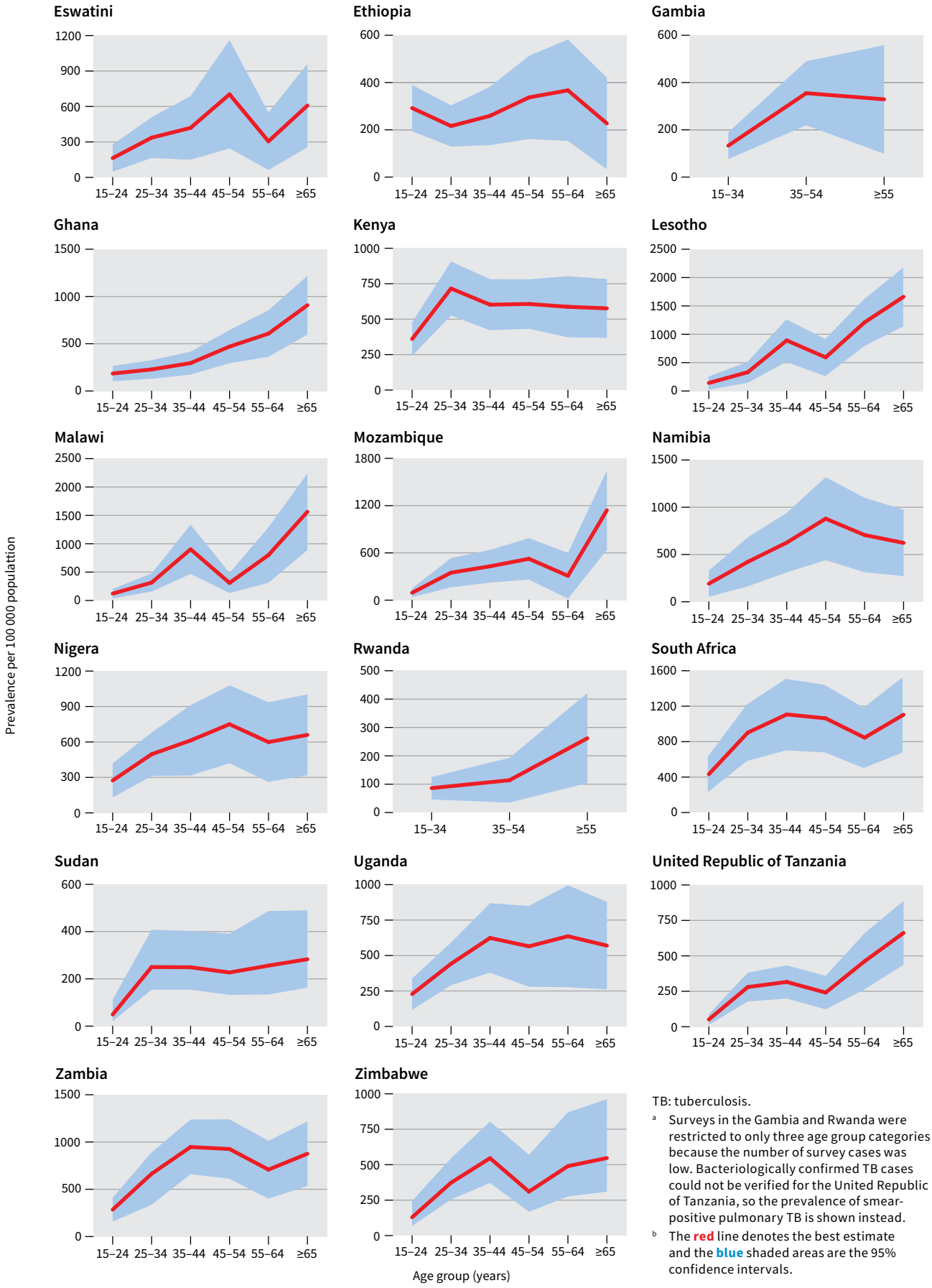


TB: tuberculosis.

[a] The **red** line denotes the best estimate and the **blue** shaded areas are the 95% confidence intervals.

Fig. 20.5

Estimated age-specific prevalence of bacteriologically confirmed pulmonary TB for national TB prevalence surveys implemented in African countries,[a] 2010–2019[b]



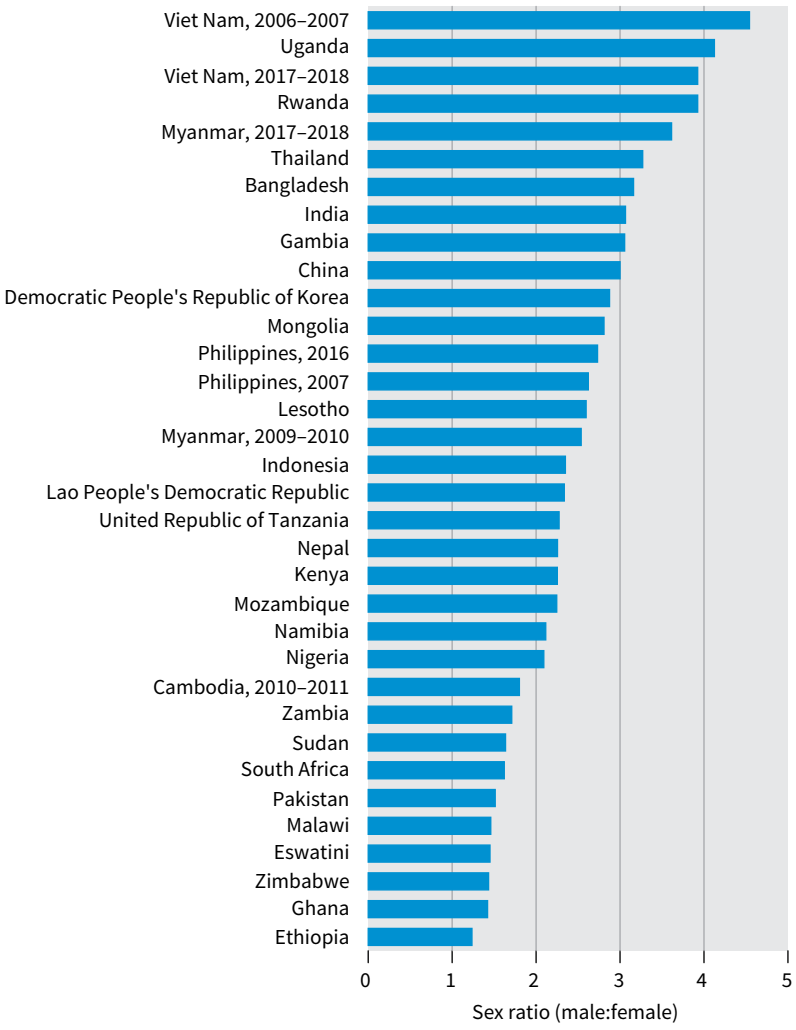
TB: tuberculosis.

[a] Surveys in the Gambia and Rwanda were restricted to only three age group categories because the number of survey cases was low. Bacteriologically confirmed TB cases could not be verified for the United Republic of Tanzania, so the prevalence of smear-positive pulmonary TB is shown instead.

[b] The **red** line denotes the best estimate and the **blue** shaded areas are the 95% confidence intervals.

Fig. 20.6

The M:F ratio of bacteriologically confirmed TB cases detected in national TB prevalence surveys implemented, 2007–2021[a]



M:F: male to female; TB: tuberculosis.

[a] Owing to laboratory challenges during the survey in the United Republic of Tanzania, it was only possible to directly estimate the prevalence of smear-positive (as opposed to bacteriologically confirmed) pulmonary TB.

women (e.g. smoking and harmful use of alcohol) contributes to the difference in burden by sex.

20.2 Results beyond estimates of TB disease burden

Results from national TB prevalence surveys are not restricted to estimates of TB disease burden. When analysed alongside TB case notification data, survey data allow assessment of case-detection gaps and how these vary by sex.[1] All surveys implemented according to methods recommended in WHO guidance provide evidence about the symptomatic status of people with undiagnosed, bacteriologically positive TB in the community (because these methods include screening based on symptoms and chest X-ray [CXR]).[2] A large subset of surveys in both Asian and African countries have included collection of data about health care seeking behaviour by people with TB or people who reported TB-related symptoms; such data can help to inform actions needed to ensure prompt diagnosis and treatment. A large subset of surveys in African countries included collection of data about HIV status, which provided evidence about the prevalence of HIV among people with TB and allowed comparison of access to care according to HIV status. One survey included both collection of data about people on TB treatment at the time of the survey and analysis of whether they had been reported as a TB case within the national TB surveillance system, to assess underreporting of people diagnosed with TB.

This section provides a summary of results for each of these topics that are available from surveys implemented between 2007 and 2021, along with examples of how findings have been used in practice at the country or global level.

20.2.1 Case-detection and reporting gaps

Ratios of prevalence to notification (P:N, expressed in years) can be used to assess case-detection or reporting gaps.[3,4] The numerator (P) is the prevalence of bacteriologically confirmed pulmonary TB per 100 000 population, as measured in a prevalence survey. The denominator (N) is the case notification rate of bacteriologically confirmed pulmonary TB per 100 000 population in the year of the survey. This indicator can be disaggregated by sex and, in theory, it can also be disaggregated by age group, but the numbers of cases in some age groups may mean that such analysis is not particularly useful.

The higher the P:N ratio, the longer the time taken for a prevalent case to be notified to the NTP. Some cas-

[1] In theory, case-detection gaps by age group can also be assessed *(3)*. However, the number of cases in some age groups is often too small to make such analysis useful; for this reason, such results are not included in this chapter.

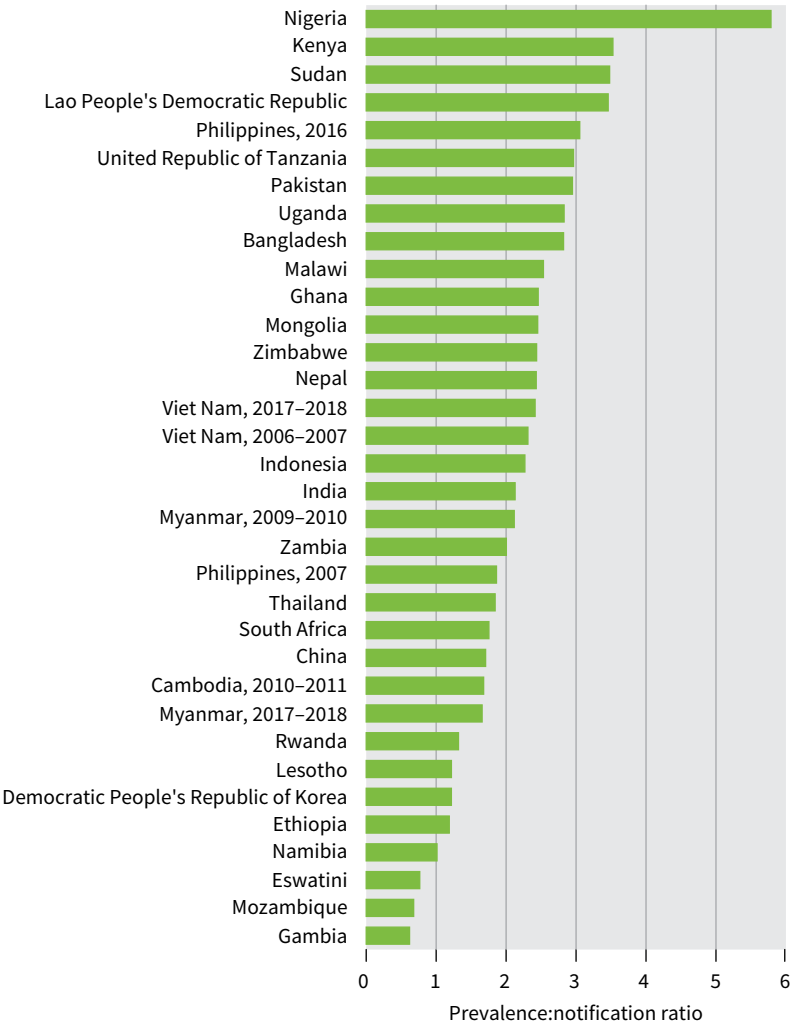
[2] As discussed in **Chapter 3** and as set out in previous guidance *(4)*.

[3] The inverse of this indicator (referred to as the patient diagnostic rate) was first described in 2004 *(22)*.

[4] The indicator is most useful for assessing relative gaps, comparing across countries and between particular groups (e.g. men versus women). Other things being equal, the P:N ratio will be higher when the screening and diagnostic methods used in surveys are more sensitive than those used in routine services.

Fig. 20.7

The P:N ratio in countries that implemented national TB prevalence surveys in the period 2007–2021



P:N: prevalence to notification; TB: tuberculosis.

es may exit the pool of prevalent cases without being notified; for example, because they self-cure or die, or because they are detected and treated by providers not linked to official reporting systems.

Surveys implemented between 2007 and 2021 showed considerable variation among countries in terms of the overall P:N ratio (**Fig. 20.7**). The consistent finding in most surveys (with only 3 exceptions) was a much higher P:N ratio among men than in women (**Fig. 20.8**). The combination of a higher disease burden in men (**Fig. 20.6**) and larger gaps in detection and reporting has demonstrated a need for multifaceted strategies to improve access and use of health services among men.[1]

Some countries have attempted to address the issues of a higher disease burden in men and larger gaps in detection and reporting. Following the prevalence survey in Ghana, one of the actions included in the national strategic plan for TB in the period 2015–2020 was the initiation of active TB screening in hospitals and targeted TB screening, especially among men in older age groups (see also **Section 20.3.1**). Following the survey in Myanmar, policies were adapted to targeted screening activities to find and treat men with TB, especially in areas where men predominate (e.g. construction, mining, migrant worker communities and prisons), and conducting screening into the evenings and over the weekends. Similarly, in the Philippines, policies were developed to undertake active case-finding in male-dominated occupations and workplaces (e.g. taxi drivers and construction sites), in addition to the development of male-specific communication materials and the opening of TB clinics outside of regular office hours.

In Nigeria, the country with the highest P:N ratio (**Fig. 20.7**, **Fig. 20.8**), the survey provided clear evidence of the need to improve access to TB diagnosis and treatment, especially in the context that many of those found to have TB during the survey already had symptoms (**Fig. 20.9**). Subsequently, efforts were made to improve access to TB diagnostic services, which were intensified over time. Since 2019, the number of TB case notifications has increased substantially, suggesting major improvements in access to TB care *(24, 25)*. Greater efforts to collect and analyse notification data disaggregated by sex has further assisted their understanding of the gender gap.

20.2.2 Symptomatic status of people with TB disease in the community

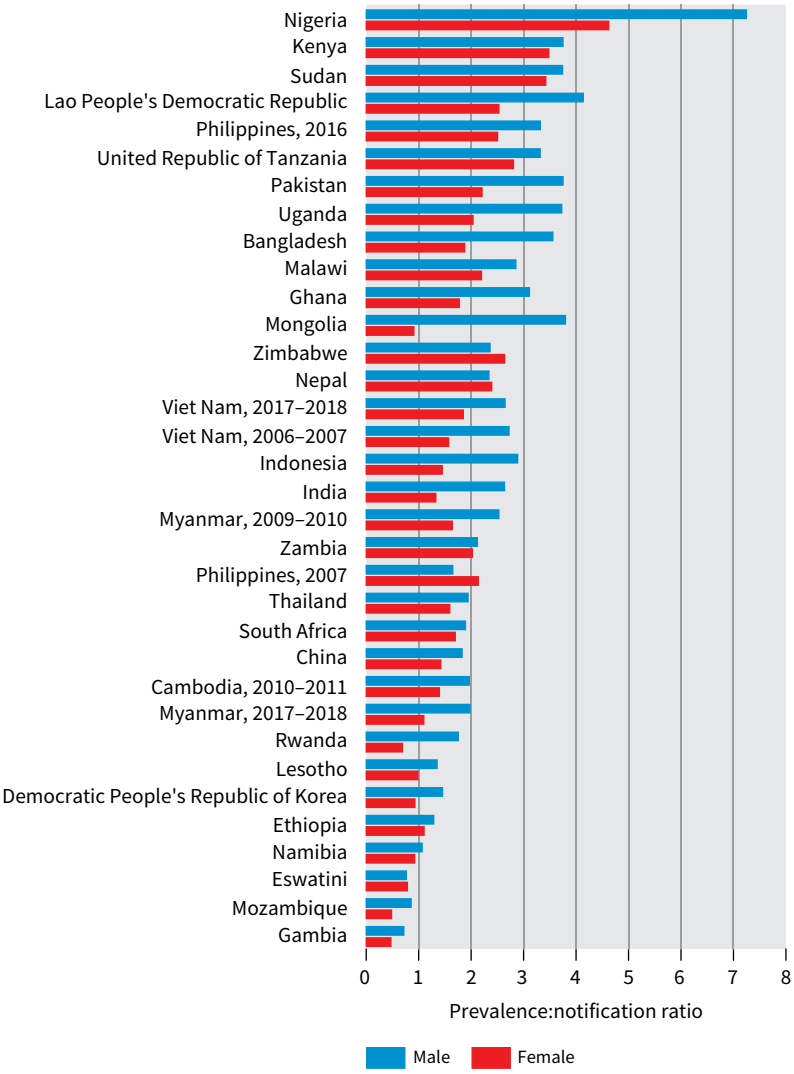
The screening algorithm of a prevalence survey provides information on the symptomatic status of people diagnosed with TB during the survey. A large proportion of people with bacteriologically confirmed pulmonary TB did not report having any of the screening symptoms at the time of the survey[2] and were only tested for TB

[1] This is consistent with findings reported elsewhere *(21, 23)*.

[2] These symptoms generally include cough (either a cough of any duration, or one that has lasted for at least 2 weeks); productive cough with sputum production; or haemoptysis, fever, chest pain or weight loss over the past month (see the country-specific publications listed in **Chapter 19**).

Fig. 20.8

The P:N ratio disaggregated by sex, for countries that implemented national TB prevalence surveys in the period 2007–2021



P:N: prevalence to notification; TB: tuberculosis.

based on CXR results.[1] This proportion was higher in Asian countries than in African countries, and varied from 30% in Malawi to 86% in Myanmar (**Fig. 20.9**).

These findings have highlighted the importance of using CXR in TB case-finding. As a result, many countries have scaled up X-ray use for active case-finding and outpatient screening activities. Examples include Cambodia, Ghana and South Africa (see also **Section 20.3**). Survey data on CXR screening have also contributed to the evidence base for WHO guidelines on TB screening guidance *(26, 27)*.

Survey data that revealed the large share of people with undiagnosed TB who did not report symptoms drew considerable attention to "asymptomatic TB",[2] including its role in community-based transmission, implications for WHO guidelines on TB prevention, diagnosis and treatment, and research priorities (**Box 20.1**).

20.2.3 Health care seeking behaviour

Prevalence surveys can provide information about the health care seeking behaviour of people found to have TB as well as those who meet TB symptom screening criteria. In turn, this information can help to identify ways to improve health services, including through updated screening and case-finding policies, to ensure more prompt TB diagnosis and treatment (see also **Box 6.1** in **Chapter 6**).

A large proportion of participants who reported symptoms that met survey screening criteria had not sought care (**Fig. 20.10**). Some participants thought that their symptoms were not serious enough to warrant attention, and others faced financial, geographical or stigma-related barriers to accessing care *(41–44)*. Typically, those with a comorbidity (e.g. HIV or diabetes) tended to seek care for their symptoms more than those who were not already being treated for an underlying condition (see also **Section 20.2.4**).

The health facility where people with symptoms first sought care varied by country (**Fig. 20.11**). Among participants with symptoms, around one third initially sought care at a public health facility *(1, 2)*. Going to private health facilities and pharmacies was generally more common in Asia than in Africa. Examples of in-depth indicators that could be obtained from survey data are provided in **Annex 20.1**.

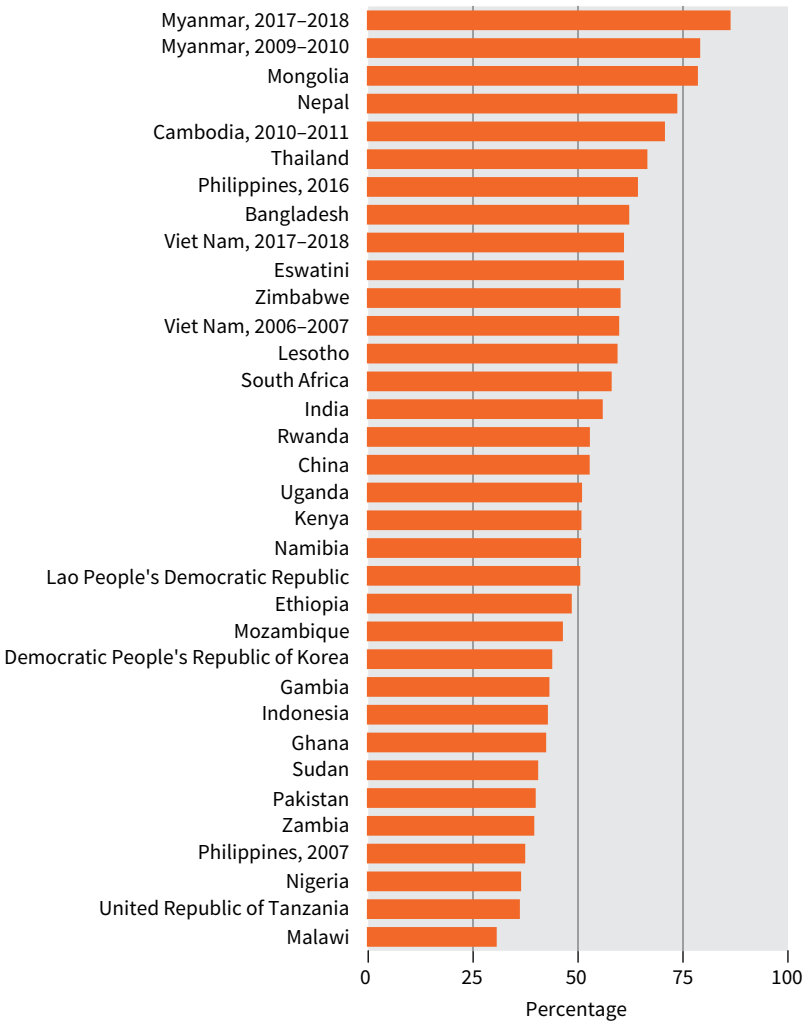
Many participants diagnosed with TB during surveys had previously sought care but had not been diagnosed. This showed that TB diagnostic services needed improvement, especially in the health facilities where people are most likely to initially seek care, and that health workers needed to be better trained to act on TB symptoms reported by their patients. Ghana is one example of a country that took action to address such findings, including by engaging pharmacies to conduct

[1] Surveys cut the time to diagnosis by finding people with TB disease before they develop symptoms or before they seek care, and finding people who had sought care but were not diagnosed (see also **Section 20.3**).

[2] In journal articles and other literature published before the end of 2024, this was referred to as "subclinical TB". Following a WHO consultation on subclinical TB held in October 2024 *(8)*, it was agreed to replace the term "subclinical TB" with "asymptomatic TB".

Fig. 20.9

Proportion of people detected with bacteriologically confirmed pulmonary TB in national TB prevalence surveys who did not report symptoms during screening, 2007–2021



TB: tuberculosis.

screening and referral of people with presumptive TB, expanding community interventions to improve health care seeking behaviour and sensitizing health workers to increase their awareness of TB-related signs and symptoms (see also **Section 20.3.1**). A second example is Cambodia. Following the first survey in 2002, actions taken included strengthening diagnostic capacity for outpatients with respiratory symptoms, more extensive use of CXR for people with any respiratory symptom, a referral system for people with smear-negative presumptive TB to a health facility equipped to carry out CXRs and the replacement of smear microscopy with rapid molecular tests (see also **Section 20.3.2**).

Data on health care seeking behaviour can also be used to help with the prioritization of interventions to reduce losses along the "cascade of care", and can be used on an ongoing basis to track programmatic efforts *(12)* (**Annex 20.2**).

20.2.4 Prevalence of HIV among people with TB and access to care according to HIV status

At the end of 2024, data on the prevalence of HIV among people with TB who were identified during a national prevalence survey were available from 11 countries in the WHO African Region. The prevalence of TB (per 100 000 population) was lower among survey cases than the prevalence of HIV among people who had been diagnosed and notified as a TB case (see **Fig. 20.12**). This may indicate better case detection among people living with HIV than for those without HIV, possibly due to greater investments in HIV programmes (e.g. such investment has enabled a high coverage of screening for TB among people living with HIV). It may also reflect earlier health care seeking behaviour among people living with HIV.

HIV testing is recommended in all national TB prevalence surveys, especially in countries with a high prevalence of HIV (**Chapter 10**).

20.2.5 Underreporting of people diagnosed with TB

Surveys include the collection of data for people who had already been diagnosed with TB at the time of the survey and were on TB treatment. These data provide an opportunity to assess the level of underreporting of people diagnosed with TB to the national TB surveillance system, and whether any corrective actions to ensure more complete reporting are needed.

Indonesia is a good example of a country that identified a need to address underreporting of people diagnosed with TB through a national TB prevalence survey. Following completion of the survey in 2013–2014, a follow-on study was conducted to assess whether there was a record in the national TB surveillance system for survey participants who reported that they were currently on anti-TB treatment (including those still bacteriologically positive) *(45)*. The study found that only 19% of these survey participants were included in the TB electronic registration (SITT) (**Table 20.1**). Although it was recognized that there may have been delays in data entry and reporting to SITT, and that more people would have been reported and included within local TB registers, the study suggested that there was a substantial amount of underreporting of people diagnosed with

BOX 20.1
NATIONAL TB PREVALENCE SURVEYS AND ASYMPTOMATIC TB

Data from national TB prevalence surveys that demonstrated the large share of people diagnosed with TB who did not report symptoms generated considerable interest and further analysis; WHO played a key role in liaising with countries to facilitate access to detailed survey datasets that were requested by researchers.

Using data from 12 surveys, Stuck et al. *(28)* estimated that up to 83% of adults in the community with culture-confirmed TB reported no cough persisting for 2 or more weeks, up to 63% reported no cough of any duration, and up to 28% reported no TB-suggestive symptoms (i.e. cough, fever, chest pain, night sweats or weight loss). TB without persistent cough or any cough was significantly more frequent among women than among men. The study also estimated that among people with smear-positive pulmonary TB, the proportion without persistent cough was as high as 29% and the proportion with no cough was as high as 23%. These results have provided further illustration of the prevalence of asymptomatic TB and its contribution to the burden of TB overall.

A re-analysis of data from national prevalence and tuberculin surveys implemented in Viet Nam in 2007 by Nguyen et al. *(29)* was used to assess the contribution of asymptomatic TB to transmission. This was done by assessing the relationship between the clinical status of people with TB and the tuberculin skin test (TST) positivity status of children aged 6–14 years, at household level. Results indicated a significantly increased risk of TST positivity in children living with people who had smear-positive pulmonary TB with 2 or more weeks of cough, compared with those living with people without TB (adjusted risk ratio [aRR]: 3.04; 95% CI: 2.00–4.63) and with those living with people who had TB but with no chronic cough (aRR: 2.26; 95% CI: 1.03–4.96).

Emery et al. *(30)* analysed data from 15 national TB prevalence surveys across Africa and Asia to assess the share of global transmission of TB that could be attributed to asymptomatic TB: the estimate was about 68% (27–92%, 95% prediction interval [PrI]).

Hamada et al. *(31, 32)* conducted an individual participant data meta-analysis of national and subnational TB prevalence survey data to assess the risk of symptomatic and asymptomatic TB in people with noncommunicable diseases or related risk factors. The analysis indicated that being a current smoker was associated with both symptomatic and asymptomatic TB. People with self-reported diabetes were also more likely to have symptomatic TB, but the association was less clear for asymptomatic TB. The analysis suggested that systematic screening could be prioritized for people who smoke and people with diabetes.

Further exploration is warranted for the classification and natural history of people with asymptomatic TB, their contribution to overall transmission at the population level and implications for case-finding and treatment *(30, 33–40)*. Nonetheless, strategies that specifically address asymptomatic TB may be required to achieve global milestones and targets for reductions in TB disease burden that have been set in WHO's End TB Strategy and the SDGs.

TB to national authorities. In response, various actions were implemented to improve the completeness of reporting, including a 2016 Health Ministerial Decree on the mandatory reporting of TB cases by all health care providers.

For more accurate assessment of the level of underreporting of people diagnosed with TB to the national TB surveillance system, Indonesia implemented a national TB inventory study in 2017 *(46)*. This resulted in an estimate that the level of underreporting of detected TB cases (i.e. the proportion of detected cases not in SITT) was 41% (95% CI: 36–46%). This underreporting was further disaggregated by type of health facility: it ranged from 15% in primary health centres to 65% in hospitals and 96% in the combined category of general practitioners, clinics and laboratories *(46)*.

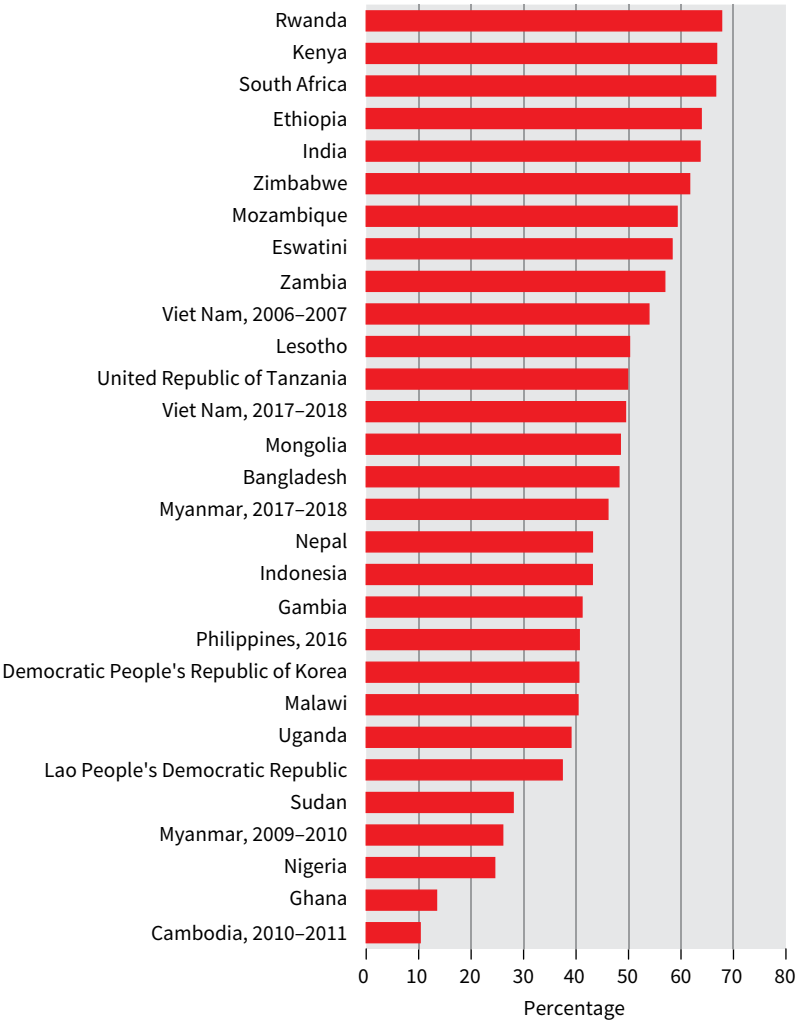
A repeat inventory study conducted in 2023 *(6)* showed large reductions in underreporting since 2017 (to a level of about 16%), demonstrating that the actions taken to correct high levels of underreporting since 2016 have been successful.

20.3 Country examples

Section 20.1 and **Section 20.2** have highlighted the results that can be produced using survey data, and how these can be applied in practice, for two major result categories and 10 topics. This section showcases country examples that illustrate how a range of survey

Fig. 20.10

Proportion of national TB prevalence survey participants who did not seek care for their symptoms, 2007–2021[a]



TB: tuberculosis.

[a] Results were not available from surveys conducted in Namibia, the Philippines (2007) and Thailand.

results have been used in practice – for three countries that have results from one survey, and for four countries that have conducted a repeat survey.

Detailed country profiles are available elsewhere *(3)* and further details can be found in individual survey reports and journal articles.[1] Country examples have also been featured in various editions of the global TB report *(5, 47–51)*.

20.3.1 Countries with results from one national survey

Ethiopia

The first-ever national TB prevalence survey was implemented in Ethiopia in 2010–2011 *(52)*. The estimated prevalence of TB was lower than the pre-survey estimate, although uncertainty intervals overlapped. The estimate of the case-detection rate was revised upwards, from a pre-survey best estimate of about 50% to one of 72% following the survey *(53)*.

Findings from the survey created a sense that things were going well; in the context of many health priorities in the country, this unintentionally resulted in TB becoming a lower priority. In response to a subsequent downward trend in TB case notifications, Ethiopia's Ministry of Health launched an improvement plan in 2014–2015. TB returned to being a high priority, with monthly updates requested by the minister of health from all regional TB coordinators. TB case notifications increased in 2015 before resuming a steady year-on-year decline, probably reflecting a true decline in the TB incidence rate.

From 2021 onwards, case notifications started to increase again; explanations include the impact of the coronavirus disease (COVID-19) pandemic and conflict in the northern regions of the country. In 2024, Ethiopia was considering a repeat survey, to provide an up-to-date and direct measurement of the burden of TB disease and to assess trends since the first survey in 2010–2011.

Ghana

Ghana's first national TB prevalence survey was implemented in 2013–2014 *(54)*. It revealed a much higher TB disease burden than previously estimated. Also, the survey indicated that a large proportion of the people found to have TB during the survey had already visited public health facilities without being diagnosed.

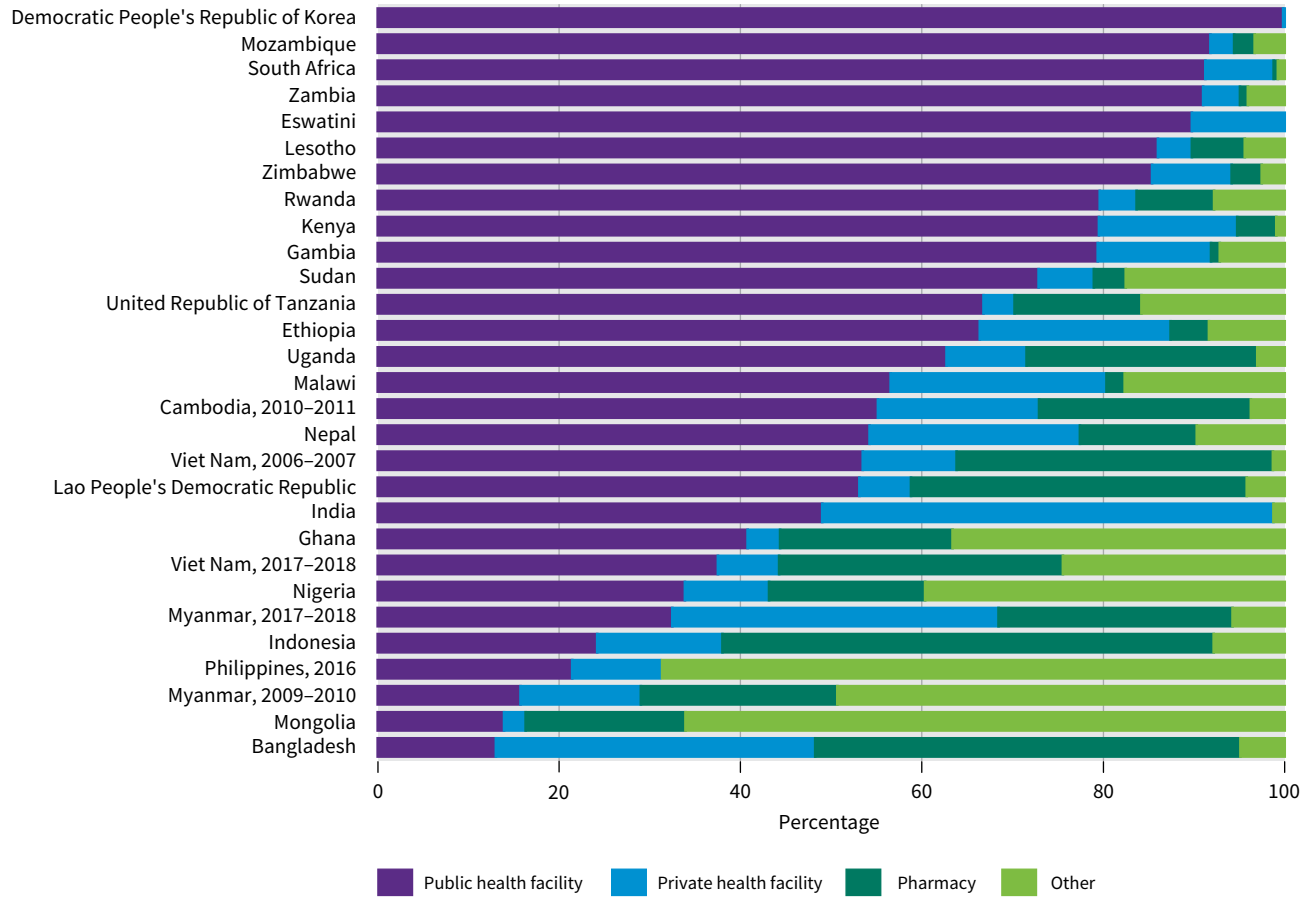
Based on the survey findings, a national TB strategic plan 2015–2020 was developed *(54)*. This gave particular emphasis to actions needed to reduce the number of people in the community with undiagnosed TB. These actions included:

- revision of the national TB screening and diagnostic algorithms routinely used in health facilities, including the addition of CXR, to increase their sensitivity;
- deployment of 54 digital CXR machines in high-volume hospitals in 2016 and 2017;
- scaling up the use of rapid molecular tests as the initial diagnostic test for TB and associated expansion of GeneXpert®-based platforms, from 2017 onwards;
- introduction of sputum sample transportation to

[1] A full list is provided in **Chapter 19**.

Fig. 20.11

Place of initial health care seeking among national TB prevalence survey participants who reported symptoms that met screening criteria and had sought care, 2007–2021[a]



TB: tuberculosis.

[a] Results were not available from surveys conducted in Namibia, the Philippines (2007) and Thailand.

increase access to onsite diagnostic tests in 1000 high-volume health facilities;

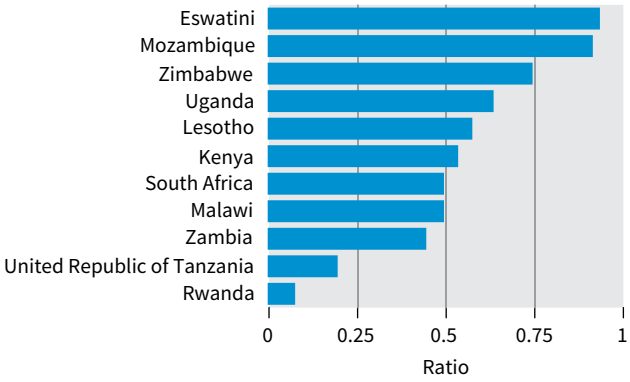
- initiation of active TB screening in hospitals and targeted TB screening, especially among men in older age groups;
- engagement of pharmacies to conduct screening and referral of people with presumptive TB;
- expansion of community interventions to improve health care seeking behaviour; and
- sensitization of health workers to increase their awareness of TB-related signs and symptoms.

South Africa

South Africa's first national TB prevalence survey was implemented in 2017–2019 *(19)*. One of the main findings was that about 60% of TB cases identified in the community did not report having symptoms (**Fig. 20.9**). This prompted the updating of new national guidelines on TB screening, especially in the general community and in outpatient departments, in which use of digital CXR screening was included from the start *(55)*.

Fig. 20.12

HIV prevalence (per 100 000 population) in TB survey cases compared with HIV prevalence (per 100 000 population) in notified TB cases, expressed as a ratio, in national TB prevalence surveys implemented, 2008–2021



HIV: human immunodeficiency virus; TB: tuberculosis.

Table 20.1

Distribution of participants from the national TB prevalence survey of Indonesia (2013–2014) who reported being under TB treatment by place of treatment, and the matching national TB electronic register (SITT) *(45)*

PLACE OF TREATMENT	PARTICIPANTS REPORTED UNDER TB TREATMENT		PARTICIPANTS REPORTED UNDER TB TREATMENT AND STILL BACTERIOLOGICALLY POSITIVE	
	SURVEY	SITT (%)	SURVEY	SITT (%)
Public health centre	34	11 (32)	8	3 (38)
Public hospital	34	8 (24)	6	2 (33)
Private hospital	26	1 (3.8)	1	0 (0)
Private clinic	7	3 (43)	2	1 (50)
Private practitioner	19	0 (0)	1	0 (0)
Others	5	1 (20)	0	0 (-)
Total	125	24 (19)	18	6 (33)

TB: tuberculosis.

Adherence guidelines were developed to address integrated care among those with chronic conditions and TB, especially older people (given their high P:N ratio) *(56)*. Similarly, owing to delayed health care seeking among survey participants for TB-related symptoms, a new strategy was developed to target interventions to improve health care seeking and increase knowledge and awareness.

South Africa was one of the first countries that used Xpert® MTB/RIF Ultra (Xpert Ultra) and liquid culture in a TB prevalence survey. This experience contributed to the development of clinical guidance on the management of people with trace-positive results (i.e. to include consideration of an individual's past history of TB) *(55)*.

Although South Africa has a high burden of HIV, the survey identified that most people with undiagnosed TB in the community were HIV-negative. This probably reflects the great investment in, and effect of, a strong HIV programme to find and treat people with HIV and TB coinfection.

20.3.2 Countries with results from a repeat survey Cambodia

Cambodia conducted national TB prevalence surveys in 2002 *(57)*, 2010–2011 *(58, 59)*, and 2023–2024. The second survey showed that the prevalence of TB had fallen significantly in the 9 years after the first survey. A key factor in this reduction was the expansion of TB diagnostic and treatment services so that they were provided in health centres as well as hospitals. Beyond health facilities in the public sector, community-based care and engagement with the private sector were also developed and enhanced. Enormous efforts were made by the NTP and its development partners to detect and treat the most infectious cases, and to increase the treatment success rate to more than 90%. Other factors that could have contributed to a reduction in TB prevalence included a reduction in the prevalence of HIV and a more than doubling of gross national income (GNI) per capita between 2002 and 2011 (US$ 320 to US$ 810) *(3, 60)*.

There were clear differences in the extent to which the prevalence of TB fell in those screening symptom-positive (56% decline, 2002–2011) compared with those screening symptom-negative (8% decline, 2002–2011). These differences were consistent with the emphasis on passive detection of people with symptomatic TB who self-referred for care. In 2002, there were more people with symptomatic smear-positive pulmonary TB with a cough of 2 weeks or longer or haemoptysis (62%) than people with smear-positive pulmonary TB who did not report symptoms (38%). By 2011, the proportion of people with smear-positive pulmonary TB who reported symptoms had fallen to 44%. Only 23% of people with smear-negative, culture-positive pulmonary TB met the 2011 NTP definition of an individual with presumptive TB.

This evolution in the TB epidemic had two major programmatic implications. The first was a need to strengthen diagnostic capacity for outpatients with respiratory symptoms, by reviewing and updating the diagnostic algorithm that had previously relied heavily on smear microscopy. Updates included more extensive use of CXR for people with any respiratory symptom, including a referral system for people with smear-negative presumptive TB to a health facility equipped to carry out CXR, and the replacement of smear microscopy with more sensitive diagnostic tools, such as Xpert MTB/RIF. The second implication was that active case-detection activities should be expanded to specific groups with a high prevalence of TB, such as elderly people, household contacts of people with smear-positive TB and people coinfected with HIV.

The survey also showed that there was a need to improve the capacity of health workers to clinically recognize TB disease: 55% of people with smear-positive

pulmonary TB and cough of any duration identified in the second survey had already sought care (45% of whom had consulted a public health facility) but had not been diagnosed with TB. Among people with smear-negative, culture-positive TB and a cough of any duration identified in the second survey, 55% had also previously sought care.

Based on the survey results, it was also recognized TB preventive treatment should be expanded, especially among older people with a CXR suggestive of inactive TB and negative bacteriological test results.

A third national TB prevalence survey was completed in 2024; provisional results available in September 2024 suggested a large decline in TB burden since 2010–2011 *(61)*.

Myanmar

Myanmar conducted national TB prevalence surveys in 1972 *(62)*, 1994 *(63)*, 2009–2010 *(64)* and 2017–2018 *(18)*. The third and fourth surveys used screening and diagnostic methods recommended by WHO *(4)*.

The 2017–2018 survey showed that the burden of TB was still high, with an estimated prevalence of bacteriologically confirmed pulmonary TB of 468 (95% CI: 391–546) per 100 000 in those aged 15 years and older. Nonetheless, the most recent survey showed that there had been a substantial reduction in the prevalence of culture-positive pulmonary TB between 2009–2010 and 2017–2018, from 520 to 256 per 100 000 population – a reduction of 51% in 7–8 years. In addition to a national estimate, subnational estimates were obtained for three geographical areas and for rural and urban areas separately. These helped to inform planning that was adapted to varying TB epidemiology within the country.

As found in other surveys, the prevalence per 100 000 population was higher in men than women and increased with age. The P:N ratio was similarly high, suggesting that men and older age groups were more likely to get TB and experience longer delays to diagnosis and poorer access to TB diagnostic services. Myanmar subsequently implemented targeted screening activities to find and treat men with TB (e.g. those working in construction or mining, migrant workers and prisoners). The fact that the number of people in the community who were not previously diagnosed with TB was greater than the number of people already on TB treatment suggested considerable delays in diagnosis; also, it indicated that many people remain bacteriologically positive without a TB diagnosis for a long period of time, thus contributing to ongoing transmission.

The low prevalence of people with symptomatic TB suggested that the increased emphasis on identifying such cases in the interval between the third and fourth surveys had an impact. However, it was also clear that symptom screening alone was not sensitive enough to detect all people with TB in the most recent survey.

The 2017–2018 prevalence survey identified smoking as the biggest risk factor for TB. In 2023, WHO estimated that about 26 000 cases of TB in Myanmar were attributable to tobacco smoking *(6)*.

Following ongoing migration from rural to urban areas, the 2017–2018 survey identified a higher prevalence of TB (relative to population) in the more urbanized and congested areas of the country. In these areas, many symptomatic survey participants initially sought care in the private health sector (e.g. private clinics, private hospitals or pharmacies). This showed that greater engagement with the private sector would be crucial for increasing overall case detection. Similarly, few people with TB received treatment (or were even diagnosed) at basic TB health facilities, indicating a need for further decentralization of basic TB services, including access to more sensitive diagnostics (rapid molecular tests) in rural areas and their integration into primary health facilities.

The Philippines

The Philippines conducted national TB prevalence surveys in 1997 *(65)*, 2006–2007 *(66)* and 2016 *(67)*. The prevalence of bacteriologically confirmed pulmonary TB was among the highest found in all national surveys implemented globally since 2007. Although it was not surprising that the use of Xpert MTB/RIF increased the overall diagnostic yield, the prevalence of culture-confirmed TB alone was high (587 per 100 000 population; 95% CI: 488−687) and showed that the Philippines was facing one of the highest burdens of TB in the world. TB prevalence declined significantly between 1997 and 2006–2007, but there was no evidence to suggest there was a decline between 2006–2007 and 2016.

Plausible explanations for the lack of decline in TB prevalence since 2007 included case-detection gaps, significant delays in diagnosis, health system weaknesses, and broader social and economic influences on the TB epidemic. These broader influences included the level of poverty, with 22% of people living below the national poverty line in 2015; the level of undernourishment, with a prevalence of 14% in the general population in 2015 and no improvement since 2008; and low coverage of health insurance and social protection (e.g. coverage of only 4% in the poorest quintile in 2013), leading to financial barriers to accessing health services and high levels of TB-affected households facing catastrophic costs (42% in 2016–2017) *(67, 68)*. Poor and disadvantaged people require adequate social protection strategies and increased benefit packages to reduce catastrophic costs associated with TB, especially drug-resistant TB.

Strategic actions were implemented with the full support of the Philippines Department of Health, and full mobilization of the health sector. Measures that were agreed included the deployment of sufficient human resources at national and subnational levels; increased domestic funding; a presidential executive

order for drug regulation; establishment of a high-level steering group; and ensuring financial protection and sustained poverty alleviation efforts for more than 90% of the poor, through increased coverage of the national health insurance scheme and expanded social protection programmes.

Viet Nam

National TB prevalence surveys were conducted in 2006–2007 *(69)* and 2017–2018 *(20)*. Between the two surveys, the prevalence of culture-positive pulmonary TB decreased by 37% (95% CI: 11.5–55.4%), from 199 (95% CI: 160–248) per 100 000 in 2006–2007 to 125 (95% CI: 98–159) per 100 000 in 2017–2018 *(70)*. The prevalence of smear-positive pulmonary TB dropped by 53% (95% CI: 27.0–69.7%), from 99 (95% CI: 78–125) per 100 000 to 46 (95% CI: 32–68) per 100 000, with the largest reductions being among men. In contrast, there was limited change in the prevalence of culture-positive but smear-negative pulmonary TB.

The declining trend in both culture-positive and smear-positive pulmonary TB occurred in the context of a range of interventions that were implemented following the first survey. These included improvements to case-finding and curative treatment, implementation of TB preventive treatment, the roll-out of new diagnostics and contact tracing. Alongside these measures, the country experienced considerable economic growth, with gross domestic product (GDP) per capita increasing at a rate of between 5.2% and 7.1% per year between 2007 and 2017. This probably contributed to better access to health care and improved nutritional, housing and employment conditions, all of which are associated with lower levels of TB disease burden.

Survey results also suggested that replacing sputum smear microscopy with rapid molecular tests for TB diagnosis and screening for TB using digital CXR to enhance rapid case-finding and treatment could help to achieve further reductions in the burden of TB disease.

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Annex 20.1 Indicators related to the health care seeking behaviour of survey participants who reported symptoms

This annex provides examples of indicators related to health care seeking behaviour of people who reported symptoms that met survey screening criteria. The indicators listed should be computed after adjusting for the clustered sampling design (**Chapter 17**).

A20.1.1 Indicators related to participants eligible for sputum examination based on presence of symptoms (as defined by the survey)

- Percentage of symptomatic participants who did NOT seek care for their symptoms:
  - among them, the percentage reporting a financial barrier;
  - among them, the percentage reporting having no health insurance; and
  - among them, the percentage reporting a geographical barrier to accessing health services.
- Percentage of symptomatic participants who did seek care for their symptoms:
  - among them, the percentage reporting having sought advice in a public clinic or hospital;[1]
  - among them, the percentage reporting having sought advice in a private clinic or hospital;
  - among them, the percentage reporting having sought advice at a traditional healer, pharmacy or other health care provider;
  - among them, the percentage who self-treated; and
  - among them, the diagnostic investigations undertaken.
- Percentage of people with tuberculosis (TB) (prevalent case) who reported symptoms but were not on anti-TB treatment at the time of the survey, who reported that:
  - they could not afford to pay for their prescribed investigations;
  - they could not access free medical services; and
  - they did not believe their symptoms were serious enough to seek care.[2]

A20.1.2 Indicators related to people with TB on anti-TB treatment at the time of the survey

- Ratio of the number of people with TB (prevalent cases) in the survey to the number diagnosed with TB before the survey and currently on anti-TB treatment.[3]
- Among people diagnosed with TB before the survey and currently on treatment, the average time between the onset of symptoms and the start of treatment.[4]
- Among people diagnosed with TB before the survey and currently on treatment, the percentage who were recorded as a TB case in the national TB surveillance system.[5]
- Among people diagnosed with TB before the survey, currently on treatment and not recorded in the national TB surveillance system, the percentage who were diagnosed in the public sector.[6]

[1] This indicator may be defined separately for initial and last medical contact.

[2] This indicator should be compared between symptomatic people with TB and symptomatic people not diagnosed with TB.

[3] A low ratio indicates a high level of performance of the national TB programme (NTP) expressed in terms of the capacity to diagnose and notify most incident cases.

[4] This indicator will provide information about the duration of disease before diagnosis under routine programme conditions, but the information is expected to be imprecise owing to low numbers and recall bias.

[5] This indicator will provide information on the coverage of TB reporting but is expected to be imprecise owing to low numbers.

[6] This indicator will provide information on providers failing to report TB but is expected to be imprecise owing to low numbers.

Annex 20.2 Care cascade analysis using data from a national TB prevalence survey

The cascade is the individual's pathway from health care access to TB diagnosis, treatment initiation and successful treatment completion. Examples of the indicators that can be calculated using prevalence survey data, which can inform planning for priority gaps in the quality of care, are listed below. They are disaggregated into three groups.

Participants not seeking care:

- ratio of prevalent TB cases to notified TB patients (rates);
- proportion of symptom-screen positive participants who did not seek care;
- reasons why care was not sought when symptoms suggestive of TB were present; and
- factors associated with the risk of having pulmonary TB.

Participants who sought care but were NOT diagnosed or notified:

- location where care was sought;
- proportion of participants with TB who had sought care but were not diagnosed with TB before the survey;
- proportion of participants with a history of TB treatment (current or past, or both), and not recorded in the national TB surveillance system (i.e. notified to the national TB programme [NTP]);
- reasons why survey TB cases were not diagnosed by health care providers; and
- reasons why previously diagnosed TB cases (excluding those not currently on treatment) were not recorded in the national TB surveillance system (i.e. notified to the NTP).

Participants who were notified to the NTP but NOT successfully treated:

- proportion of survey participants who reported history of TB treatment (current or past, or both), disaggregated by treatment location.

For further information please contact:

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