Module 1

EPIDEMIOLOGY OF CHILDHOOD TB

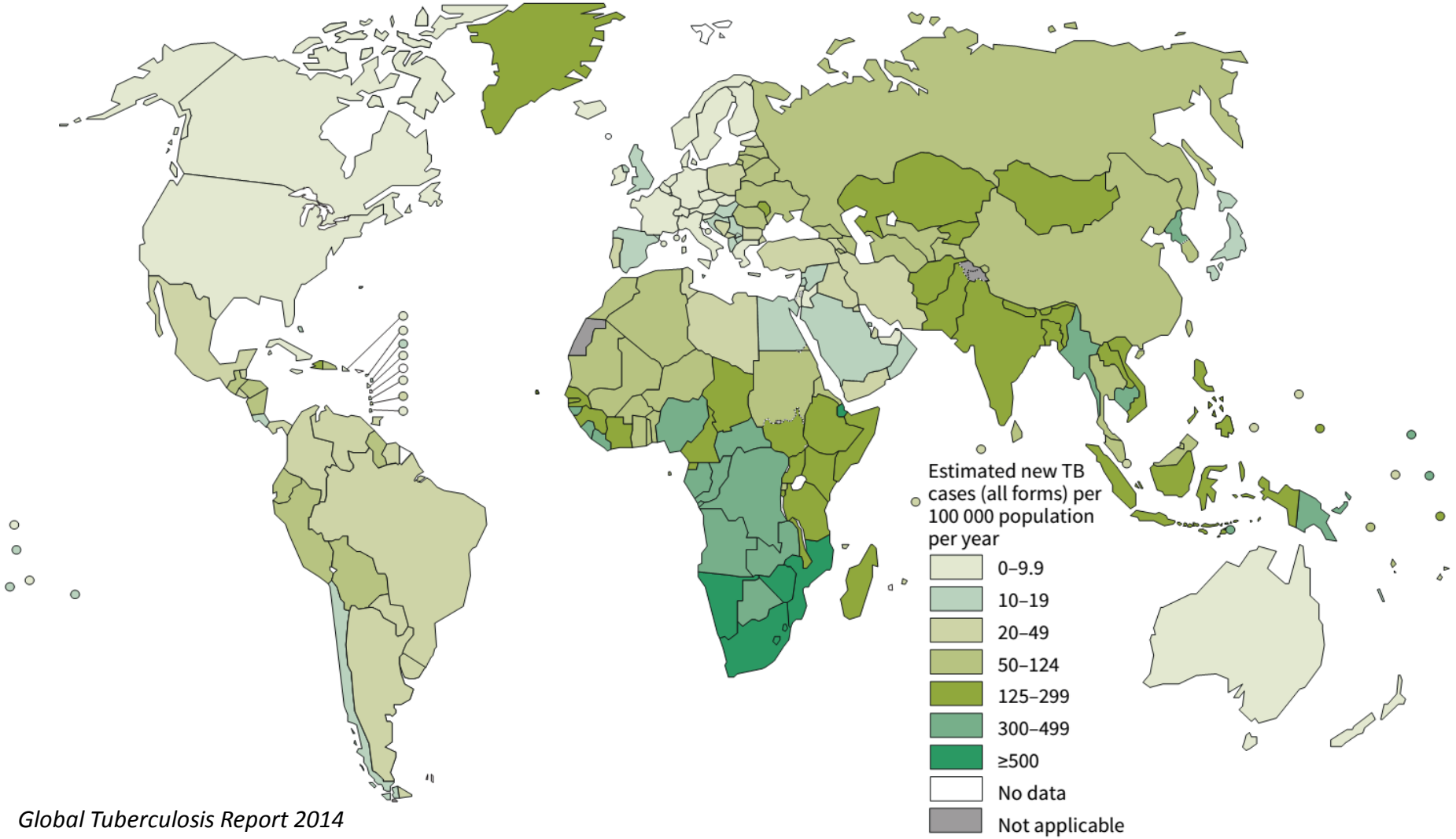
International Union Against Tuberculosis and Lung Disease

World Health Organization

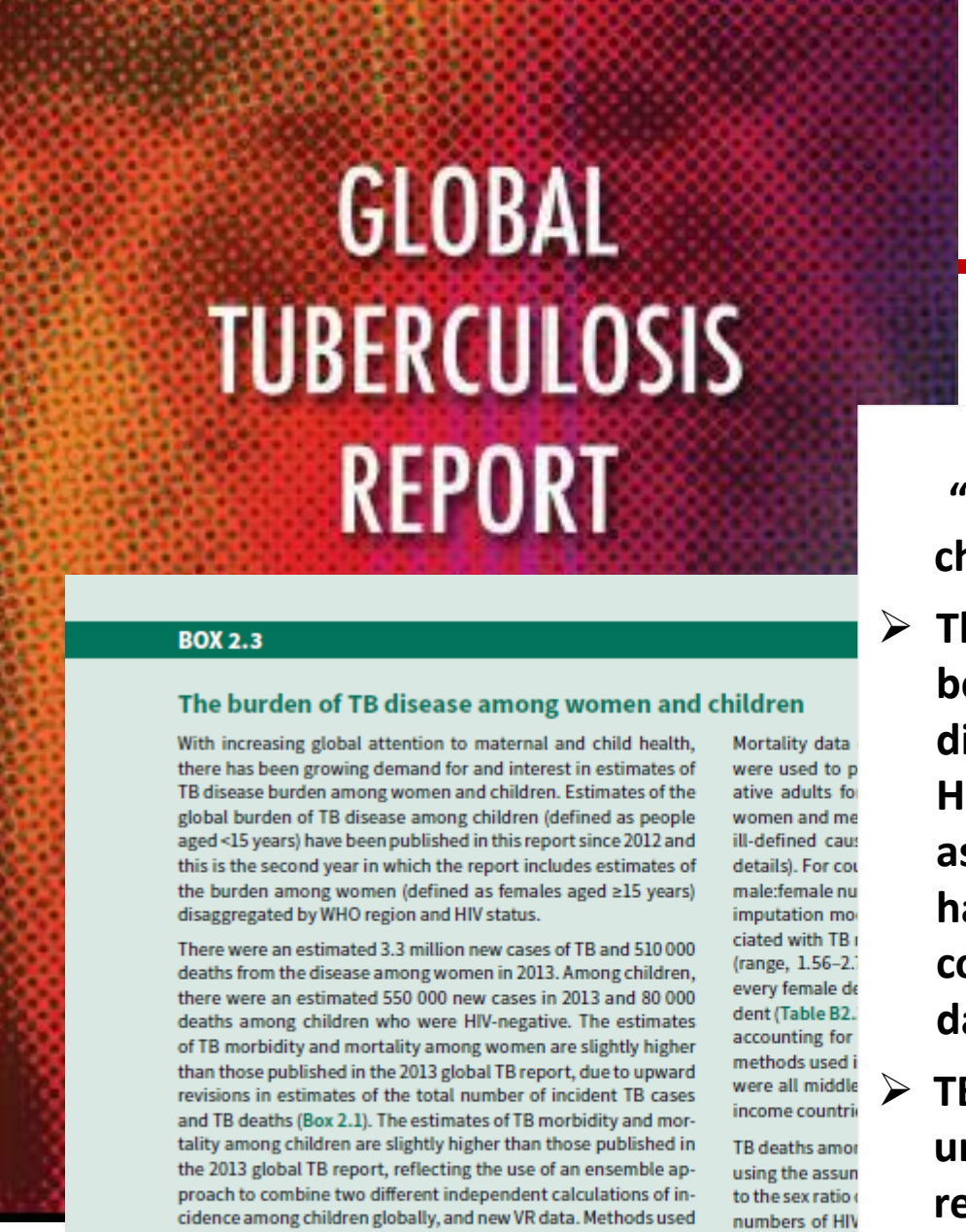
Burden of TB in children

- Tuberculosis (TB) in children is common wherever TB is common in adults i.e. TB endemic settings
- TB is an important cause of illness and death in children in many TB endemic countries
- At least 550 000 children become ill with tuberculosis (TB) each year.
- Up to 80 000 HIV-uninfected children die of TB every year*.
- 70–80% of children with TB, have the disease in their lungs (pulmonary TB). The rest are affected by TB disease in other parts of the body (extrapulmonary TB).
- There were over ten million orphans due to parental TB deaths in 2010.
- An understanding of the risks for infection and disease due to TB in children is critical for improved diagnosis and preventive management
- The HIV epidemic has increased the burden of childhood TB and the clinical challenges
- The main benefit of neonatal BCG is protection against severe disseminated TB in children

Estimated TB incidence rate, 2013



Global Tuberculosis Report 2014



BOX 2.3

The burden of TB disease among women and children

With increasing global attention to maternal and child health, there has been growing demand for and interest in estimates of TB disease burden among women and children. Estimates of the global burden of TB disease among children (defined as people aged <15 years) have been published in this report since 2012 and this is the second year in which the report includes estimates of the burden among women (defined as females aged ≥15 years) disaggregated by WHO region and HIV status.

There were an estimated 3.3 million new cases of TB and 510 000 deaths from the disease among women in 2013. Among children, there were an estimated 550 000 new cases in 2013 and 80 000 deaths among children who were HIV-negative. The estimates of TB morbidity and mortality among women are slightly higher than those published in the 2013 global TB report, due to upward revisions in estimates of the total number of incident TB cases and TB deaths (Box 2.1). The estimates of TB morbidity and mortality among children are slightly higher than those published in the 2013 global TB report, reflecting the use of an ensemble approach to combine two different independent calculations of incidence among children globally, and new VR data. Methods used to produce these estimates and further details about results are provided below.

The burden of TB in women: estimates of TB incidence and mortality, 2013

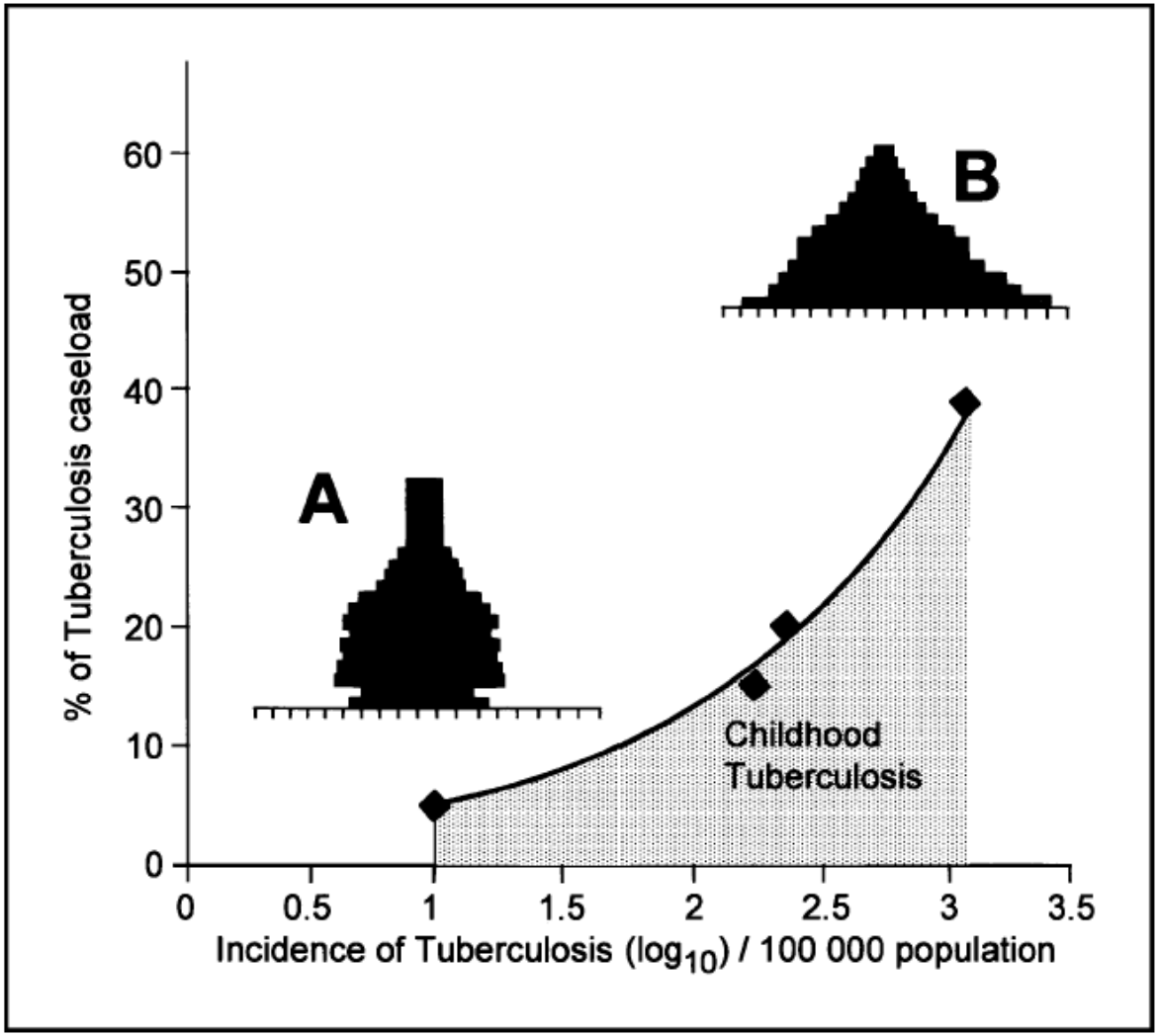
Mortality data
were used to p
ative adults fo
women and me
ill-defined caus
details). For cou
male:female nu
imputation mo
ciated with TB
(range, 1.56–2.
every female de
dent (Table B2.
accounting for
methods used i
were all middle
income countri

TB deaths amor
using the assun
to the sex ratio
numbers of HIV
and women (Fig
al variations (T
occurred amon
deaths were est

"best estimates" of 550 000 cases of TB in children per year = 6% of the global burden

- **The proportion of cases among children may be different in countries for which age-disaggregated data were not available. However, this is becoming less of a problem as the reporting of cases disaggregated by age has been improving and the number of countries not reporting age-disaggregated data was low in 2013**
- **TB-related deaths in children are underrepresented in this report because TB-related deaths in children are often attributed to HIV or pneumonia or malnutrition**

Figure 1. Percentages of the tuberculosis caseload



The percentage of the tuberculosis caseload made up by children <15 years of age in relation to the incidence of tuberculosis/100,000 population and the population pyramids typical of an (A) developed and a (B) developing community.

Donald PR. Curr Opin Pulm Med 2002

National TB control data

- *This slide could include recent data of TB control indicators from your National TB control programme or regional data*

Stockholm declaration

Home › Get Involved

CALL TO ACTION for CHILDHOOD TB

Read the Call in French, Read the Call in Russian

Sign the Call to Action

We, participants gathered at the 'International Childhood Tuberculosis Meeting' held March 17-18, 2011 in Stockholm, Sweden recognize that:

Childhood TB and public health

- Public health approach: Proper identification and treatment of infectious cases will prevent childhood TB

- Child TB historically afforded a low priority by NTPs:
  - Diagnostic difficulties
  - Usually not infectious
  - Limited resources
  - Lack of recording and reporting

But …..

- **this disregards the impact of TB on childhood morbidity and mortality**

- **child TB reflects recent TB control**

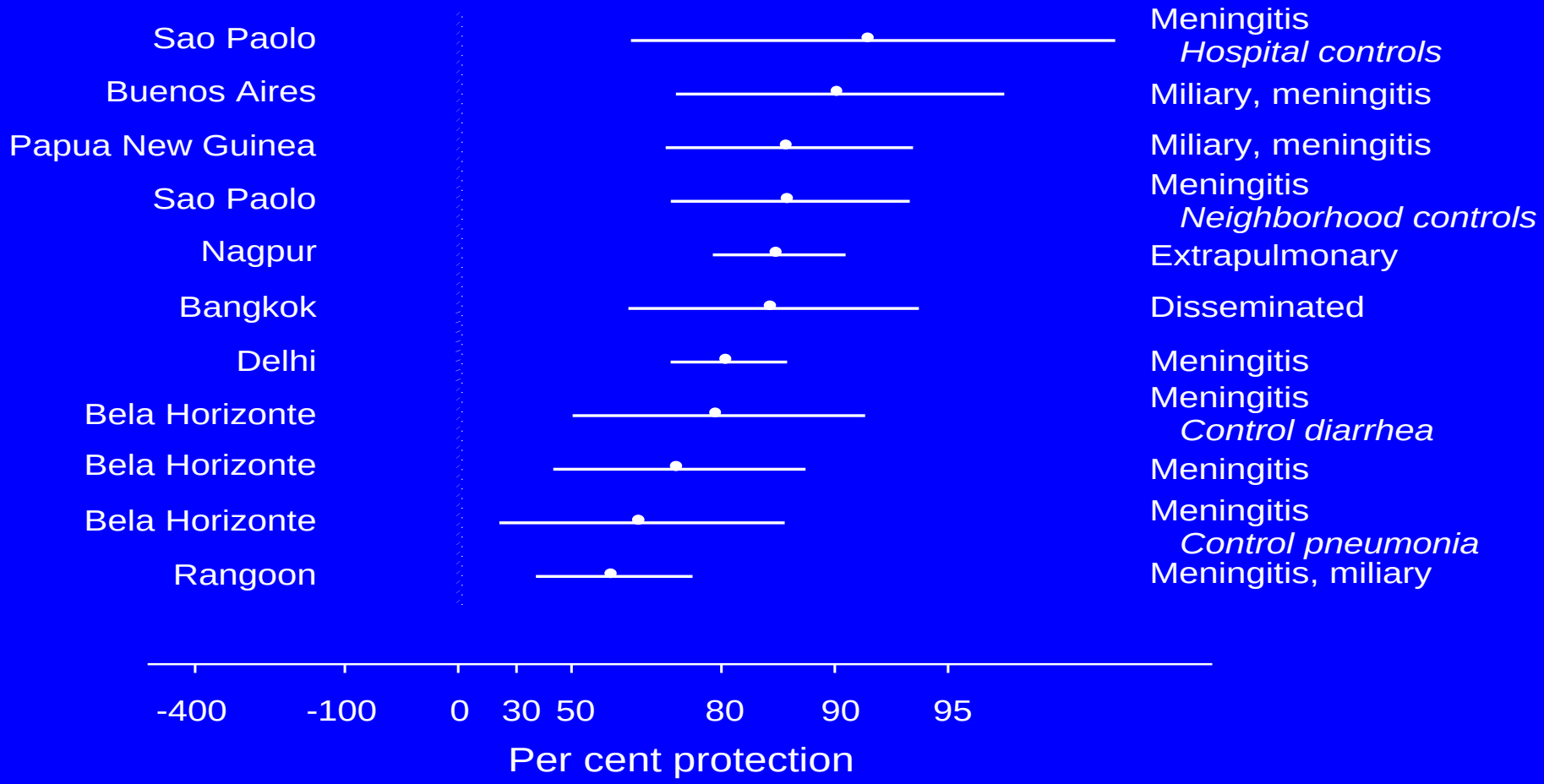
- **infected children become adults with disease**

Pathogens found in lungs from autopsy studies of African children

Causes of pneumonia	HIV-infected N=473	HIV-uninfected N=338	Total N=811
Bacterial	238 (50%)	132 (39%)	370 (46%)
PcP	145 (31%)	11 (3%)	156 (19%)
CMV	121 (26%)	7 (2%)	128 (16%)
M.tuberculosis	**50 (11%)**	**27 (8%)**	**77 (9%)**
Co-infection	98 (21%)	5 (1.5%)	103 (13%)

Combined data from 7 autopsy studies from five TB endemic countries shows that tuberculosis is a common diagnosis in children dying with lung disease including HIV-uninfected children

Protection from BCG Vaccination - Retrospective Studies
Protection Against Death, Disseminated, and Meningeal Tuberculosis



From: Reider HL. Interventions for Tuberculosis Control and Elimination, IUATLD 2002

Studies from many TB endemic settings consistently show that BCG protects against severe disseminated forms of TB in children ---------- and leprosy

Risk factors for TB infection and disease in children

For TB infection

- Contact with source case
  - Closeness of contact
  - Duration of contact

- **Source case**
  - Smear positivity
  - Cavities on CXR

- **Increased exposure**
  - Living in high TB endemic communities
  - Children of families living with HIV

Risk factors for TB infection and disease in children

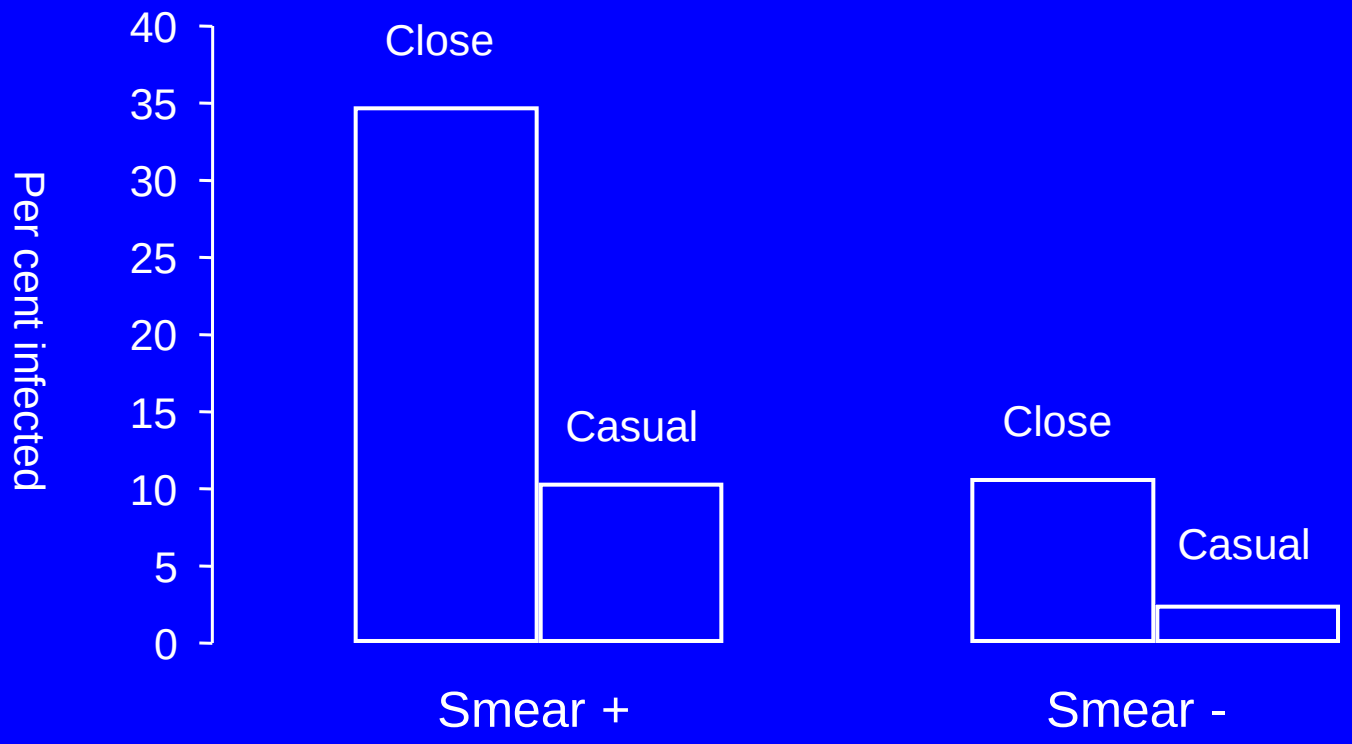
For TB infection

- Contact with source case
  - Closeness of contact
  - Duration of contact
- **Source case**
  - Smear positivity
  - Cavities on CXR
- **Increased exposure**
  - Living in high TB endemic communities
  - Children of families living with HIV

For TB disease

- Young age
  - Especially 0-2 years
- **HIV infection**
  - Risk of infection and disease
- **Other immunosuppression**
  - Malnutrition
  - Post-measles
- **Not BCG vaccinated**
  - Risk of disseminated disease

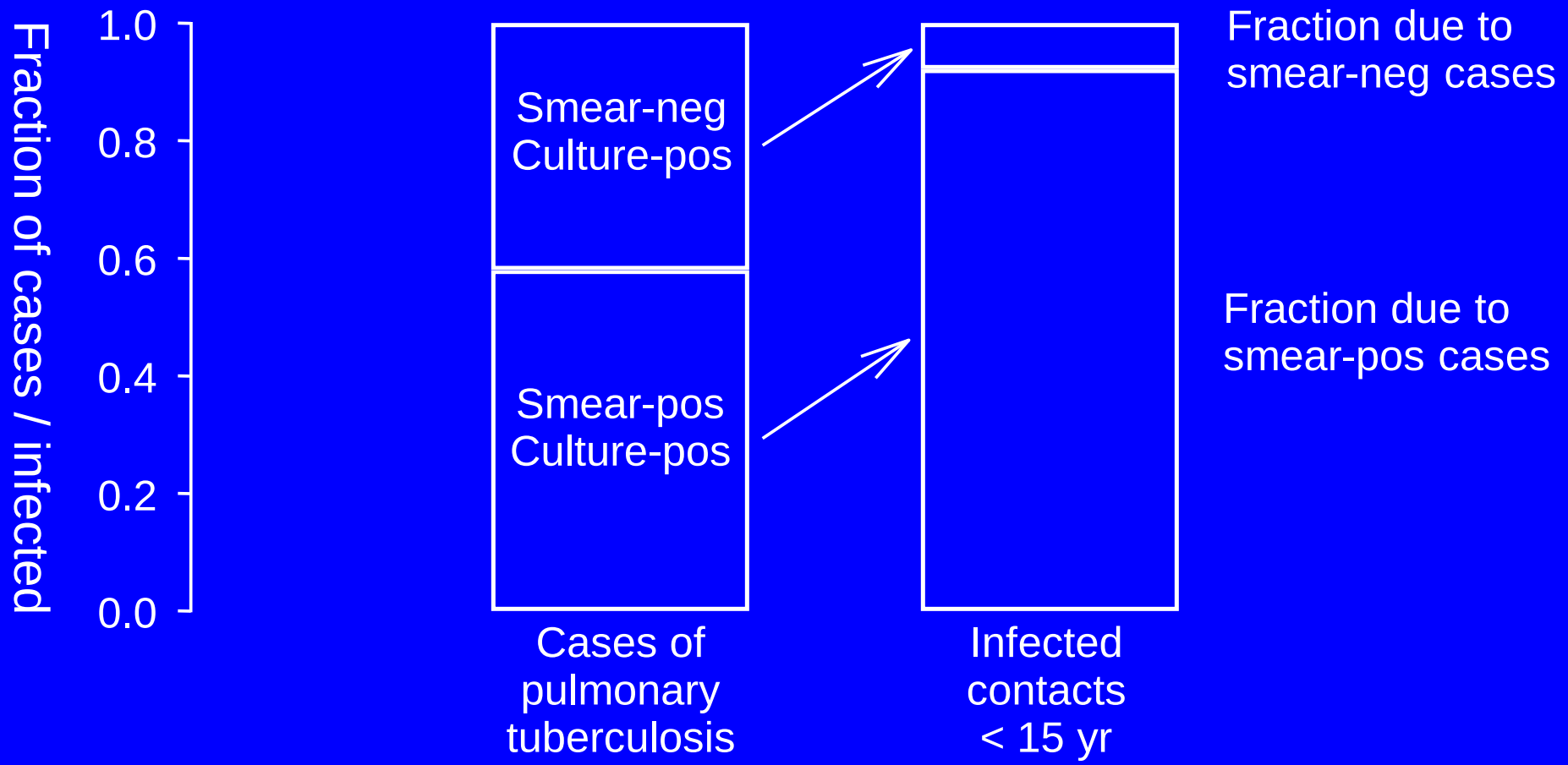
The risk of infection with tuberculosis (as measured by TST) is greatest if the contact is close and with a case of sputum smear-positive disease



Grzybowski S, et al. Bull Int Union Tuberc 1975

Adapted from: Reider HL. Epidemiological Basis of Tuberculosis Control, IUATLD 1999

Infection with TB can occur from contact with a sputum smear-negative source case but it is less common than from smear-positive cases



Grzybowski S, et al. Bull Int Union Tuberc Lung Dis 1975

Studies of child contacts in African communities

- One-third to two-thirds of child household contacts of TB cases have evidence of TB infection i.e. TST positive
- Incidence of TB disease among household contacts is very high – reported as >1,000 cases/100,000 population
- Likelihood of infection is related to closeness/proximity of contact to and sputum smear positivity of index case
- Risk of infection greatest when the index case is the child's carer e.g. mother, grandmother
- HIV-infected children are at increased risk of exposure to TB

Kenyon TA et al, Int J Tuberc Lung Dis 2002; Sinfield R, et al Ann Trop Paediatr 2006; Jackson-Sillah D, et al Trans R Soc Trop Med Hyg 2007; Morrison J, et al Lancet Infect Dis 2008

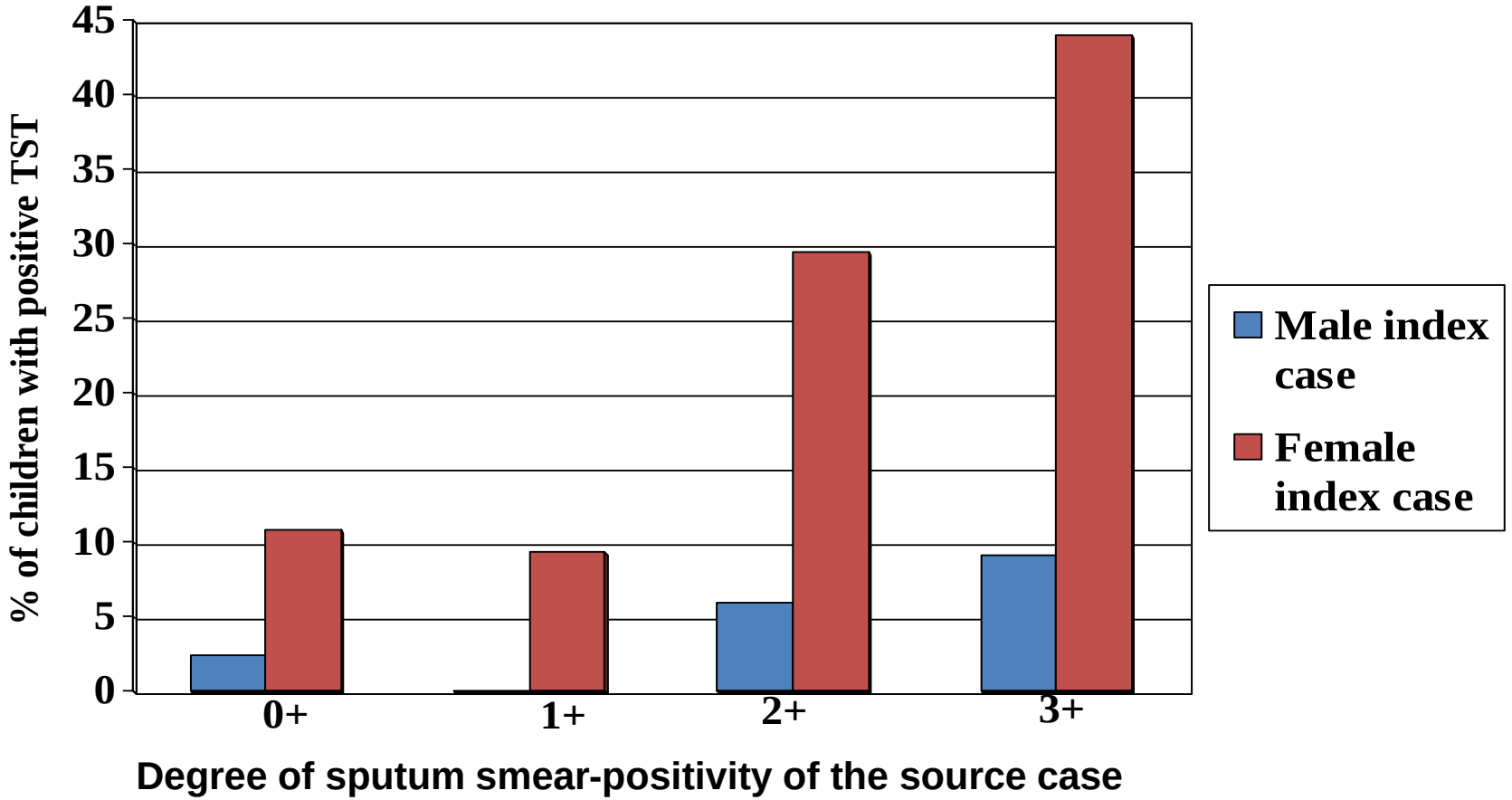
Studies of child contacts in Asian countries

Study	Location	No. of child contacts	Proportion with TB infection	Proportion with TB disease
Andrew et al	India	398	39 %	5.5 %
Narain et al	India	790	24 %	NR
Kumar et al	India	142	NR	3 %*
Singh et al	India	281	34 %*	3 %*
Rathi et al	Pakistan	151	27 %	NR
Salazar et al	Philippines	153	69 %	3 %
Tornee et al	Thailand	500	47 %	NR
Nguyen et al	Lao PDR	148	31 %	NR
Okada et al	Cambodia	217	24 %*	9 %*

* Data only for < 5 years; NR: not recorded

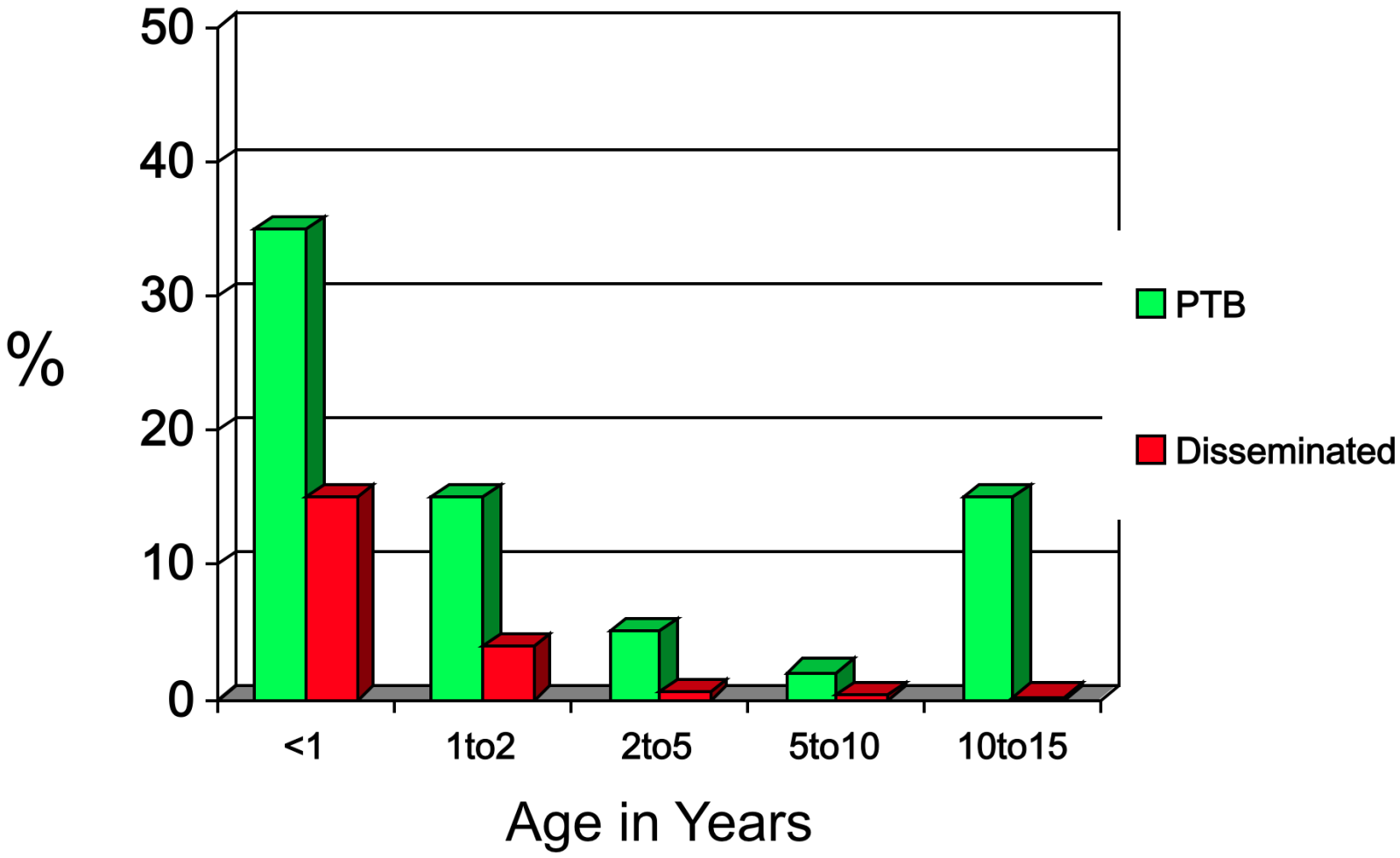
From Triasih R et al, J Trop Med 2012

Proportion of children with TB infection (positive TST) by degree of smear positivity of the source case

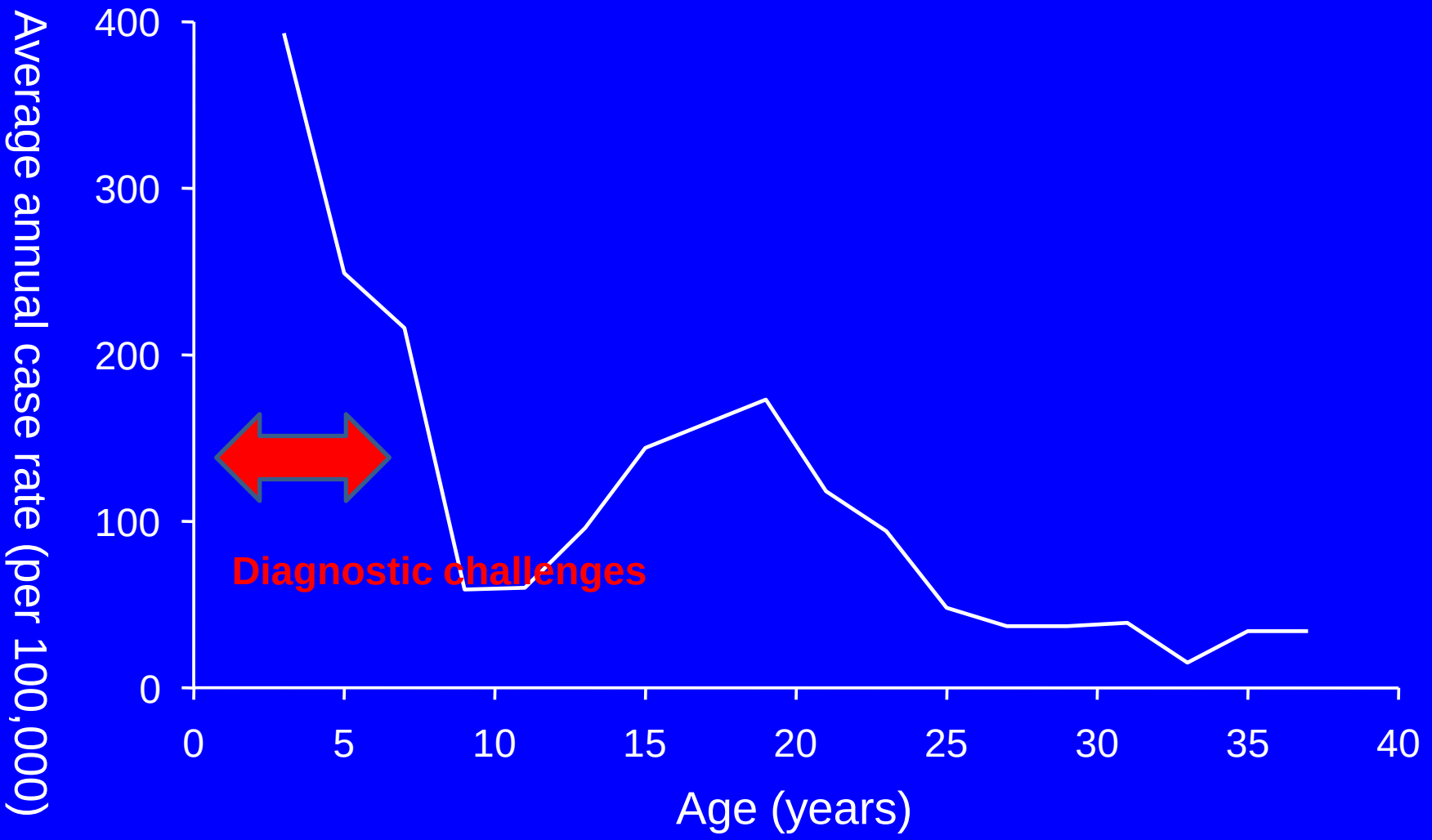


Kenyon TA et al, Int J Tuberc Lung Dis 2002

Risk of TB disease following infection by age



Incidence by age when TB was first diagnosed



Comstock GW, et al. Am J Epidemiol 1974;99:131-8

TB disease in children

- Most cases occur in young children (<5years)
- Most disease occurs within 2 years after exposure/infection
  - The majority within 1 year

- Most cases in children are pulmonary TB
  - Smear negative or smear not done are the majority
  - Extrapulmonary TB is also common and the type depends on age
  - Smear positive disease is usually older children

Childhood TB caseload: Malawi 1998

Malawi NTP, 1998	numbers (proportion of childhood caseload)	proportion of total caseload
Total caseload	22,982	
Total childhood	2,739	11.9%
0-4 years	1,615 (59 %)	7%
5-14 years	1,124 (41 %)	4.9%
Smear-positive PTB	127 (5 %)	1.3%
Smear-negative PTB	1,804 (65 %)	21.3%
EPTB	808 (30 %)	15.9%

Harries AD, et al. Int J Tuberc Lung Dis 2002

Types of childhood EPTB disease in 2 endemic settings

	Malawi NTP, 1998	PNG, 2005-6
EPTB cases	808	1097
Lymphadenitis	331 (41%)	342 (31%)
Pleural effusion	101 (12%)	94 (9%)
Spinal	83 (10%)	41 (4%)
Pericardial	60 (7%)	12 (1%)
Abdominal	39 (5%)	173 (16%)
Miliary	34 (4%)	64 (6%)
Meningitis	30 (4%)	257 (23%)
Bone disease	12 (1%)	15 (1%)
Not indicated/others	118 (14.6%)	99 (9%)

Harries AD, et al. Int J Tuberc Lung Dis 2002; Law I, et al. Int J Tuberc Lung Dis 2009

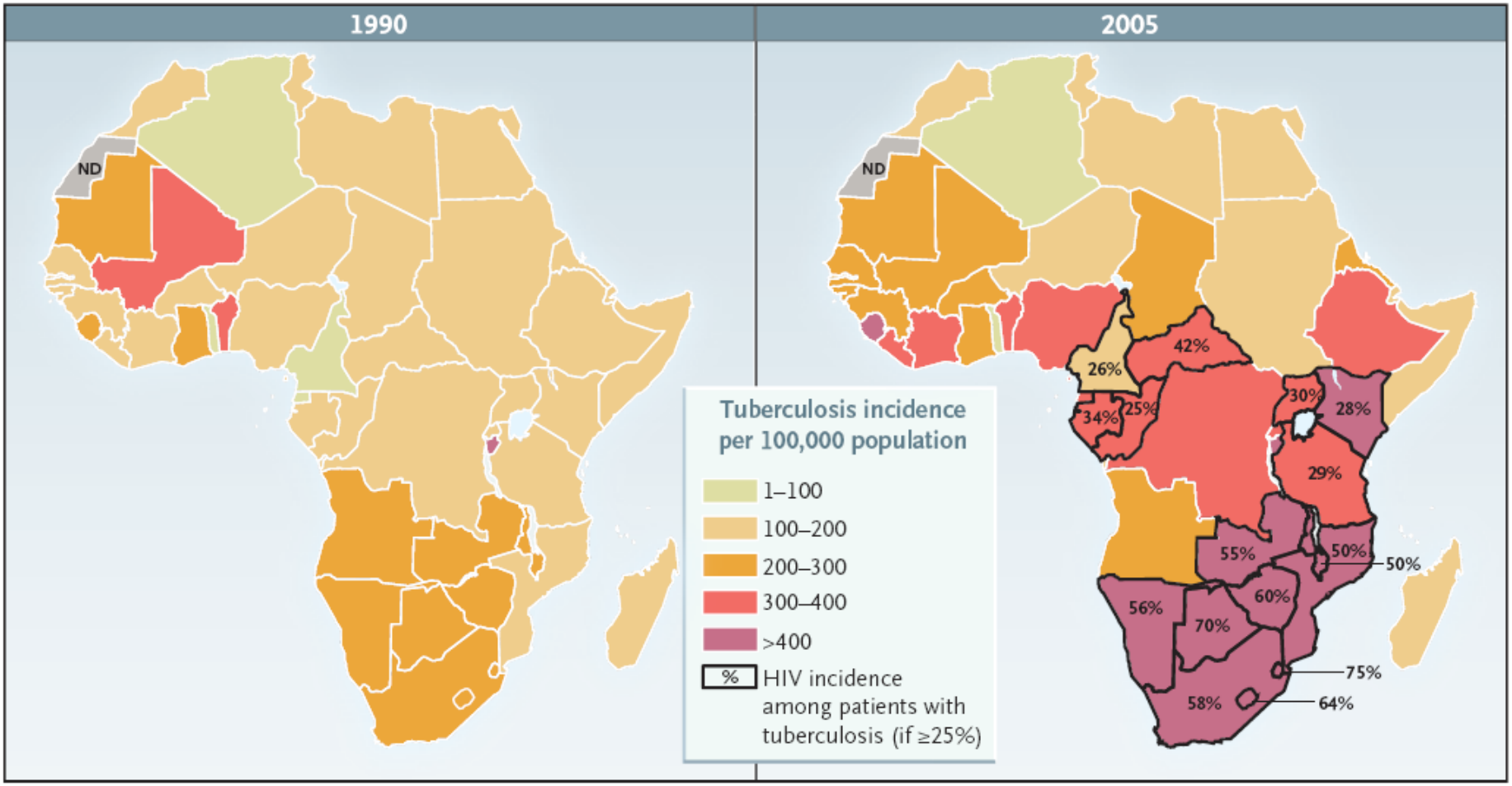
Child TB data and NTP

- The burden of TB in children at a national or global level is uncertain
- The burden of TB in children is an important indicator of ongoing transmission within the community
- Children with TB are often not registered with or reported by NTP - but should be
- Important data include age, TB disease type, HIV status and treatment outcomes

The challenge of HIV and TB/HIV

- Increased caseload of child TB
- Greater difficulty with diagnosis
- Poorer response to TB treatment
- Drug interactions
- Implementation of the “three I’s”

TB/HIV epidemiology

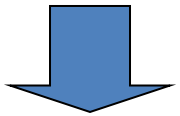


Estimated Incidence of Tuberculosis per 100,000 Population in African Countries in 1990 and 2005.

Child TB/HIV epidemiology

HIV epidemic

Large increase in TB cases in young adults



Increased number of child TB cases

HIV-infected children at risk of PTB because:

1. immune suppressed
2. more likely to be a contact of an adult with TB

The TB notification rate and notification rate of smear-positive disease rose in Malawi in the wake of the worsening HIV epidemic

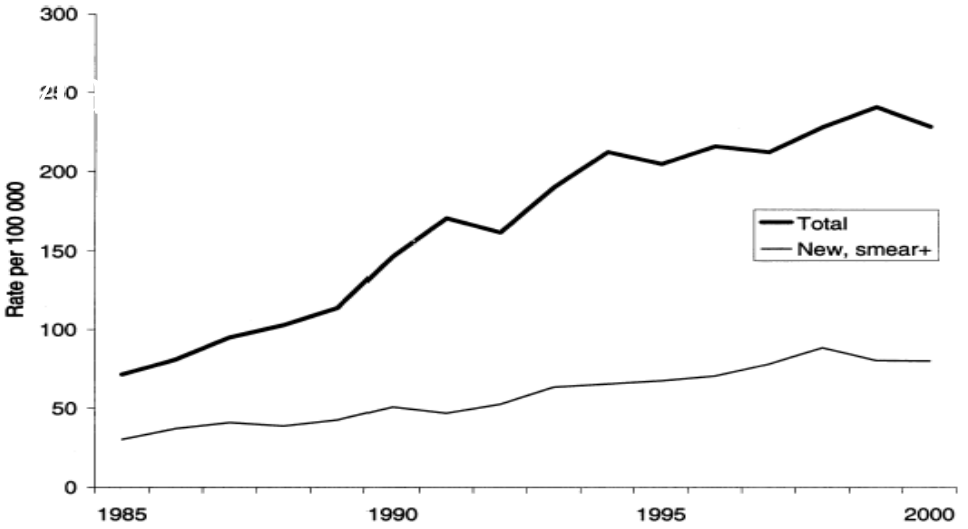
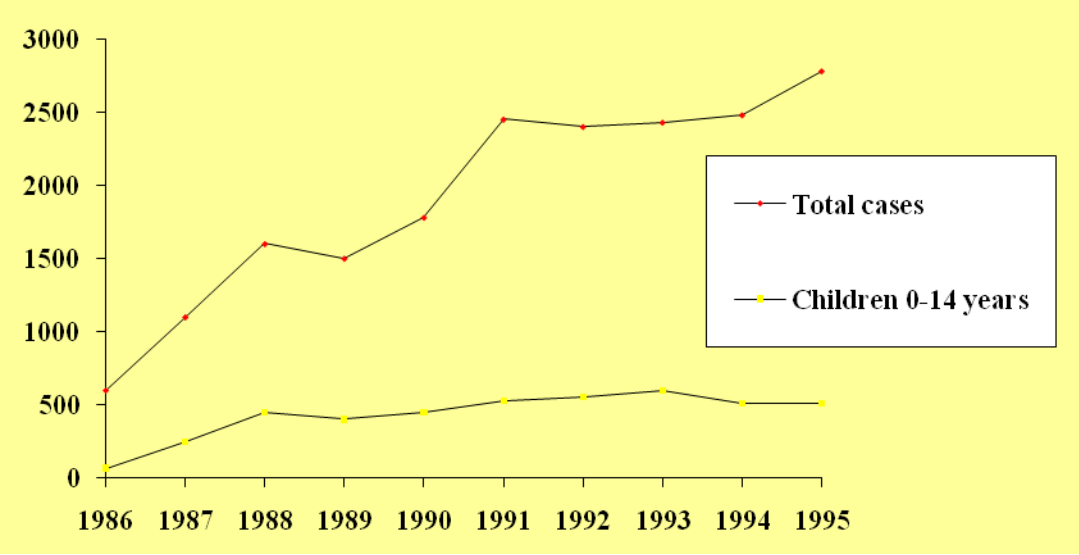


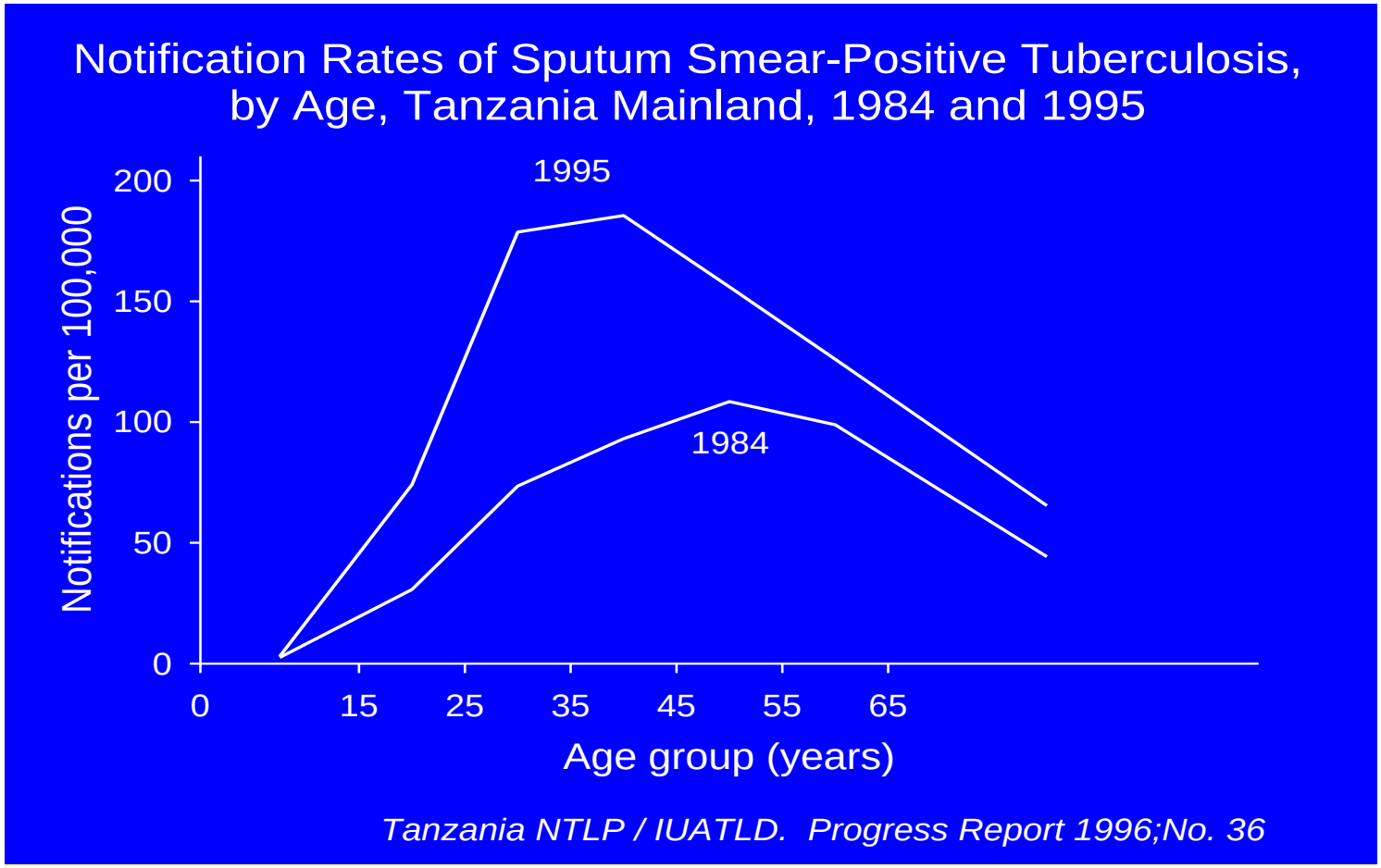
Figure 1 Tuberculosis notification rates in Malawi, 1985–2000. smear+ = smear positive.

Childhood tuberculosis notifications in Blantyre district, Malawi, increased 8-fold from 1986 to 1995 as the TB epidemic worsened

Harries AD, et al. Int J Tuberc Lung Dis 1997



Increased risk of TB exposure among young children in HIV-endemic countries



Child TB and TB/HIV

- Risk of culture-confirmed TB is far higher in HIV-infected than in HIV-uninfected children

  Madhi SA et al, Clin Infect Dis 2000; Hesseling AC et al, Clin Infect Dis 2008

- TB risk is higher in HIV-infected children with low CD4% < 15% compared to HIV-infected children with higher CD4%

  Elenga N et al, Pediatr Infect Dis J 2005

- Mortality significantly higher in HIV-infected especially if not receiving ART

Impact of HIV on TB treatment outcome

HIV infection was associated with a very poor outcome from TB in children in the pre-HAART era

	Complete recovery			Mortality		
	HIV+	HIV-	p value	HIV+	HIV-	p value
South Africa Jeena et al 1994	65%	95%	0.002	15%	0%	<0.05
Cote d'Ivoire Mukadi et al 1995				23%	3%	<0.01
Dominican Republic Espinal et al 1994	63%	97%	<0.001	16%	0%	<0.001
Ethiopia Palme et al 2002	55%	73%	0.01	38%	6%	<0.001

Three “I”s for TB control

1) **I**ntensified Case Finding
2) **I**NH Prevention Treatment (IPT)
3) **I**nfection Control

….and a fourth?

Integration

of TB/HIV including maternal TB/HIV

of other health services such as maternal child health/IMCI

Maternal TB/HIV impact

- TB in pregnancy or post-partum is common especially in HIV-infected women
- Associated with maternal mortality
- Associated with LBW and poorer infant outcomes
- Associated with risk of TB and of HIV transmission

Child TB data and NTP

- Children diagnosed and treated for TB should be routinely registered, recorded and reported
- Important information includes age, TB type, HIV status and treatment outcome
- Such data are important for M&E as well as informing training activities, drug procurement, strategic plans etc.
- NTP should have a designated child TB working group that oversees and facilitates child TB activities

A few points to keep in mind…….

- Tuberculosis (TB) in children is common wherever TB is common in adults i.e. TB endemic settings
- TB is an important cause of illness and death in children in many TB endemic countries
- An understanding of the risks for infection and disease due to TB in children is critical for improved diagnosis and prevention
- The HIV epidemic has increased the burden of child TB and the clinical challenges
- The main benefit of neonatal BCG is protection against severe disseminated TB in children
- NTP should register and report all child TB cases!

Revision and self-assessment

List three important risk factors for TB exposure and infection

(3 marks)

List three important risk factors for developing TB disease if infected

(3 marks)

True or False: (4 marks)

1. The risk of infection for children has been reduced in the HIV endemic setting
2. Extrapulmonary TB is usually more common than pulmonary TB in children
3. Careful contact history is an important diagnostic tool in young children with suspected TB
4. Neonatal BCG immunisation has limited protective efficacy against TB in children