TRAINING MODULE ON **MALARIA CONTROL**

Epidemiological approach for malaria control

GUIDE FOR **TUTORS**

World Health Organization

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Second edition

World Health Organization

Contents

Foreword

Malaria is a major global public health problem and a leading cause of morbidity and mortality in many countries. Malaria caused an estimated 219 (range 154–289) million cases and 660 000 (range 490 000–836 000) deaths in 2010. Approximately 80% of the cases and 90% of the deaths occur in Africa while the remaining cases and deaths occur mainly in the South-East Asia and Eastern Mediterranean Regions.[1]

The World Health Assembly and Roll Back Malaria (RBM) targets for malaria control and elimination are to achieve at least a 75% reduction in malaria incidence and deaths by 2015.

Elimination of malaria is defined as the reduction to zero of the incidence of locally acquired infection by human malaria parasites in a defined geographical area as a result of deliberate efforts. Elimination programmes require more technical malaria expertise than standard malaria control programmes, and require by national expertise in malaria epidemiology and entomology.

To achieve the objectives of malaria control and elimination programmes, appropriately planned and targeted delivery of essential malaria interventions is critical, including: diagnostic testing and prompt treatment of confirmed infections with effective artemisinin-based combination therapy (ACT); chemoprevention of malaria in pregnant women (Intermittent preventive treatment during pregnancy – IPTp), infants (Intermittent preventive treatment during pregnancy – IPTi) and children (Seasonal malaria chemoprevention – SMC), where appropriate; and application of appropriate vector control interventions, particularly the use of insecticide- treated nets (ITNs/LLINs) and indoor residual spraying (IRS).

This training module on the epidemiological approach for malaria control has been developed to support the staff involved in the planning and management and in the monitoring and evaluation of malaria control and elimination programmes.

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[1] WHO (12). *World Malaria Report.* Geneva, World Health Organization. http://www.who.int/malaria/publications/world_malaria_report_2012/en/index.html

Abbreviations

ABER	Annual blood examination rate
ACT	Artemisinin-based combination therapy
ANC	Antenatal clinic
API	Annual parasite index
CFR	Case fatality rate
CSP	Circumsporozoite protein
DALY	Disability-adjusted life year
DHS	Demographic and health survey
EIR	Entomological inoculation rate
ELISA	Enzyme-linked immunosorbent assay
GIS	Geographical information system
HBI	Human blood index
IEC	Information, education and communication
IPT	Intermittent preventive treatment
IRS	Indoor residual spraying
ITN	Insecticide-treated mosquito nets
IVC	Integrated vector control
KAP	Knowledge, attitudes and practices
LLIN	Long-lasting insecticidal nets
MDA	Mass-drug administration
MICS	Multiple indicator cluster survey
MIS	Malaria indicator survey
NGO	nongovernmental organization
NMCP	National malaria control programme
PCR	Polymerase chain reaction
POPs	Persistent organic pollutants
PPOA	Preparedness plan of action
RBM	Roll Back Malaria
RCT	Randomized clinical trial
RDT	Rapid diagnostic test
SPR	Slide positivity rate
SMPH	Summary measures of population health
TPR	Test positivity rate
WHO	World Health Organization

Acknowledgements

Development of the module

The content of the module is based on current WHO guidelines and other evidence-based technical documents.

This training module is arranged in four parts. The main framework of each part was developed at different times, and has been evaluated and reviewed in various separate education programmes. The decision to combine these four parts into a training module was made through technical expert meetings held in 2008 and 2009.

The training module was updated under the guidance of technical experts representing malaria training and academic institutions, malaria researchers, country programme managers, and WHO regional offices, who guided the process of reviewing and updating the module. The process included the following steps:

▸ Three consultations of technical experts (7–9 April 2008; 14–16 October 2008 and 15–17 April 2009) were held to review the existing WHO training materials on the epidemiological approach for malaria control and elimination, and to identify areas for update in view of the developments of new tools, technologies and strategies for malaria control and the changing disease epidemiology.

▸ Technical experts were commissioned to incorporate the recommended updates in the module.

▸ The revised module was then reviewed for content and completeness by the technical experts, the WHO technical staff and additional external experts in malaria epidemiology.

▸ The updated module was field-tested in several national and international courses.

▸ Based on feedback from field tests, and in consultation with technical experts, the text was finalized for publication.

Introduction

This *Guide for Tutors* is designed primarily to help those responsible for the training on epidemiological approach for malaria control of health personnel responsible for the planning, implementing and evaluation of malaria control activities. In this module, tutor or facilitators will rely on intensive exchange of knowledge and experiences between the participants. After completion of the training course the participants will each receive a copy of the *Guide for Tutors* for future reference. For individual study, trainees can be provided with both the Guide for Participants and the *Guide for Tutors*, the latter serving as an "answer book". Ideally this module should be learned through group learning, and not through individual study. This module uses a problem-solving approach in which the tutor and facilitator provide minimal assistance to the participants in carrying out the exercises.

Potential users of this training module

The module is designed for health professionals involved in planning, implementing, and monitoring the malaria control and elimination programmes. The target group of the module include medical officers, medical assistants, public health officers, environmental health officers, parasitologists and entomologists involved in malaria control and working either in a national programme or non governmental or civil society organization supporting or complementing the work of the national programme.

Design and content of the training module

The training module is intended to facilitate the teaching of malaria epidemiology for better prevention and control, planning and management. The principal objectives of the training are listed in the Introduction of the *Guide for Participants*, which the tutor needs to explain at the beginning of the course. This module is designed to stimulate active learning by working through the series of exercises which will be carried out on the basis of the *Guide for Participants*, usually in small groups. The exercises focus on different aspects of malaria epidemiology using problem-based learning approaches, and the solutions to these particular problems are provided in this *Guide for Tutors*. The answers provided are often indicative and may not be the unique solutions to the problems posed.

Learning objectives summarize the knowledge, skills and competences that each participant should have acquired by the end of each Learning Unit. The tutor and facilitators should be satisfied that each trainee has achieved the stated objectives before proceeding to the next Learning Unit (methods of evaluating progress are described later).

Responsibility for running the course

The tutor is responsible for organizing and running the course. The *Guide for Participants* and *Guide for Tutors* will assist, but the final results will largely depend upon the tutor's efforts. Whether the tutor is organizing and running such a course for the first time, or has had extensive teaching experience, the *Guide for Participants* and the *Guide for Tutors* should be used together in conducting the course.

The job will be simplified, and teaching more effective, if the tutor is assisted by colleagues who act as facilitators throughout the course. The facilitators should have knowledge and experience in the subject. The class can be divided into small groups of 4–8 participants, with one facilitator allocated to each group. This allows greater interaction between the participants and the facilitators resulting in better learning and understanding. The facilitator's role is to explain the questions asked in the small group exercises, as required, and facilitate the discussions to keep them on the focus.

As the overall manager of the training module, the tutor will be responsible for designing the timetable, explaining the learning tasks to the participants, and discussing with the facilitators what help will be required from them in explaining or demonstrating activities and watching the performance of the participants. The facilitators should also be ready to admit to participants when they are unable to answer a question and refer it to the tutor. (Reassure the facilitators that no one person can be expected to know everything about every subject.)

Many problems can be avoided by giving the facilitators plenty of time to read the *Guide for Participants* and *Guide for Tutors*, other relevant resources or handouts and to discuss any parts that may need clarification. It may be helpful for the tutor and the facilitators to go through the module together; the tutor may then assess their knowledge through questions and discussion.

Why a *Guide for Participants* is provided

Providing participants with a full set of notes ensures that:

▶ All participants have exactly the same basic materials and guidelines on how to proceed with exercises;

▶ Tutor and facilitators can refer to any part of the *Guide for Participants* knowing that all participants can find the right page quickly;

▶ Participants can spend more time reading the notes, and therefore have a greater opportunity for thinking, discussion and formulation of ideas;

▶ There is no possibility of participants making errors in note-taking;

▶ After the course, each participant can keep a copy of the *Guide for Participants* and the *Guide for Tutors* as a helpful reference in his or her daily work and perhaps also to use in teaching others.

Running the training course

To facilitate learning by all participants, the teaching of this subject will encourage the participants to learn from each other as well as from the tutors and facilitators, particularly in the group discussions. Each participant will therefore be expected to take part actively throughout the course. In working through the Learning Units, there will be opportunities to put into practice, individually or collectively, what has been learnt.

Presentations

Formal presentations (e.g. lectures) will usually be kept to a minimum and will be replaced by limited introductory remarks by the tutor at the beginning of each subject and short examples to overcome points of common difficulty. Most of the information provided in such sessions is already contained in this guide and the participants will not need to take extensive notes. A lecture will usually be combined with a demonstration. The participants will be asked frequently to present their work in plenary session. This will provide experience on how to make a presentation, both by presenting and by learning from the observations and suggestions made during discussion.

Small group work

Most of the work will be carried out in small groups, e.g. 2 or 3 groups of 4–8 participants. Preferably each group should have its own room, with the following: computer with projector or slide projector or overhead projector, whiteboard, blackboard, and flipcharts. For each learning unit the group selects among its members a moderator and a rapporteur by rotation, so that each participant should perform both functions at least once.

The sessions provide good opportunities for participants to express their opinions, develop ideas and learn from one another. The participants will usually have different backgrounds, in terms of training and experience, so that they should have much to learn from each other. The exchange of experiences among participants contributes to most of the training material, with the *Guide for Participants* providing a lead for discussions and work. The moderator chosen by the members of each group will lead discussions on the specific subjects proposed in the Learning Units.

At the end of the group work the results and conclusions from each group will be presented in a plenary session by the moderators and discussed by all participants, with comments by the tutor. The group compositions can be changed occasionally or left the same throughout the course, as preferred by the tutor.

Training facilities

A number of basic facilities and equipment must be organized before training can begin. In some countries these are readily available but in others it may be necessary to improve or modify existing resources. However, the training should not be delayed unnecessarily because of lack of the best equipment.

One large room should be available for plenary presentations and discussions. The small groups may use separate rooms, or work in the main room, according to availability and preference of the tutor. Whatever the conditions, the tutor should ensure that the participants are as comfortable as possible in the circumstances, and much can be achieved even with relatively limited facilities.

Teaching equipment

For teaching sessions and group discussions, the following items should be available:

- overhead projector

- slide projector or computer with projection

- screen for projection (a white sheet is an adequate substitute but the white-board is unsuitable because it will reflect projected light)

- flipcharts – one for each small group of participants. Supplies of "butcher's paper" or "newsprint" are usually cheap and readily available.

- chalk board or white board

- chalks for blackboard or marker pens for white-board, in a selection of colours.

- acetate sheets for overhead projector

- coloured marker pens for acetate sheets (including some permanent markers for diagrams that may be kept)

Participants' supplies

The equipment listed below should be provided for each participant. Where supplies have to be ordered, this should be done well in advance of the course; many items are difficult to obtain at short notice.

- Copy of the *Guide for Participants* and *Guide for Tutors* (the latter to be given at the end of the course)

- Notebook: this should be used only for occasional notes or instructions; in general note-taking should not be necessary during training sessions

- Sheets of paper for the exercises during the working groups

- Ballpoint pen

- Set of pencils (medium-hard graphite, plus red, blue, brown and black) for during charts and graphs during practical sessions

- Pencil sharpener

- Eraser

- Ruler

- A simple hand-held calculator

Syllabus and timetable

The table of contents represents the syllabus – the list of subjects to be covered – for the training course. The tutor should go through each of the Learning Units and assess how much time will be needed and what kind of training activity would be most suitable for the topic.

The course is designed to include the following learning activities:

Group discussion

Once participants become accustomed to group discussions, the two-way exchange of information between them and the facilitators makes this a very effective learning activity. People share their knowledge and experiences with the rest of the group and stimulate each other's thoughts on the subject in hand.

Practical exercises

Practical exercises may be done individually or in groups in the classroom. Their purpose is to give participants the opportunity to practise the procedures involved. The more practice they have, the more competence they will acquire

Demonstrations, examples

These are designed to reinforce the learning process. Clear examples help to clarify concepts and establish principles. The tutor and facilitators should have many examples ready to use, but in addition trainees should also be invited to give examples. This is a much stronger reinforcement.

Once the amount of time that needs to be spent on each unit has been calculated, all the various learning activities must be fitted into the framework of the training programme. The duration of the programme may be something over which the tutor has little control; for instance, the programme may have to be limited to fewer days because of shortage of funds, although the planned duration may have been longer. In such cases, the tutor and the facilitators will need to spend time reorganizing the timetable so that all the learning activities can be fitted into the time available.

In planning the timetable, time should be allowed for evaluation both during and after the course, and for the hidden activities, such as getting settled into group work, delays in transportation to the training facility etc.

The module is designed for 12 days of training (see proposed timetable in page 8). As the course progresses, the tutor may consider that further discussion is necessary on some topics. These activities can be fitted into the "free" periods and a discussion session on the afternoon of the last day can also be used in a flexible manner.

Use of the *Guide for Tutors*

Participants will follow the group training activities using the *Guide for Participants* plus other materials provided by the tutor. As noted above, a copy of the *Guide for Tutors* will be given to each participant at the end of the training. The way in which the tutor and facilitators should make the best use of the guides will become apparent in working through the training module.

When qualified facilitators are not available the tutor must, to the extent possible, replace the facilitators. The guides may also be used in combination by individuals for study and reference.

Evaluation

Judging whether or not the course was successful involves answering the following questions:

▸ *How well did the participants learn?*

▸ *How did the participants view the training?*

Evaluation of the participant

Whether this module is used for group training or individual learning, assessment of progress made by the trainee in gaining skills and competence in the subject matter is essential. This can be accomplished by means of a pre-test and a post-test using a multiple-choice questionnaire (MCQ). The pre-test will be given before the trainee reads the *Guide for Participants* and the post-test will be administered after all the Learning Units have been completed. Since the answers to the questions and to the exercises are included in this *Guide for Tutors*, it is essential that participants do not have access to it until after the training activity has been completed. During the pre-and post-test evaluations, participants must be seated apart from one another and work alone.

The results of the pre-test can be used in two ways. The tutor may use the test to ascertain the general level of knowledge on the subject in the group, and have an indication of common weak areas that need emphasis or re-emphasis. It could also be used to identify individuals who might be used as facilitators for specific subject areas. The other major use for the pre-test is as an individual base-line comparator for measuring the gain in knowledge, skills and competence at the end of the training as revealed by the post-test.

If the test results are to be valid, the questions in the pre-tests and post-tests should be of the same degree of difficulty and both tests should be given under the same conditions and the same length of time. The only way to ensure that the questions in the post-test are of equal difficulty to those in the pre-test is to give the same questions in a different order, and in the case of MCQ questions, with the answers also in a different order. It is therefore essential that the pre-test papers be collected and retained (not handed back to the participants). The participants do not need to know the results of the pre-test until the end of the training when it is used to assess progress.

The tutor is encouraged to develop a bank of questions that can be used for pre- and post-testing for subsequent training sessions. The answers are scored equally because each question is considered, in this instance, to be of equal value. The preferred answers have been provided but in some cases alternative responses are acceptable, and these have been noted.

Evaluation of the training by the participants

The entire training activity, including the organization and content of the course, the suitability of the learning methods, and the quality of the teaching and training materials, competence of the tutors and facilitators will be assessed by the participants through a questionnaire, and at a plenary feedback and discussion session after the questionnaires have been completed. This evaluation will take place at the end of the training period in order to provide as much feedback from the participants as possible. All participants are encouraged to make suggestions for improvement on the part of the tutor and facilitators as well as in the content of the course and the training facilities.

Feedback provided through this exercise allows the tutor to assess how well the training has been received and to make any modifications that seem necessary for improving future programmes.

Certificate

The attendance and performance of each participant should be noted during the course and the record retained for future reference. Participants should receive a certificate of successful completion of the training course.

Note: it is important to stress to the participants that they must take time to read each Learning Unit carefully before attending the class in which it will be considered. The time allotted for the course is based on the assumption that the corresponding unit in the Guide for Participants has been studied in advance.

SUGGESTED TIMETABLE

TIME	DAY 1	DAY 2	DAY 3	DAY 4	DAY 5	DAY 6
08:30–10:00 PRE-TEST	**Introduction to the training LU 1**	LU 4	LU 6	Field work: conducting the KAP* study	LU 7	LU 10
10:00–10:30			BREAK			
10:30–12:00	LU 2	LU 5	LU 6 (cont'ed)	Field work: conducting the KAP study (cont'ed)	LU 7 (cont'ed)	LU 10 (cont'ed)
12:00–13:30			BREAK			
13:30–15:30	LU 2 (cont'ed)	Practical: computer and group work for **LUs 3–5**	Field work: design of a KAP study*	Field work: **analysis of the KAP studies and conclusions**	LU 8	LU 11
15:30–16:00			BREAK			
16:00–18:00	LU 3	Practical: computer and group work for **LUs 3–5**	Field work: development of a questionnaire for KAP survey	Field work: presentation of findings of the KAP survey. Application of **LUs 1–6**	LU 9	LU 11 (cont'ed)

TIME	DAY 7	DAY 8	DAY 9	DAY 10	DAY 11	DAY 12
08:30–10:00	LU 12	LU 13 (cont'ed)	LU 15 (cont'ed)	LU 17	LU 19 (cont'ed)	LU 21 (cont'ed)
10:00–10:30			BREAK			
10:30–12:00	LU 12 (cont'ed)	LU 14	LU 16	LU 18	LU 20	LU 22
12:00–13:30			BREAK			
13:30–15:30	LU 13	LU 15	LU 16 (cont'ed)	LU 18 (cont'ed)	LU 20 (cont'ed)	LU 23
15:30–16:00			BREAK			
16:00–18:00	LU 13 (cont'ed)	LU 15 (cont'ed)	LU 16 (cont'ed)	LU 19	LU 21	**Post-test and evaluation of the course**

* KAP: knowledge, attitude, perception

LEARNING UNIT **1**

Introduction to epidemiology

Learning Objectives:
by the end, participants should be able to...

- Provide a definition of *epidemiology*

- Define descriptive studies and describe their purpose

- Describe the major types of descriptive studies and their primary uses

- Describe the major types of analytic studies

- Provide a definition of *random error*, *bias*, *confounding* and *validity*

After allowing approximately 20 minutes for participants to read through the Introduction to epidemiology.

For this Learning unit, the tutor should provide a definition of epidemiology and briefly describe the purpose of various descriptive and analytic studies. The tutor should check that participants have understood the role of these studies for the control of tropical diseases. Stimulate discussion; be particularly careful to explain any items that might be misunderstood, so that misconceptions can be eliminated from the outset.

Answers

Exercise 1.1

1.	Descriptive study	h.	Describes patterns of disease occurrence by time, place, and person
2.	Analytic study	g.	Test hypotheses concerning the relationship between suspected risk factor and an outcome
3.	Case series	f.	Describes characteristics of persons with a similar diagnosis
4.	Ecological study	e.	Compares disease frequencies in a population at different points in time as a function of a particular exposure
5.	Cross-sectional study	d.	Examines the relationship between a disease and other variables of interest in a population at a particular point in time
6.	Case-control study	c.	Start with cases of disease and unaffected controls and determine rates of exposure to risk factors in each group
7.	Cohort study	b.	Start with exposed and unexposed groups and determine if rates of occurrence of outcome in the two groups differ
8.	Interventional study	a.	Subjects are randomized into exposed and unexposed groups and followed over time to compare rates of disease development

Exercise 1.2

1.	Random error	d.	Large divergence of a study result from the true value due to a small study sample size
2.	Selection bias	c.	Assessing outcomes of uncomplicated malaria among patients admitted to a hospital
3.	Information bias	b.	Collecting information regarding malaria treatment through a household survey conducted months after the treatment was received
4.	Confounding	a.	Studying the relationship between bednet use and occurrence of malaria if age is associated with both use of bed nets and susceptibility for symptomatic malaria infection

Exercise 1.3

a) High validity and low reliability

LEARNING UNIT **2**

Ratios, proportions and rates

Learning Objectives:
by the end, participants should be able to...

■ Define the terms ratio, proportion and rate

■ Differentiate between incidence rate and prevalence rate, and give examples of their use

■ Calculate ratios, proportions and rates using appropriate numerators, denominators and constants

■ Apply the concepts of relative risk and risk differences

As an introduction to the unit, the tutor should describe briefly the terms mentioned above, the purposes for which these measurements are used and their primary users.

The presentation should be illustrated with simple examples.

Exercises

For conducting the exercise session it is preferable to have the participants work individually. However, for any who are unfamiliar with the calculations, it may be useful to have them work in pairs with those who have greater facility. The tutor and facilitators may wish to circulate among the participants as they work to help anyone who is having difficulties.

For some of the calculations, the participants may write their results in a slightly different way than expressed here. For example, 9/100 can also be expressed as 90/1000. In general, one should either follow convention (e.g. infant mortality is always expressed per 1000 live births) or use the number that leaves one digit to the left of the decimal point for the smallest rate in a series.

Answers

Exercise 2.1

a. *The number of cases has increased steadily, and in 2005 there were more than twice as many cases as in 2001.*

b. *The incidence rate per 100 is calculated by taking the number of cases divided by the population and multiplying by 100.*

Year	Rate per 100
2001	6.3
2002	6.2
2003	6.2
2004	6.3
2005	6.5

The rate has been relatively stable over the 5-year period, although it appears to be increasing slightly in 2005.

c. *While the number of cases has increased very rapidly, so has the population. The rate, therefore, has remained relatively stable.*

d. *The rate is the most appropriate measure to monitor trend, because it takes into account the changes in population size, provides a more realistic idea of the amount of disease in the population.*

Exercise 2.2

a. *The incidence rate in Province Z is 9.0/100, much higher than the rate of 6.5/100 seen in Province X.*

b. *Although the disease rate is much higher in Province Z, this province has a much smaller population. A decision on allocation of funds will depend on a variety of factors. If the goal of the malaria*

programme is to prevent as many cases of malaria as possible, funds may be better spent in Province X, where the rate is somewhat lower but the population and total number of malaria cases is much larger. One should also find out if the rate in Province Z is stable or is changing rapidly.

Exercise 2.3

a. The parasite rate in Region A is 47%.

b. It is a prevalence rate since it measures all cases of parasitaemia at the time of the survey, some of which may have just occurred and some of which are likely to have been going on for some period of time.

Exercise 2.4

a. Ratio = 49 140:23 250 = 2.1:1 (division of each number by 23 250)

b. % males   = [49 140 / (49 140 + 23 250)] = 0.679 = 67.9%

   % females   = [23 250 / (49 140 + 23 250)] = 0.321 = 32.1% or: 1 – 0.679 = 0.321 = 32.1%

Exercise 2.5

a. The age group 15 years and over.

b. The 1–4 year age group.

c. The age-group ≥15 years accounts for half of the cases, but also for over half of the population. The group at greatest risk of developing disease is not the ≥15 year-old group, it is the 1–4-year olds.

For planning hospital beds or ordering antimalarial drugs, the percentage value may be more useful.

For deciding who is at risk for purposes of an intervention programme, the age-specific incidence rate will be more useful.

Exercise 2.6

a. The relative risk is the ratio of the 2 rates:

   (10 / 1000) / (2 / 1000) = 5

b. Gem miners are 5 times more likely to contract malaria than farmers living in the same villages.

c. The risk difference is obtained by subtracting the 2 rates:

   (10 / 1000) – (2 / 1000) = 8 / 1000

d. 8 of the 10 cases likely to occur among 1000 gem miners can presumably be attributed to going into the forest; if they stopped going into the forest, their disease rate would drop from 10 cases per 1000 to 2 cases per 1000.

LEARNING UNIT **3**

Data presentation: tables, graphs and charts

Learning Objectives:
by the end, participants should be able to...

- List the features of good tables, graphs, and charts
- Plot and label a series of tables, graphs and charts correctly from raw data
- List the uses for semi-logarithmic presentation

In introducing the session, the tutor should explain the importance of good data presentation. Each of the methods should be described in detail using examples to illustrate them clearly. Time should be allowed for questions.

Exercises on data presentation

The first 3 exercises should be done one at a time with the whole class. The tutor should allow ~2 minutes for participants to think about the answers, and then request the answers from the class. Not more than 5–10 minutes should be allowed for these exercises, as the graphing exercise will take a lot of time. Instructions for organizing the groups for practical graphing are given at the beginning of Exercises 4 and 5 in this Unit.

Answers

Exercise 3.1

Advantages of using surveillance data:

▶ Readily available

▶ Usually collected from many different types of health facilities (health stations, clinics, hospitals, etc.) and therefore may be more representative than data abstracted from individual clinics or hospitals.

Disadvantages of using surveillance data:

▶ Changes over time may reflect changing reporting practices, changes in diagnosic testing, changes in case definition, etc. rather than actual disease trends.

▶ The information available is often not sufficiently detailed.

▶ Useful for looking at trends, but may not give an accurate picture of the relative frequency of the individual diseases, since this may be influenced by the accuracy of diagnosis, or the likelihood that someone with this disease will seek medical care, etc.

Other sources of surveillance data:

▶ Hospital discharge data. This provides more information on who has the disease, but hospitalized cases may represent only a small fraction of the total cases and may not be representative of all cases of a disease.

▶ Data from health surveys in the population (household survey). These are more representative than either of the above sources and can provide more information on who has the disease, but do not allow the assessment of trends, unless more than one survey has been performed over time.

Exercise 3.2

The DMO also needs the number of children in the district each year so that the disease rates can be calculated. This is particularly important in areas with rapid population growth or significant in- or out-migration.

Exercise 3.3

Knowing the population of children < 5 years-of-age in 2000 and the rate of natural increase in the population allows the DMO to estimate the population for each year.

The 2000 population in this age-group was 56 650, with an annual rate of increase at 3.3% per year. The 2001 population can be estimated at 56 650 × 1.033 = 58 520

2002: 58 520 × 1.033 = 60 450   *2003:* 60 450 × 1.033 = 62 450

2004: 62 450 × 1033 = 64 510   *2005:* 64 510 × 1.033 = 66 630

(results rounded to the nearest 10)

Note for Exercises 3.4 and 3.5

Exercises 3.4 and 3.5 are best done with 3 groups of 2 participants each. If there are more in a group, the two pairs should perform the same task independently (i.e. if there are 8 participants, 2 pairs will independently prepare the graph for question 4a; one pair should do 4b, and the other pair should do 4c).

Assuming there are 3 groups of 6, each with 3 pairs, the tasks should be distributed as follows:

Group 1, pair 1	=	4a, 5a for Disease A
Group 1, pair 2	=	4b, 5b for Disease A
Group 1, pair 3	=	4c, 5c for Disease A
Group 2, pair 1	=	4a, 5a for Disease B
Group 2, pair 2	=	4b, 5b for Disease B
Group 2, pair 3	=	4c, 5c for Disease B
Group 3, pair 1	=	4a, 5a for Disease C
Group 3, pair 2	=	4b, 5b for Disease C
Group 3, pair 3	=	4c, 5c for Disease C

Thus, each group will have a full set of graphs showing the incidence, mortality, and case fatality rate for "their" disease.

Ask the participants to work in pencil. They should be provided with arithmetic and if possible with semi-log paper, which can be photocopied. The participants should work individually and decide how they want to do the graphs. For those working on semi-log paper, the tutor and facilitators may need to help them decide how to set up the cycles and how to use the paper. Some will choose arithmetic and others semi-log paper for the same graph; it will be interesting to compare the patterns observed with each.

As the participants complete their work, the tutor and facilitators should check that all graphs have adequate titles and that axes and curves are clearly labelled.

U3

Exercise 3.4
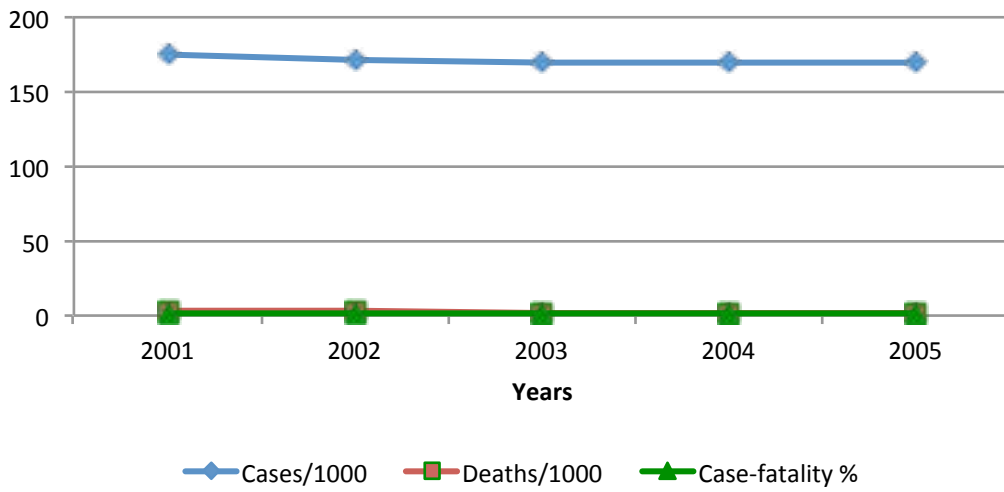
Figure 3.1a Incidence, mortality and case fatality for disease A, District W, 2001–2005
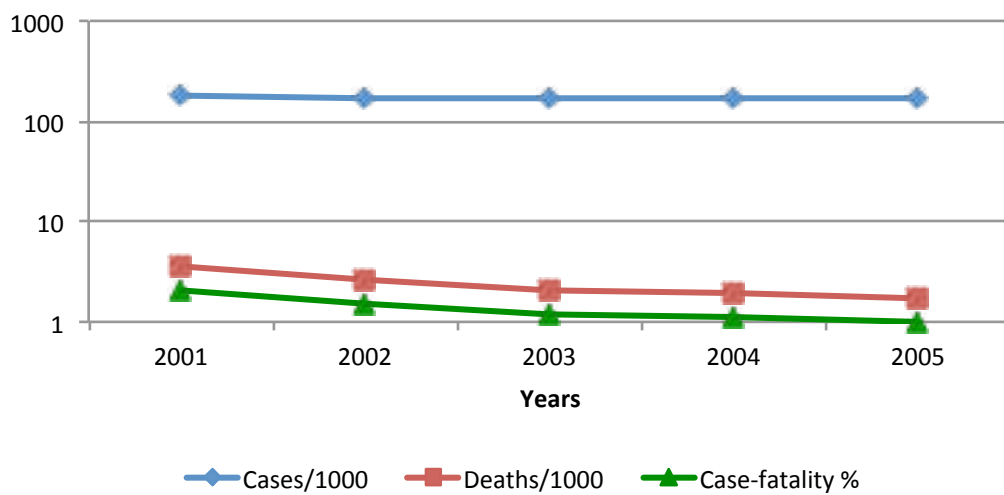
Figure 3.1b Incidence, mortality and case fatality for disease A, District W, 2001–2005
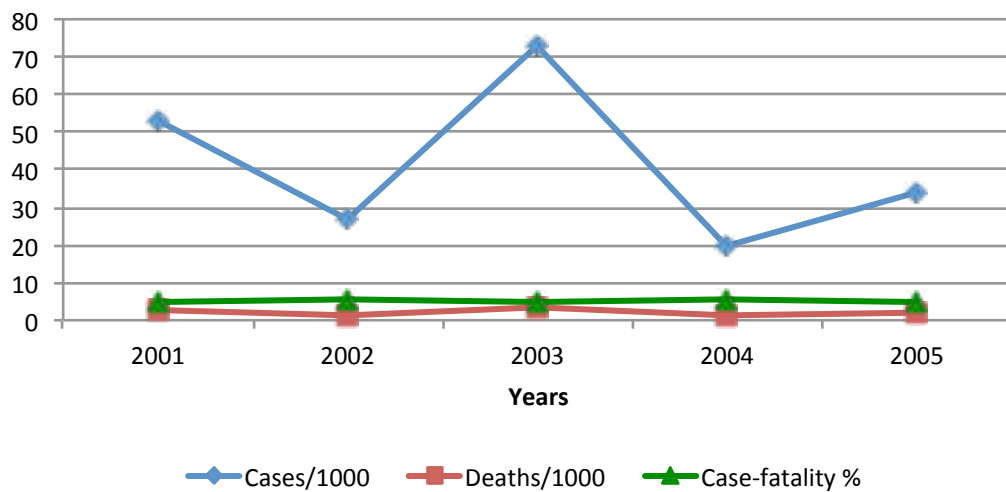
Figure 3.2a Incidence, mortality and case fatality rates for disease B, District W, 2001–2005
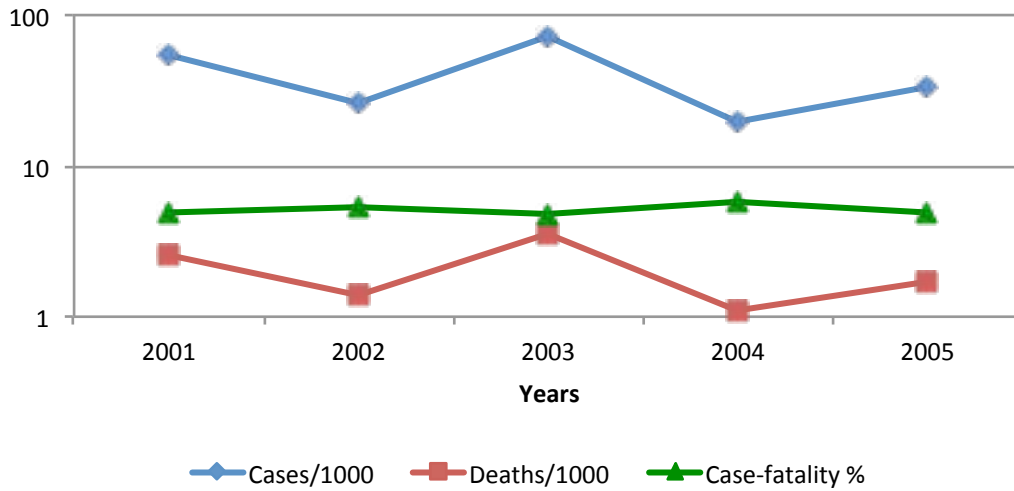
Figure 3.2b Incidence, mortality and case fatality rates for disease B, District W, 2001–2005
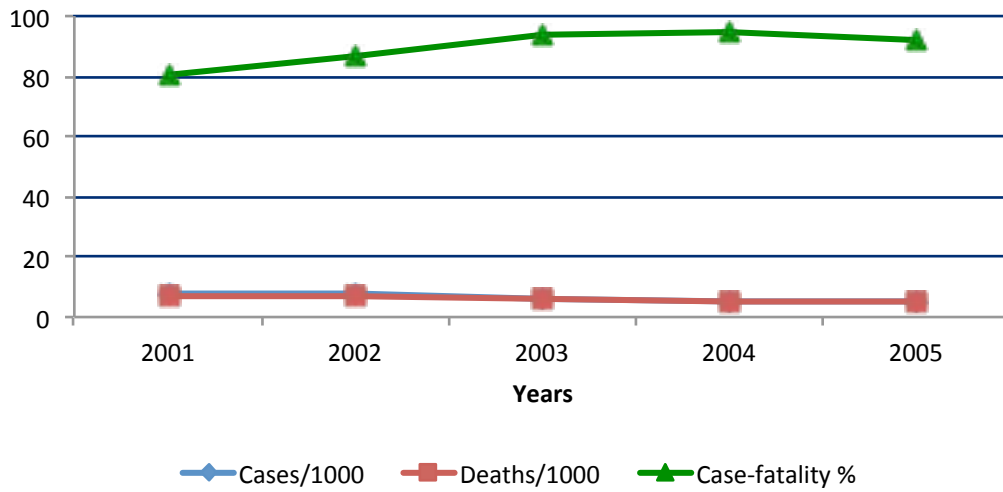
Figure 3.3a Incidence, mortality and case fatality for disease C, District W, 2001–2005
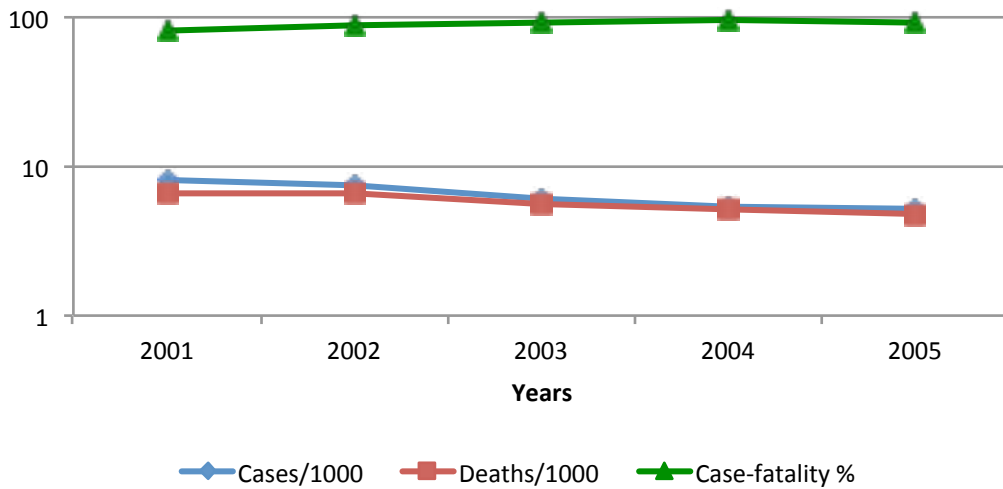
Figure 3.3b Incidence, mortality and case fatality for disease C, District W, 2001–2005

U3
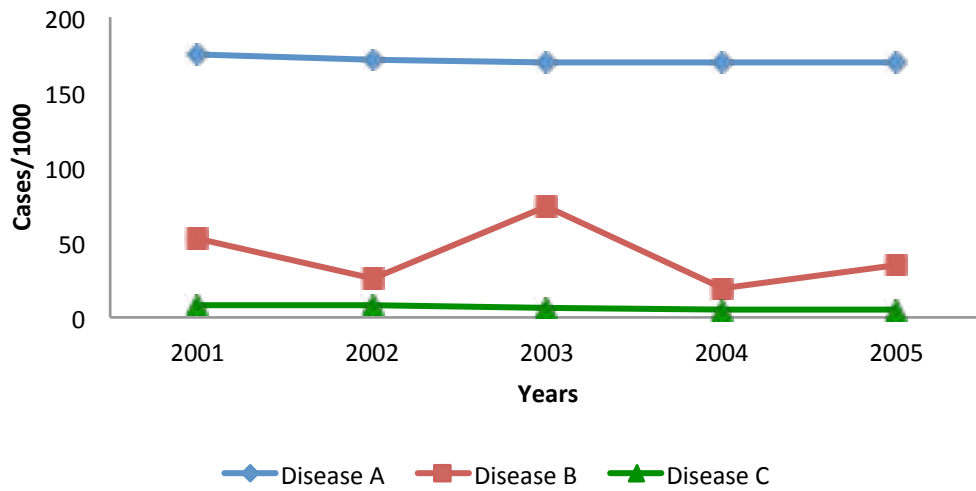
Figure 3.4a Incidence of diseases A, B and C, District W, 2001–2005
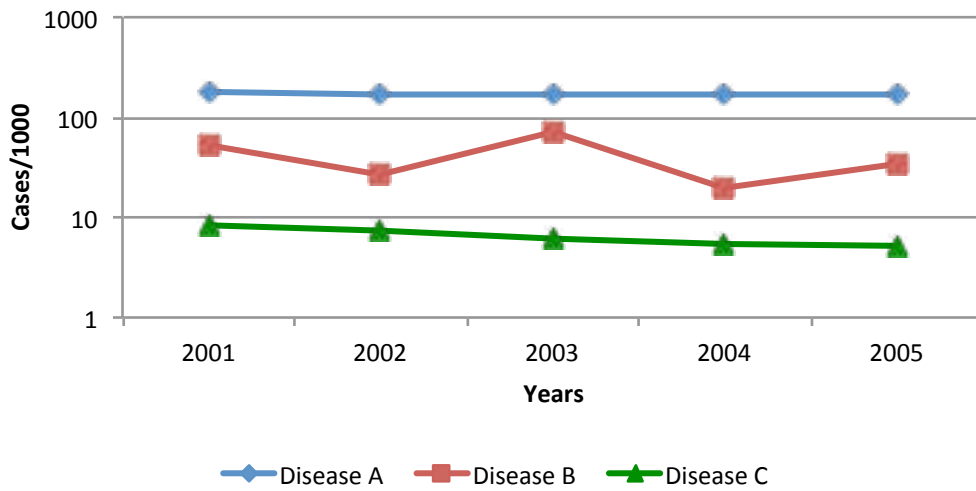
Figure 3.4b Incidence of diseases A, B and C, District W, 2001–2005 (Logarithmic scale)
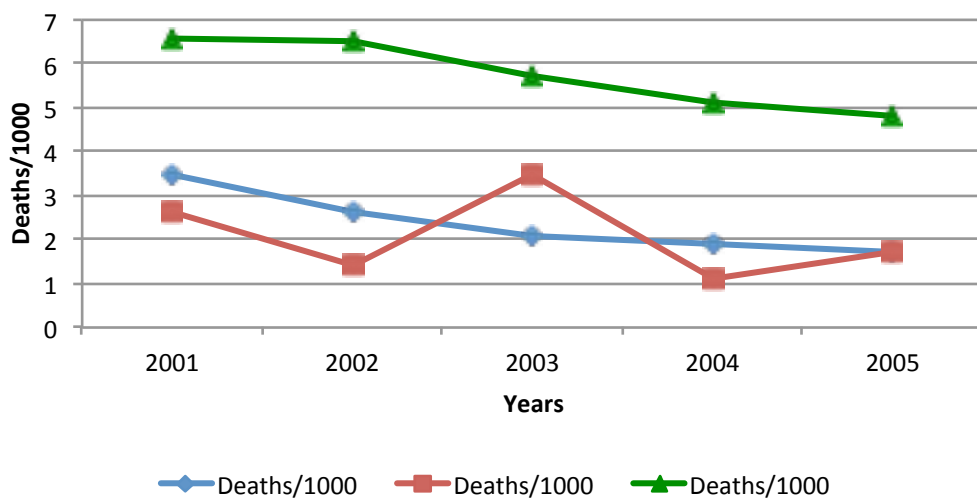
Figure 3.5   Incidence of death for diseases A, B and C, District W, 2001–2005
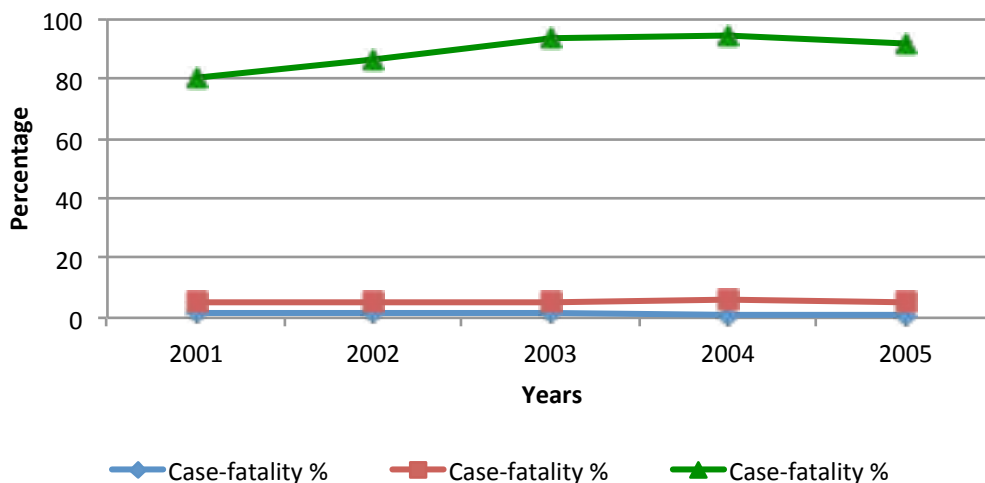
Figure 3.6a Case-fatality rate (%) for diseases A, B, C, District W, 2001–2005
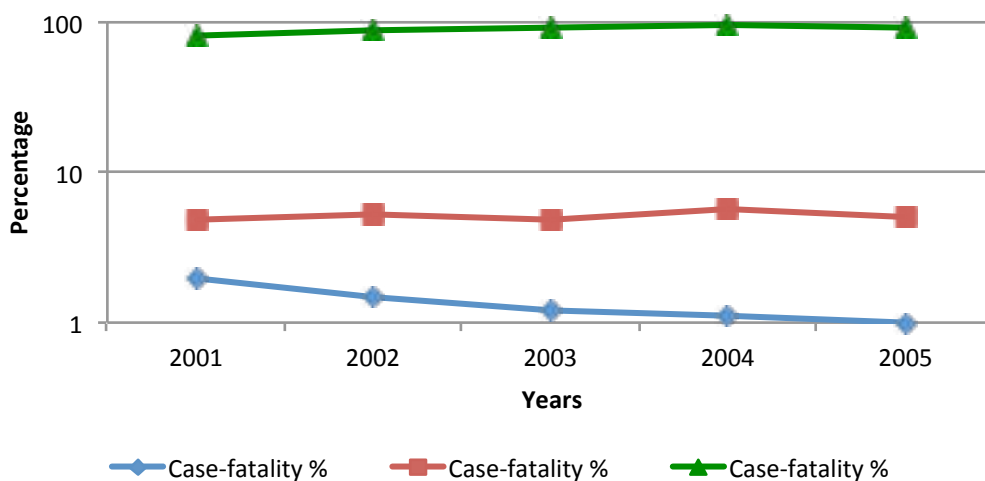
Figure 3.6b Case-fatality rate (%) for diseases A, B, C, District W, 2001–2005 (logarithmic scale)

Exercise 5
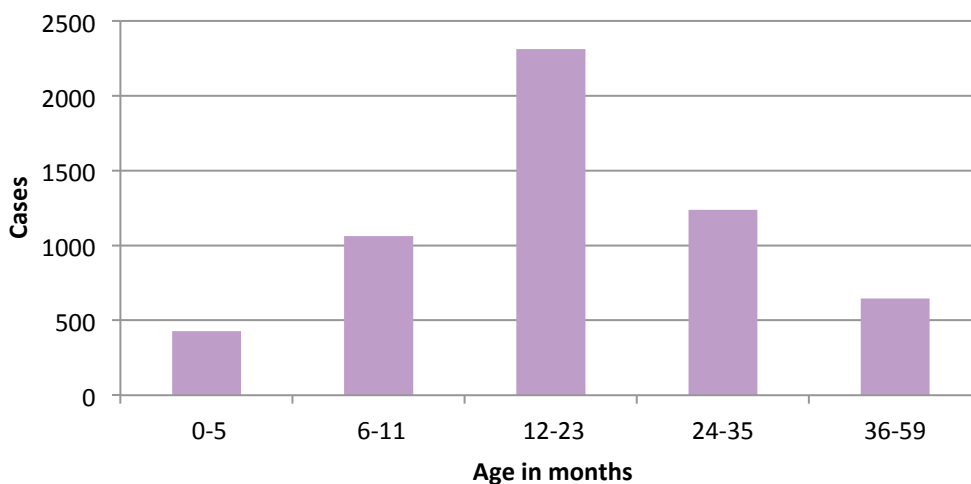
Figure 3.7   Age distribution for disease A, District W, January–December 2001
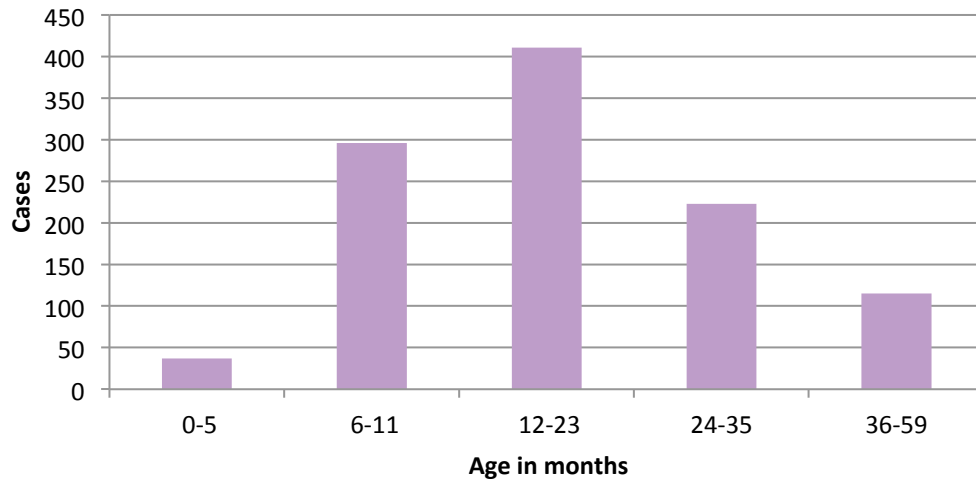
Figure 3.8   Age distribution for disease B, District W, January–December 2001
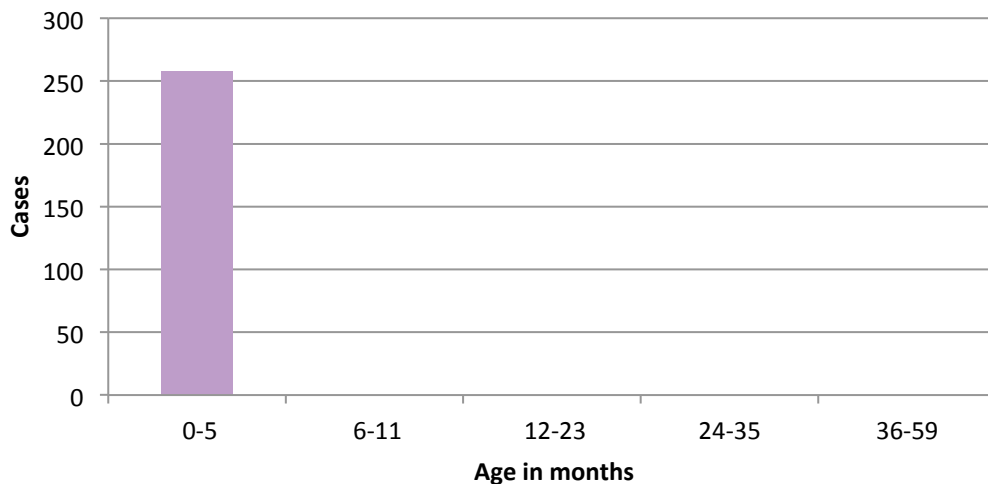
Figure 3.9   Average monthly distribution for Diseases A, B and C, District W, 2001

Exercise 3.6

In commenting on the graphs drawn by the participants at the end of their presentations (Table 3.1 in the Guide for participants, the tutor may wish to review the advantages and disadvantages of arithmetic versus semi-log paper). Below is the possible descriptions of the trends for incidence, mortality and case fatality as well as age distribution and seasonality of the three diseases.

Disease A is diarrhoea (high incidence, low mortality, low case fatality; seasonal distribution also common with diarrhoea, as is age distribution with peak after weaning age). Recent declines in mortality may be due to improved treatment. Incidence is largely unchanged; it might be reduced by improvements in water sanitation, hand washing, etc.

Disease B could be either malaria or measles, although measles is much more likely given the cyclical trends over the years. This disease is characterized by fairly high incidence, low but non-negligible mortality, and a higher case-fatality rate than for disease A. The age distribution is also fairly characteristic for measles, as it is a seasonal pattern. The decline appears to be due

to immunization, without much improvement in treatment, as indicated by the stable case-fatality rate.

Disease C is neonatal tetanus based on its relatively low incidence, very high case fatality, unusual age distribution, and lack of seasonality. The changes over time may be due to better maternal immunization coverage and/or better delivery practices. The increase in case fatality may be real and due to the cases being more severe or to poorer case management. On the other hand, the numbers for this disease are relatively small, and the year-to-year changes may simply reflect random variation.

U3

LEARNING UNIT 4

Measures of central tendency

Learning Objectives:
by the end, participants should be able to...

■ Define the terms mean, median, and mode

■ Describe the advantages and disadvantages of using the mean versus the median

■ Calculate means, medians and modes from individual and from grouped data

In introducing the session, the tutor should define the terms mean, median and mode and describe the advantages and disadvantages of using the mean versus median. The participants should then work individually on the exercises provided in the *Guide for Participants*.

Exercises on measures of central tendency

If the group includes participants who are not familiar with the calculations, it may be preferable to have them work in pairs with someone who is more experienced. The tutor and facilitators may wish to circulate among the participants to answer any questions or work with any who may be having difficulties.

Answers

Exercise 4.1

a. *The mode is 3 years, which is represented 5 times in the data set.*

b. *The median is the (20 +1) / 2 or 10.5th value when the ages are put in rank order:*

Age	1	1	1	2	2	2	3	3	3	3	3	4	4	5	6	7	12	22	26	64
Value	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*	*15*	*16*	*17*	*18*	*19*	*20*

In this case, both value number 10 and value number 11 are 3. The 10.5th value is the average of these 2 values: $(3 + 3) / 2 = 3$ years.

c. *The mean is:*

$$(4+3+3+1+2+26+64+3+2+5+7+4+22+3+1+1+12+2+3+6) / 20 = 8.7 \text{ years.}$$

d. *The mean and median are different in this case because the distribution of ages is skewed to the right by the 3 cases that are considerably older than the rest.*

e. *Because of these "outliers", the median probably gives a better idea of the age distribution of the population.*

Exercise 4.2

a. *There are 2 modes: 4 days and 5 days.*

b. *The median is the (11 + 1) / 2 or 6th value. In this case, it is 5 days.*

c. *The mean is 64 / 11 or 5.8 days.*

d. *The mean and median are closer because the distribution has fewer outliers (it is more bell-shaped or normal).*

e. *In this case, either would be acceptable.*

Exercise 4.3

Begin by determining the midpoint of each of the categories by adding the lowest value in the category to the highest and dividing the result by 2. For example, the midpoint of the first category would be (2999 + 1000) / 2 or 1999.5 parasites/1000 WBC (see the box below). Multiply the number of observations in that category by the midpoint value. In the first category, this is 20 × 1999.5 or 39 990. Then sum the values for all categories and divide this sum by the total number of observations.

a. *The **mean parasite density** is 5249.5 (1 049 900 / 200) parasites/1000 WBC*

CATEGORY	MIDPOINT (MP)	FREQUENCY (F)	MP x F
1000–2999	1999.5	20	39 990.0
3000–4999	3999.5	70	279 965.0
5000–6999	5999.5	80	479 960.0
7000–8999	7999.5	25	199 987.5
9000–10999	9999.5	5	49 997.5
		200	**1 049 900.0**

To calculate the median, determine the midpoint of the data, which in this case is the:

$(200 + 1) / 2$ or 100.5^{th} observation.

Calculate the cumulative total of the frequency distribution for the categories and decide which interval contains the midpoint:

CATEGORY	FREQUENCY (F)	CUMULATIVE FREQUENCY
1000–2999	20	20
3000–4999	70	90
5000–6999	80	170
7000–8999	25	195
9000–10999	5	200

The 100.5^{th} observation falls in the 5000 – 6999 category, which contains observations 91–170.

Apply the formula, median $= L + JW / f,$

where: L is the **true** lower limit of the class interval containing the midpoint

           J is the number of cases in this interval below the midpoint (calculated as: number of cases below the midpoint minus cumulative number of cases up to but not including this interval

           W is the **true** width of the class interval

           f is the total number of cases in this interval.

Here:

- the **true** lower limit of the interval L is 5000
- the width of the interval W is 2000
- the number of cases in the interval f is 80
- the cumulative number of cases below the interval C is 90

           J is then calculated as the midpoint minus C or 100.5 minus 90 = 10.5

           J / f is 10.5 / 80 = 0.13

           $J / f \times W$ is therefore 0.13 × 2000 = 260

b. *The **median parasite density** is:*

    $(L + WJ / f)$ or 5000 + 260 = 5260

c. *The **modal parasite density** is the interval 5000 – 6999.*

Exercise 4.4

The following data set is typically skewed distribution of malaria of malaria parasite densities. It is then important to consider differences between mean values and median.

Patient number	Parasite density (per µl)	Patient number	Parasite density (per µl)
1	1069	13	22827
2	3941	14	23585
3	4514	15	29648
4	8048	16	32265
5	8793	17	32739
6	11654	18	38000
7	12736	19	40684
8	13680	20	66211
9	17614	21	67231
10	18630	22	159091
11	21186	23	196500
12	22099		

The mean and the median of the above data set are 37075 and 22099, respectively. The mean and median are different because the distribution of parasite densities is skewed. If the two highest parasite densities are excluded, the mean and median will be 23674 and 21186, respectively. The mean value decreased considerably when the two highest values are excluded while the median just shifted slightly. This shows that the mean value is dependent on all values, and is very much influenced by extreme values. The median is not at all affected by the extreme values

Instead of using the median when the series of values include one or more values exceptionally high, another approach is to use the geometric mean. The geometric mean is the antilog of the average of logarithmic values of the series.

If you convert the above series in their logarithmic values, you will obtain the following table.

Patient number	Log parasite density (per µl)	Patient number	Log parasite density (per µl)
1	3.03	13	4.36
2	3.60	14	4.37
3	3.65	15	4.47
4	3.91	16	4.51
5	3.94	17	4.52
6	4.07	18	4.58
7	4.11	19	4.61
8	4.14	20	4.82
9	4.25	21	4.83
10	4.27	22	5.20
11	4.33	23	5.29
12	4.34		

▶ The mean of the logarithm is 4.3123; antilog of this is 20525 , namely the geometric mean.

The geometric mean is closer to the median since using the log-transformation yields a mean which is less sensitive to extreme values. When the mean and the median are almost the same, the data is considered symmetric.

LEARNING UNIT **5**

Measures of variability and normal distribution

Learning Objectives:
by the end, participants should be able to...

■ Define the terms *range, standard deviation* and *normal distribution*

■ Describe the advantages and disadvantages of using *range, standard deviation* and *normal distribution*

■ Calculate a *range* and *a standard deviation*

■ Calculate and interpret a chi-squared value

The tutor should introduce the session by defining the terms *range* and *standard deviation* and describing the advantages and disadvantages of using the range and the standard deviation. The chi-square test should be explained and discussed. The participants should then work individually or in pairs on the exercises provided in the *Guide for Participants*.

The tutor should make sure the concepts of square and square roots are known by everyone in the class, and give an explanation if necessary. It may be preferable for any participants who are not familiar with the calculations to work in pairs with someone who is more experienced. Tutor and facilitators may wish to circulate among the participants to answer questions or work with those who may be having difficulties.

Answers

Exercise 5.1

a. *The range is 4–18 days (it can also be expressed as 14 days)*

b. *The mean is (6 + 7 + 10 + … + 6 + 11) / 24 = 10.5 days*

c. *The standard deviation is calculated as follows:*

$$SD = \sqrt{\frac{\sum x^2 - (\sum x)^2 / n}{n - 1}}$$

where: $\sum x^2 = 2981$

$(\sum x)^2 = 64\ 009$

$(\sum x)^2 / n = 2667.04$

$$SD = \sqrt{\frac{2981 - 2667.04}{23}} = \sqrt{13.6} = 3.69 \text{ days}$$

d. *The standard deviation is the better indicator here, because mathematically it takes into account the distance of each value from the mean value of the group and thus describes the dispersion (or variation) within data for each range*

Exercise 5.2

a. *The range is 58 – 83 beats per minute*

b. *The mean is 83 + 72 + 77... + 58 + 65 + 77/10 or 68.5 beats per minute*

c. *The standard deviation is calculated as follows:*

$$\sqrt{\frac{\sum x^2 - (\sum x)^2 / n}{n - 1}}$$

where: $\Sigma x^2 = 47\ 629$

$(\Sigma x)^2 = 469\ 225$

$(\Sigma x)^2 / n = 46\ 922.5$

$$SD = \sqrt{\frac{47629 - 46922.5}{9}} = \sqrt{78.5} = 8.9 \text{ beats per minute}$$

Exercise 5.3

Values given

		Insecticide-treated nets		
		In regular use	Other	Total
Blood slide	Positive	34		94
	Negative	80		106
	Total			200

a. Tabulation of the information

▶ Observed values (O) for all cells

Observed values (O)		Insecticide-treated nets		
		In regular use	Other	Total
Blood slide	Positive	34	60	94
	Negative	80	26	106
	Total	114	86	200

Expected value for "regular users/positive slide"
E = 94 × 114 / 200 = 10716 / 200 = 53.58

▶ Expected values (E) for all cells

Expected values (E)		Insecticide-treated nets		
		In regular use	Other	Total
Blood slide	Positive	53.58	94 – 53.58 = 40.42	94
	Negative	114 – 53.58 = 60.42	86 – 40.42 = 45.58	106
	Total	114	86	200

▶ (O–E) for all cells (absolute value). In a 2 by 2 grid, this is a constant, but this is not the case in other grids

0 – E		Insecticide-treated nets		
		In regular use	Other	Total
Blood slide	Positive	34 – 53.58 = 19.58	60 – 40.42 = 19.58	94
	Negative	80 – 60.42 = 19.58	26 – 45.58 = 19.58	106
	Total	114	86	200

▸ $(O–E)^2$ for all cells

(O – E)²		Insecticide-treated nets		
		In regular use	Other	Total
Blood slide	Positive	$(19.58)^2 = 384$	$(19.58)^2 = 384$	94
	Negative	$(19.58)^2 = 384$	$(19.58)^2 = 384$	106
	Total	114	86	200

▸ $(O–E)^2 / E$ for all cells

(O – E)² / E		Insecticide-treated bednets		
		In regular use	Other	Total
Blood slide	Positive	384/53.58 = 7.2	384/40.42 = 9.5	94
	Negative	384/60.42 = 6.4	384/45.58 = 8.4	106
	Total	114	86	200

Calculation of chi-squared as the sum of : 7.2 + 6.4 + 9.5 + 8.4 = 31.4

For 1 degree of freedom, the threshold value of chi-squared is

3.84 for $p = 0.05$ and

6.64 for $p = 0.01$

b. 37.7 is greater than 6.64 and the chi-square value is therefore significant

LEARNING UNIT **6**

Assessing the accuracy of a test

Learning Objectives:
by the end, participants should be able to...

■ Define the terms *sensitivity, specificity, positive predictive value, negative predictive value,* and describe their importance to health practitioners and patients

■ Describe the trade-offs between sensitivity and specificity

■ Describe the effect of prevalence and incidence on positive predictive value

■ Calculate and interpret sensitivity, specificity, and positive predictive value from sample data

The tutor should open the session by defining the concepts sensitivity, specificity, positive predictive value, negative predictive value and describing their application in diagnostic tests. This should be followed by discussion with the participants about the diagnostic tests' ability to detect a person with disease or exclude a person without disease. Enough time should be allowed for questions and clarification of any aspects not fully understood.

Exercises on sensitivity and specificity

The participants should work individually or in pairs. Ask them to think about the questions for a few minutes, then they should answer as a class.

For Exercise 6.2, the tutor may prefer to allow the participants to work individually for a few minutes and then work with them together as a class to carry out this exercise (see detailed instructions below on how to set up the table). The same applies to Exercise 6.3.

The participants can then work individually on Exercise 6.4, with tutor and facilitators circulating to help any who are having difficulties.

Answers

Exercise 6.1

a. In this case, "test" corresponds to " fever and rigors", and "disease" to "positive thick smear". Of 100 people with positive thick smears ("presence of disease"), 98 will have fever and rigors ("test positive"). The other 2 will have no fever and rigors ("test negative") but positive thick smears ("presence of disease") and will be considered false negatives.

TP / (TP + FN) = 98 / 100 = 98%. The sensitivity is 98%.

b. Of 100 people who have negative thick smears ("absence of disease"), 99 will not have fever and rigors ("test negative") and are thus considered true negatives. The remaining 1 will have a negative smear ("absence of disease") but will have fever and rigors and will represent a false positive.

TN / (TN + FP) = 99 / 100 = 99%. The specificity is 99%.

Exercise 6.2

Steps

- Begin by constructing the 2 × 2 cell table. Make sure that everyone realizes that in this case the "test" is "presence or absence of fever + rigors", while the diagnosis of "disease" is based on the presence or absence of malaria parasites in the thick smear.

- Place the number 100 000 in the lower right hand corner.

	Disease status		
Test	**Positive smear**	**Negative smear**	**Total**
Fever and rigors			
No fever and rigors			
TOTAL			**100 000**

- Ask the participants how they can fill in the other cells based on the numbers they already know. The first step is to multiply 100 000 by the prevalence, which gives the total number of individuals with positive thick smears (100 000 × 0.02 = 2000). This number goes in the total of the "positive smear" column. The total number with negative smears can then be derived by subtracting 2000 from 100 000 = 98 000.

Test	Disease status		
	Positive smear	Negative smear	Total
Fever and rigors			
No fever and rigors			
TOTAL	**2000**	**98 000**	**100 000**

The number of people who have fever with rigors and a positive thick smear can be calculated by multiplying the number with a positive smear by the sensitivity. The number without fever plus rigors and with a positive thick smear can then be derived by subtracting 1960 from 2000 = 40.

Test	Disease status		
	Positive smear	Negative smear	Total
Fever and rigors	1 960		2 940
No fever and rigors	40		97 060
TOTAL	**2000**	**98 000**	**100 000**

U6

The number of people who have negative thick smears and do not have fever and rigors can be obtained by multiplying the number with negative smears by the specificity, or: 98 000 × 0.99 = 97020. Note that this number goes in the lower right hand box. The number of people with a negative smear who have fever and rigors can be obtained by subtracting 97 020 from 98 000 = 980

The final table should read as follows:

Test	Disease status		
	Positive smear	Negative smear	Total
Fever and rigors	1 960	980	2940
No fever and rigors	40	97 020	97 060
TOTAL	**2000**	**98 000**	**100 000**

Thus:

a. *The number of persons receiving treatment is the total with fever + rigors = 2940.*

b. *The number unnecessarily treated would be 980, which represents the number who have fever + rigors but a negative thick smear.*

c. *The positive predictive value is 1960 (true positives) divided by 2940 (true positives plus false positives) = 0.67*

d. *The negative predictive value is 97 020 (true negatives) divided by 97 060 (true negatives plus false negatives) = 0.98*

Exercise 6.3

A positive predictive value of 0.67 means that 67% of those who have fever and rigors and are treated will actually have malaria, and that 33% of those treated will not have been malaria.

A negative predictive value of 0.98 means that among patients without fever and rigors, 98% do not have malaria. In other words, if the patient does not have fever and chills, it is highly unlikely that he/she has malaria.

Exercise 6.4

From their experience with Exercise 6.2, participants must be able to answer this question individually.

	Disease status		
Test	**Positive smear**	**Negative smear**	**Total**
Fever and rigors	196	998	1194
No fever and rigors	4	98 802	98 806
TOTAL	200	99 800	100 000

Therefore:

a. The number treated each week would be: 1194

b. The number who would actually have malaria would be: 196

c. The positive predictive value would be: 196 / 1194 = 0.16

d. The negative predictive value would be: 98 802 / 98 806 = 0.998

LEARNING UNIT **7**

Understanding malaria at regional and global levels

Learning Objectives:
by the end, participants should be able to...

■ Describe the geographical distribution of malaria in the world

This map is intended as a visual aid only and not as a definitive source of information about malaria endemicity.

Source: © WHO 2010. All rights reserved.

Countries or areas where malaria transmission occurs
Countries or areas with limited risk of malaria transmission
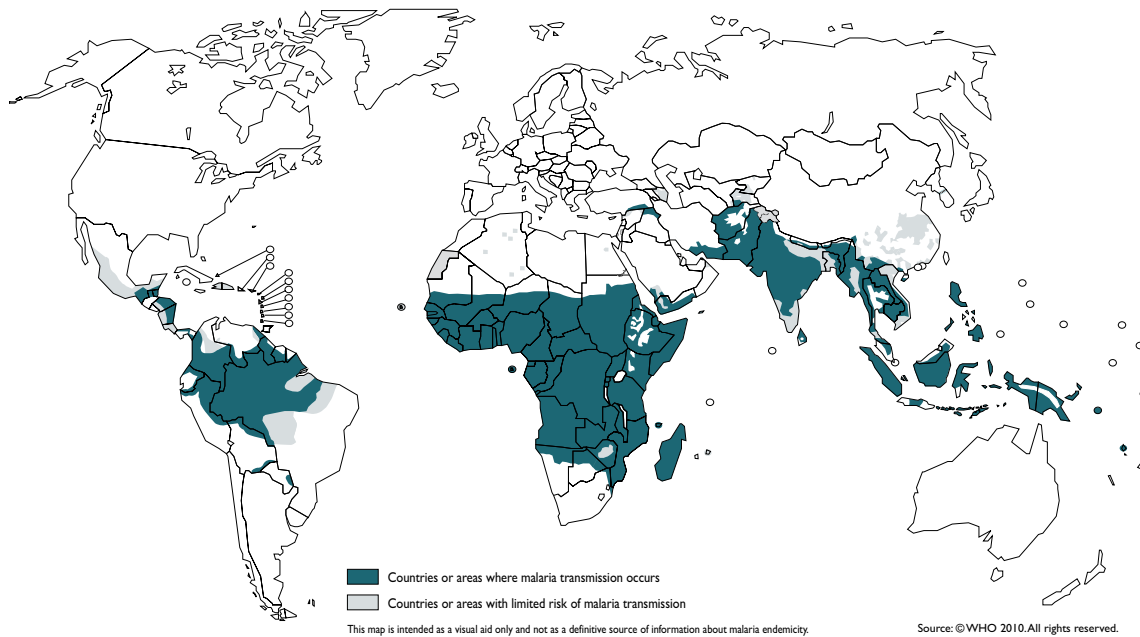
Figure 7.1   Countries or areas at risk of transmission, 2010

Answers

Exercise 7.1

Figure 7.1 shows countries or areas at risk of malaria transmission in 2010 (Fig. 7.1).

a. In 2011, an estimated 3.3 billion people (about half of the world population) lived in areas where malaria is a health risk for the population. Malaria caused an estimated 219 million cases and up to 660 000 deaths in 2010.[1] Approximately 80% of the cases and 90% of the deaths occur in Africa while the remaining cases and deaths occur mainly in the South-East Asia and Eastern Mediterranean Regions. Malaria transmission differs in intensity and regularity depending on local factors such as rainfall patterns, proximity of mosquito breeding sites and mosquito species.

b. Some areas have a fairly constant number of malaria cases throughout the year – these are malaria endemic with perennial or seasonal transmission and the latter usually coinciding with the rainy season. Other areas experience epidemic malaria which refers to unexpected increase of cases in a given population at a specific time of the year. Large and devastating epidemics can occur in areas where people have had little contact with the malaria parasite, and therefore have little or no immunity. These epidemics can be triggered by climatic change, e.g. increased temperature or abnormal rainfall, and further aggravated by complex emergencies or natural disasters.

The burden of malaria disease varies greatly from one region of the world to another, depending on the species of malarial parasite (e.g. *P. falciparum, P. vivax* and other species) and the epidemiology of malaria (e.g. high or low transmission, stable, or unstable epidemic).

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[1] WHO (2012). *World malaria report*. Geneva, World Health Organization. http://www.who.int/malaria/publications/world_malaria_report_2012/en/index.html

In high malaria transmission settings, there is a high level of mortality, severe disease concentrated in children, predominance of *P. falciparum* species. In low-transmission settings, there are few deaths due to malaria, burden of the disease is spread to all age groups (or more in adults), often a substantial fraction of disease is due to *P. vivax*, and malaria is typically focal.

c. ***Note for tutor:*** If there are participants from different regions, they could be asked to explain the situation of malaria in their regions. One option is to consider various regions of the world according to the WHO classification (noting that WHO Regions do not coincide exactly with geographic or geo-political regions). The WHO Regions are:

- ▸ African Region
- ▸ Region of the Americas
- ▸ Eastern Mediterranean Region
- ▸ European Region
- ▸ South-East Asia Region
- ▸ Western Pacific Region

African Region

The African region is generally characterised by a high intensity of malaria transmission except the countries in southern Africa with low malaria transmission, and Cape Verde which is in pre-elimination phase. Africa remains the Region that has the greatest of malaria cases (80%) and deaths (90%) in the world. Malaria was responsible for an estimated 174 (range 110–242) million cases and 596 000 (429 000–772 000) deaths in 2010, mostly occurring in children under 5 years of age in Africa south of the Sahara.[1] In most of the countries, cases of malaria are predominantly due to *P. falciparum*, with the exception of Eritrea and Ethiopia where the proportions of cases due to *P. vivax* are 50% and 37%, respectively.

Region of the Americas

About 30% of the population of the 21 countries with ongoing transmission is at some degree of risk and about 8% of the population is at high risk. In 2010, malaria cases and deaths were estimated to 1.1 (range 0.9–1.3) million and 1 100 (range 700–1 800), respectively.[1] Fifteen countries are in the control phase and the remaining (Argentina, Costa Rica, Ecuador, El Salvador, Mexico and Paraguay) are in the pre-elimination phase. Less than 60% of cases in most countries in the Region are caused by *P. falciparum*, and the remainder by *P. vivax*, except the Dominican Republic and Haiti where malaria cases are almost exclusively due to *P. falciparum*.

Eastern Mediterranean Region

Aproximately 55% of the population, reside in areas of varying risk of malaria transmission. The Region contains seven countries with areas of high malaria transmission (Afghanistan, Djibouti, Pakistan, Somalia, Sudan, South Sudan and Yemen), and two countries with low,

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[1.] WHO (2012). *World malaria report*. Geneva, World Health Organization. http://www.who.int/malaria/publications/world_malaria_report_2012/en/

geographically limited malaria transmission (Islamic Republic of Iran and Saudi Arabia) whereas Iraq has not reported locally acquired cases since 2009. The remaining countries have either eliminated malaria or preventing re-establishment of malaria transmission.

In 2010, an estimated 10.4 (range 6.4–16.6) million malaria cases and 15 300 (range 7 200–23 500) deaths were reported from the Region.[1] *P. falciparum* is the dominant species of parasite in Djibouti, Saudi Arabia, Somalia, Sudan, South Sudan and Yemen, but the majority of cases in Afghanistan and Pakistan and almost all cases in the Islamic Republic of Iran are due to *P. vivax.*

European Region

The Region reported 226 malaria cases in Azerbajan, Greece, Kyrgyztan, Tajikistan, Uzbekistan and Turkey in 2011.[1] Only 69 of the 226 malaria cases were indigenous; these were reported from Tajikistan and Azerbaijan. No locally-acquired *P. falciparum* cases have been reported since 2008. All other *P. falciparum* malaria cases found in the Region in 2011 were imported. Kyrgyzstan suffered a large outbreak in 2002 but had zero locally-acquired cases in 2011. Between 2001 and 2005, Turkey reported around half of all cases in the Region, but it had zero cases in 2011. Uzbekistan reported zero indigenous cases in 2009, 3 *P. vivax* cases in 2010, and again zero indigenous cases in 2011. Georgia reported zero indigenous cases for the first time in 2010 and continued to have zero cases in 2011. Turkmenistan and Armenia were certified malaria-free by the Director-General of WHO, in October 2010 and September 2011 respectively. However, despite the achievements made to date, the Region faces challenges due to reintroduction of malaria from neighbouring countries or through population migration from more distant countries. For instance Greece which remained malaria-free since 1974 reported three locally acquired *P. vivax* in 2010 and has experienced an outbreak in 2011.

South-East Asia Region

In South-East Asia Region approximately 70% of the population of 1.8 billion people is at some risk for malaria, with 26% at high risk. In 2010, malaria cases and deaths were estimated to 32 (range 25.9–41.9) million and 43 000 (range 31 100–60 300),[1] respectively. The majority of malaria cases in the Region are due to *P. falciparum*, although the proportion varies greatly among countries. Malaria is predominantly due to *P. falciparum* in Bangladesh, Myanmar and Timor-Leste, mostly to *P. vivax* in Nepal and Sri Lanka, and exclusively due to *P. vivax* in the Democratic People's Republic of Korea. Bhutan is pre-elimination phase and Sri Lanka is elimination phase.

Western Pacific Region

The epidemiology of malaria in the Region is highly heterogeneous. Malaria transmission is intense through most of Papua New Guinea, Solomon Islands and Vanuatu. Transmission is highly focal in the countries and areas of the Greater Mekong subregion, including Cambodia, Yunnan province (China), Lao People's Democratic Republic and Viet Nam. In these countries malaria is most intense in remote forested areas and where the disease disproportionately affects ethnic minorities and migrants. Malaria is also restricted in distribution in Malaysia,

[1.]   WHO (2012). *World malaria report.* Geneva, World Health Organization. http://www.who.int/malaria/publications/world_malaria_report_2012/en/

the Philippines and the Republic of Korea. Malaysia and Republic of Korea are in pre-elimination and elimination phases, respectively. In 2010, around 1.7 (range 1.3–2.1) million cases and 4 000 (range 2 400–6 100) deaths due to malaria were reported from the Region.[1] Most countries have transmission cycles of both *P. falciparum* and *P. vivax*, but transmission is entirely due to *P. vivax* in the Republic of Korea and in central areas of China.

Exercise 7.2

The different factors for malaria in Africa, South-East Asia and America are listed in Figure 7.1.

Table 7.1   Distribution of malaria characteristics[1]

	Americas	South-East Asia	Africa
Parasitological species of malaria cases (%)	*P. falciparum* 35% *P. vivax*/mixed 65%	*P. falciparum* 41%, *P. vivax* 38% Mixed 21%	*P. falciparum* 98%, *P. vivax* or malariae or *P. ovale* or mixed 2%
Principal malaria vectors	*A. albimanus* (Central America), *A. darlingi* (Amazon Basin)	*A. culicifacies, A. minimus, A. annularis A. dirus, A. fluviatilis, A. maculipennis A. sacharovi, A. superpictus, A. farauti*	*A. gambiae s.l. A. funestus s.l.*
Estimated proportion of population at malaria risk	21%	74%	85%
Estimated contribution to the global burden of malaria cases (%)	1.1 million (0.5%)	32 million (15%)	174.3 million (80%)

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Exercise 7.3

Yes, differences in distribution do affect the programme objectives.

Malaria is currently endemic in all continents of the world except Antarctica and Australia, with intensities of transmission that vary from very low to extremely high. The objectives of malaria programmes range from reducing the disease burden and maintaining it at a reasonably low level (countries in control), to eliminating the disease from a defined geographical area (countries in elimination) and, ultimately to eradicating the disease globally (countries eradicated malaria). These phases of malaria programme will be addressed in Learning Unit 13.

[1.] WHO (12). *World Malaria Report*. Geneva, World Health Organization. http://www.who.int/malaria/publications/world_malaria_report_2012/en/index.html

LEARNING UNIT **8**

Determinants of malaria distribution

Learning Objectives:
by the end, participants should be able to…

■ Categorize the determinants of malaria distribution

■ Describe each of these determinants

The tutor should introduce the unit by brainstorming session on the determinants that influence malaria distribution and guiding the participants to the correct answers. The tutor should ensure that the participants have understood the characteristics of these determinants and their effect on malaria transmission. Enough time should be allowed for questions and clarification of any aspect not fully understood.

Answers

8.1   Determinants of malaria distribution

Exercise 8.1

Three determinants influence the distribution of malaria:

1. The *Anopheles* mosquito must be present and be in contact with humans, so that the parasite can pass its developmental phase in the invertebrate host.

2. Humans must be present and be in contact with the mosquito, to allow the parasite to pass part of its life-cycle in the vertebrate host.

3. The malaria parasite must be present.

Interaction among these three factors leads to malaria infection. In general terms, the factors affecting malaria incidence can be classified into the following three groups:

1. Mosquito, parasite, human

2. Environmental factors

3. Global factors

Environmental factors	→	Parasite Mosquito Human	←	Global factors

8.2   Parasite

Exercise 8.2

The characteristics of the malaria parasite[1] can affect the distribution of malaria:

▶ In regions where *P. falciparum* is the predominant malaria species, because it has a higher transmission potential, the incidence of malaria tends to be higher than in regions where other species of malaria are prevalent.

▶ Whereas *P. falciparum* is absent from temperate areas of the world, *P. vivax* and *P. ovale* can survive in these areas. This is because *P. vivax* and *P. ovale* can complete the sporogonic cycle at lower temperature compared to *P. falciparum*.

▶ Virulence (severity of acute disease in non-immune subjects) differs greatly between species. *P. falciparum* is the most virulent of the four human *plasmodium* species and more likely to cause a fatal malaria disease.

[1.]   *P. Knowlesi*: is a primate malaria parasites commonly found in Malaysia, Thailand and other South-East Asian countries. It infects humans and is mainly transmitted in forests and forest fringes.

▶ *P. falciparum* readily develops resistance to antimalarial medicines which leads to treatment failures. This increases malaria morbidity, mortality and, by expanding parasite reservoir, increases malaria transmission.

8.3   Mosquito

Exercise 8.3

▶ The types of *Anopheles* present in an area at a given time will influence the intensity of malaria transmission. Not all *Anopheles* are equally good vectors for transmitting malaria from one person to another. Some species are biologically unable to carry human malaria parasites, while others are readily infected and because readily infective to humans with sporozoites in the salivery glands.

▶ In some *Anopheles* species females take preferably blood meals from humans (anthropophilic) while others prefer biting animals (zoophilic). Some species prefer to bite indoors (endophagic), and others prefer outdoor biting (exophagic). The anthropophilic species will have more frequent contacts with humans and thus will be more efficient malaria vectors. The anthropophilic *Anopheles gambiae* is an extremely potent vector and its widespread presence in Africa explains why malaria is so prevalent in Africa.

▶ The *Anopheles* mosquito can develop resistance to the insecticides used for impregnating nets and residual spraying, defeating vector control operations.

8.4   Humans

Exercise 8.4

a. Human characteristics that influence malaria distribution in the world.

1. Genetic factors

The genetic factors that can protect humans against malaria include:

▶ Specific heamoglobinopaties, such as sickle-cell trait (heterozygous for abnormal HbS gene) are protected against severe forms of falciparum infection. The selective advantage of sickle-cell trait carriers explains why hemoglobin S is more frequently found in endemic malaria zones, whereas sickle-cell disease (SS homozygotes) leads to early death, before adulthood.

▶ Negative Duffy group RBCs do not possess the necessary membrane receptor for *P. vivax* infection. This explains the rare transmission of this parasite in western and central Africa where this blood group dominates.

▶ Other genetic factors related to RBCs (HbC, G6PD deficiency) also influence malaria. Certain HLA genetic determinants also affect the risk and/or severity of disease.

2. Biological factors

▶ *Acquired immunity*

Acquired immunity is one of the most important factors that impact on the health of individuals and societies. After repeated attacks of malaria, a significant degree of species-specific immunity against malaria is acquired although immunity is never more than partial. When

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malaria occurs in partially immune people, the disease does not progress to severe illness and the symptoms end to be mild.

The acquisition of immunity and its consequences on clinical epidemiology of malaria depends on the level and the regularity of transmission. In areas where *P. falciparum* transmission is intense, newborns are passively immunized against malaria for the first few months of life by maternal antibodies. With the passage of time, and a reduction of these antibodies, young children become highly susceptible to malaria. As a result of repeated exposure to malaria infection, often after the age of 5 years they acquire a partial immunity. Therefore, in areas with a high incidence of malaria, children <5 years of age are at greatest risk.

In areas of moderate transmission, the malaria burden shifts to the older children with the peak at 5–15 years. In areas of low malaria incidence, because transmission is lower, many older children and adults do not acquire immunity to malaria. In these settings malaria occurs in all age groups.

▶ *Pregnancy and malaria*

Pregnancy leads to an increase in the susceptibility of women to malaria with negative health consequence to both the mother and the fetus. Plasmodial infection of the placenta is associated with low birth weight of neonates and a higher infant mortality rate. In high transmission areas where adult populations acquired partial immunity, clinical symptoms and parasitaemia are worse in primigravid than in multigravid women and other adult patients. In low transmission settings, women are non-immune and cerebral and other forms of severe falciparum malaria are more common in pregnancy, regardless of gravidity.

▶ *Malaria and malnutrition*

When food is scarce, children are at greater risk of malnutrition than adults. Malnutrition increases the likelihood of mortality resulting from infectious diseases. There is a high risk of mortality in severely malnourished children (children weighing less than 70% normal weight) who contract malaria. Severely malnourished children may not present the classic symptoms of malaria in spite of having high levels of parasitaemia, e.g. fever may not be present.

b. Social and economic factors that influence malaria distribution

In addition to biological and environmental factors, socioeconomic factors also influence the risk of acquiring malaria in individuals and populations:

▶ Poor people do not live in suitable houses and may not have access to mosquito nets to protect them against insect bites.

▶ Poor people may not have knowledge of preventive measures of malaria and may not be able to recognize early the disease.

▶ Financial constraints (e.g. are unable to buy medicine) or physical barriers (e.g. distance from health centres) may limit access to health services.

▶ Other man-made factors which influence malaria distribution include:

  ▶ Human activities such as deforestation, logging, road constructions can create breeding sites that are favourable for the growth of malaria larvae.

▶ Irrigation and agricultural activities (which itself is influenced by climatic conditions) may increase human-vector contacts.

▶ Raising domestic animals near housing (depending on the vector species) can lead to a reduction of man-vector contact.

▶ Armed conflict, humanitarian emergencies, immigration and tourism in endemic countries may lead to exposure of non-immune individuals to malaria.

8.5   Environmental factors

Exercise 8.5

a. Climate and its changes are largely responsible for the geographical distribution and seasonality of malaria. The presence of malaria in a region is dependent on environmental factors such as: rainfall, temperature, and humidity.

Rainfall

Rain can create pools of stagnant water where the anopheline mosquitoes are able to breed. The developmental stage of larvae and their transformation into adult mosquitoes takes place in such pools and its duration is temperature dependent and in warm regions is 9–12 days.

Floods can indirectly cause a rise in diseases transmitted by vectors due to an increase in the density of vectors. The stagnant waters created by rainfall or river overflows can generate breeding sites for the mosquitoes. Flood victims therefore have more contact with the vector and malaria transmission increases.

Example

Malaria epidemics have occurred in the wake of flooding in several endemic areas of Central and South America, including the earthquake and flood in Costa Rica in 1991, and the flood in the Dominican Republic in 2004. Recurrent floods following the El Niño-Southern Oscillation (ENSO) lead to malaria epidemics in northern Peru in 1982–1983 and 1997–1998.

Temperature and humidity

The adult anopheline mosquito requires suitable temperature, humidity and rainfall for its survival. In order to transmit the parasite, the mosquito must remain alive for sufficient time for the parasite to complete its sporogonic cycle. This cycle takes 9–21 days at 25 °C. At higher temperatures the cycle shortens and the risk of transmission increases. On the contrary, at low temperatures (< 16 °C for *P. vivax*, and < 19 °C for *P. falciparum*) the sporogonic cycle is not completed and malaria cannot be transmitted. This explains why malaria is more widespread in warmer regions of the world.

It is theorectically possible that the current process of global warming will increase the geographical distribution of malaria, with the risk of new malaria epidemics.

b. Even in tropical and subtropical regions malaria transmission does not take place in the following conditions:

▶ high altitudes,

▶ colder seasons,

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- ▶ deserts (excluding oases),
- ▶ in some islands of the Pacific Ocean where disease-transmitting anopheline mosquitoes are absent,
- ▶ in countries which have successfully eliminated malaria.

In general, in hotter areas near the equator:
- ▶ transmission is more intense,
- ▶ malaria is transmitted all year round,
- ▶ *P. falciparum* is more prevalent.

c. *In cooler regions malaria is transmitted seasonally and with less intensity. P. vivax is more common in these regions, because it is more capable of surviving lower temperatures.*

d. *Climate conditions influence human behaviour and may increase contact with anopheline mosquitoes (between sunset and sunrise), when anopheline mosquitoes are most active. In warm weather people tend to sleep outdoors and use nets less. At the time of harvest, farmers often sleep outdoors near the fields without protection.*

8.6 Global factors

Exercise 8.6

a. *Malaria is both a cause and an effect of poverty. About 90% of deaths from malaria have occurred in African countries mainly in rural settings. The burden of malaria is higher in poor countries.*

Malaria intricately linked with poverty. Countries with higher proportions of their population living in poverty (on less than USD 1.25 per person per day) have higher death rates from malaria (Fig. 8.1). Poverty is the main obstacle in the fight against malaria. Most countries lack the infrastructure and resources to combat malaria effectively. At a personal level, poverty limits access of people to use appropriate measures for prevention or cure. Malaria also affects negatively the economic growth of nations and individuals alike. These include economic cost of delivering malaria interventions, days off work and school and lost income, and medical expenditures.

Source: WHO estimates, Human Development Report 2011
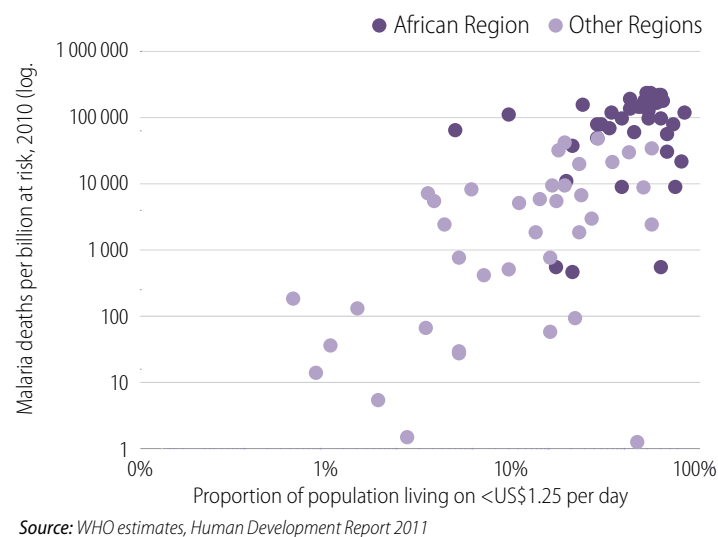
Figure 8.1 Relationship between proportion of country's population living in poverty and mortality rates

b. Change of occupation and lifestyle

The relation between irrigation, agriculture and malaria epidemics has long been known.

In recent years huge malaria epidemics have occurred in gold-mine workers in South America and South East Asia, while focal epidemics have accompanied the rural settlements which followed the construction of new roads. These epidemics spread among local populations, which have often been decimated by *P. falciparum*.

At times, economic activities have led to the establishment of endemic areas and caused epidemics.

▶ In Brazilian Amazonia, the workers' gold rush not only led to the formation of highly endemic foci, but also caused an epidemic in some of its local tribes.[1]

▶ In 1950s, malaria control programmes were hampered on the Pacific coast of Central America by the high vulnerability of cotton workers who were constantly moving to different areas because of the temporary nature of their jobs. On the other hand, malaria control was very effective in banana plantations on the Atlantic coast. The collapse of cotton cultivation in the early 1980s caused widespread migration of workers, and resulted in expansion of banana plantations on the Atlantic coasts of Costa Rica and Honduras. This transfer led to serious focal malaria outbreaks on the Atlantic coasts but eventually facilitated the success of malaria control programmes on the Pacific coast.[2]

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[1.] Veeken H (1993). Malaria and gold fever. *British Medical Journal*, 307 (6901):433–4.

[2.] WHO (1998). Malaria epidemics detection and control, forecasting and prevention. Geneva, World health Organization.

LEARNING UNIT **9**

The life-cycle of the malaria parasite
and its relation to pathogenesis, immune responses, antimalarial drugs, and field measurements

Learning Objectives:
by the end, participants should be able to...

■ Describe the life-cycle of human malaria parasites

■ Describe important characteristics of infection with each of the 4 species of human malaria parasite

■ Relate the parasite's life-cycle to pathogenesis, immune responses and potential vaccines

■ Identify, in the parasite's life-cycle, the points of impact of the main antimalarial drugs

■ Identify in the parasite's life-cycle what can be measured, using methods suitable for application in malaria control programmes.

The tutor will need to prepare in advance photocopies for each participant and use the overhead transparencies or PowerPoint presentations of Figures 9.1 to 9.6 provided in the appendix of Learning Unit 10 of the *Guide for Tutors*.

Answers

9.1   The life-cycle of the malaria parasite

Exercise 9.1

a. The participants should work in groups and each group should prepare a diagram of the parasite's life-cycle. After they have completed this task they should be given a photocopy of Figure 9.1. Each group is asked to compare it with the one they have prepared and discuss the differences.

RBCs = red blood cells
PRBCs = parasitized RBC
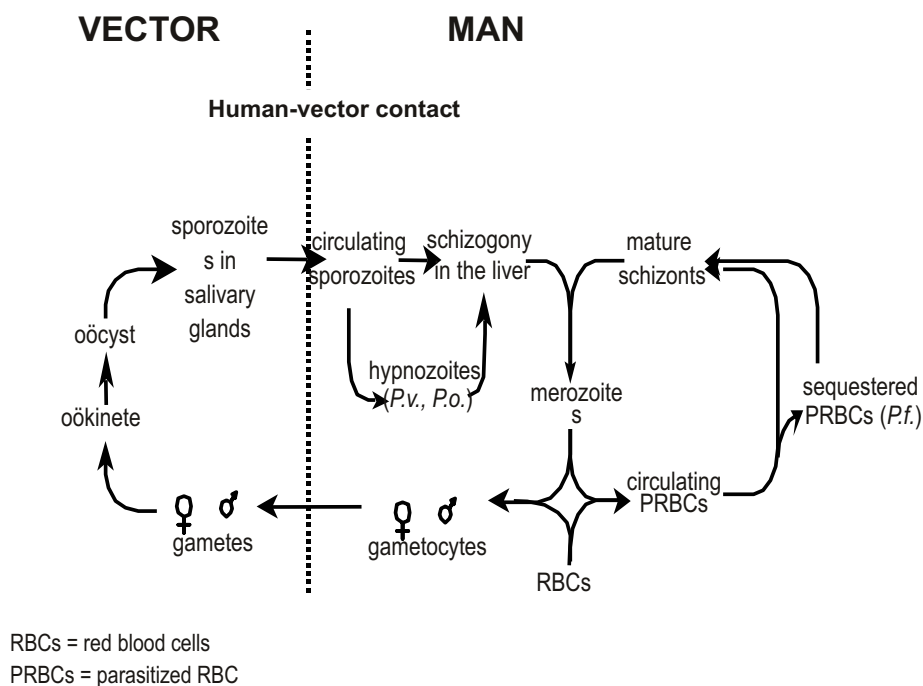
Figure 9.1   Parasite life-cycle

b. Only the zygote and ookinete are diploid, the rest of the cycle is haploid. This is significant because:

  1. *Fertilization allows recombination between gametes of different genotypes (e.g. resistance to different drugs), and*

  2. *In the haploid state, no allele (e.g. resistance to drug X) is recessive.*

Note: This unit includes many exercises that overlap with other Learning Units. The tutor and facilitators are advised to avoid entering into in-depth discussions of topics which will be covered in the units of this module.

9.2   Characteristics of infection with each of the 4 species of human malaria parasites

Exercise 9.2

The participants should work in small groups to list and discuss the characteristics of infection of *P. falciparum, P. vivax, P. ovale* and *P. malariae*.

The facilitators should provide participants with a copy of Tables 9.1 and 9.2

Time factors

Table 9.1   Time factors for the four main species of human malaria parasites

Characteristics	*P. falciparum*	*P. vivax*[a]	*P. malariae*	*P. ovale*
Prepatency period[b]	5.5 days	8 days	15 days	9 days
Incubation period[c]	9–14 days	12–17 days	18–40 days or longer	16–18 days or longer
Time of appearance of gametocytes[d]	8–15 days	0–5 days	5–23 days	5 days
Asexual cycle in the blood	48 hours	48 hours	72 hours	48 hours
Maximum duration of untreated infection	1–2 years[e]	1½ – 5 years	Up to 50 years	Probably same as *P. vivax*

[a]   except those strains with prolonged incubation periods
[b]   from infection to the appearance of detectable parasitaemia
[c]   from infection to the appearance of symptoms
[d]   after the appearance of parasitaemia
[e]   assuming uncomplicated infection

Multiplication factors

Table 9.2   Multiplication factors in man and vector

	P. falciparum	*P. vivax*	*P. malariae*	*P. ovale*
Number of merozoites per hepatic schizont	30 000	8000–20 000	15 000	15 000
Number of merozoites per blood schizont	16–32	12–18	6–12	8–10
Number of sporozoites per oocyst	10 000	1000–10 000	–	–

Other differences among parasite species

- "Hypnozoites" (intrahepatic parasites with retarded development) exist in *P. vivax* and *P. ovale* but not in *P. falciparum* and *P. malariae*. They are responsible for relapses either at relatively short intervals or after a long period;

- *P. falciparum* invades red blood cells of any age (one of the factors that make *P. falciparum* the most dangerous species) whereas *P. vivax* and *P. ovale* prefer younger red cells, and *P. malariae* seeks mature red cells;

- In *P. falciparum*, parasitized red blood cells are sequestered in various tissues (through cytoadherence to endothelial cells) during the second half of the asexual cycle (another factor making *P. falciparum* dangerous) and during maturation of gametocytes.

9.3   The life-cycle of the parasite, pathogenesis, and immunity

Exercise 9.3

a. The main mechanisms of pathogenesis

  i. The rupturing parasitized red blood cells release, in addition to merozoites, malaria toxin(s), which precipitate a complex "cascade" or network of cytokines (TNF, etc.) and effectors (nitric oxide, etc.), which cause fever.

  ii. Sequestration of parasitized red blood cells (by *P. falciparum*), plus the local release of toxin(s), cytokines and effectors causes tissue damage, in particular cerebral malaria.

  iii. Anaemia is caused by destruction of red blood cells by the parasite, plus depression of erythropoiesis (production of new red blood cells) by the effects of toxin(s) released.

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The size of the parasite population aggravates (*i*), (*ii*) and (*iii*); note that the size of the parasite population may not be indicated by the circulating parasite density (in particular for *P. falciparum*, because of sequestration).

Figure 9.2 is the same as Figure 9.1, plus the main broad pathways of pathogenesis.

RBCs = red blood cells
PRBCs = parasitized RBC
SM = severe malaria
TNF = tumor necrosis factor
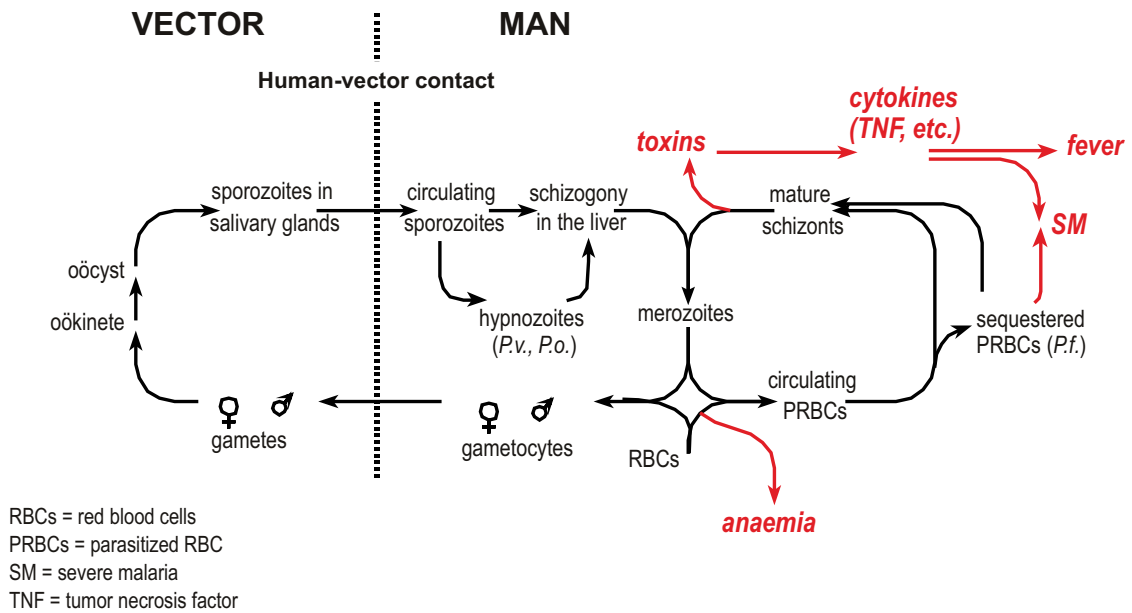
Figure 9.2   Parasite life-cycle and pathogenesis

b. Figure 9.3 is the same as Figure 9.2, plus the stages of the malaria parasites that induce a natural

TNF = tumor necrosis factor
SM = severe malaria
RBCs = red blood cells
PRBCs = parasitized RBC
IRs = immune responses
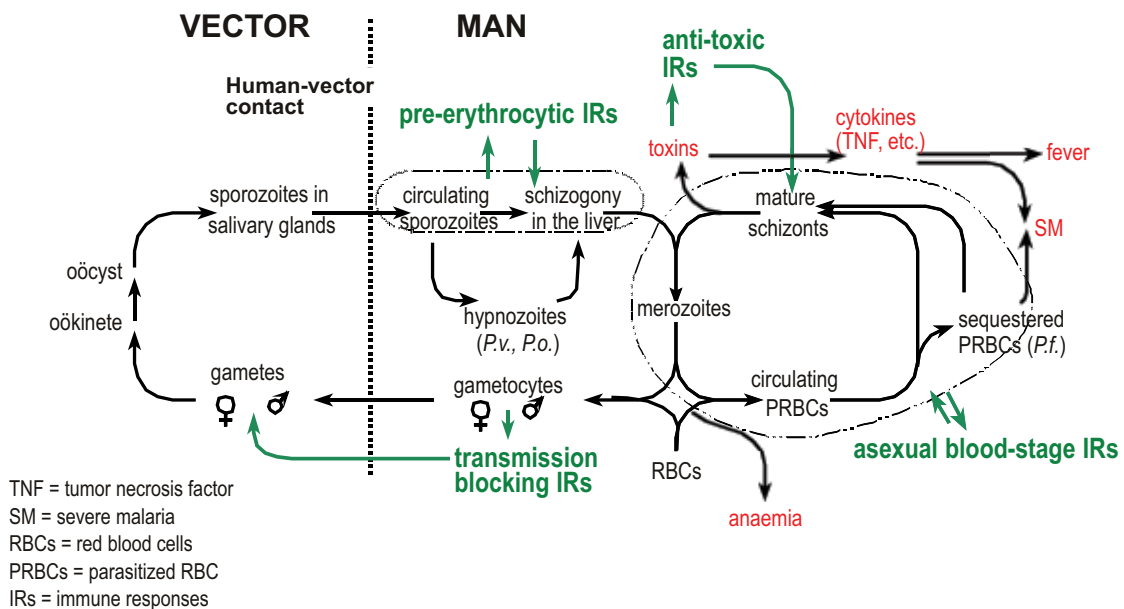
Figure 9.3   Parasite life-cycle, pathogenesis and natural immune response (IRs)

Points to note:

– IRs include protective and non-protective responses;

– All the naturally acquired IRs are only effective to a limited extent;

– Naturally-acquired transmission-blocking immunity acts in the vector's gut (through antibodies picked up with the gametocytes during the blood-meal).

c. *Figure 9.4 is the same as Figure 9.3, plus expected points of impact of different kinds of potential malaria vaccines.*

TNF = tumor necrosis factor — SM = severe malaria — RBCs = red blood cells — PRBCs = parasitized RBC — IRs = immune responses
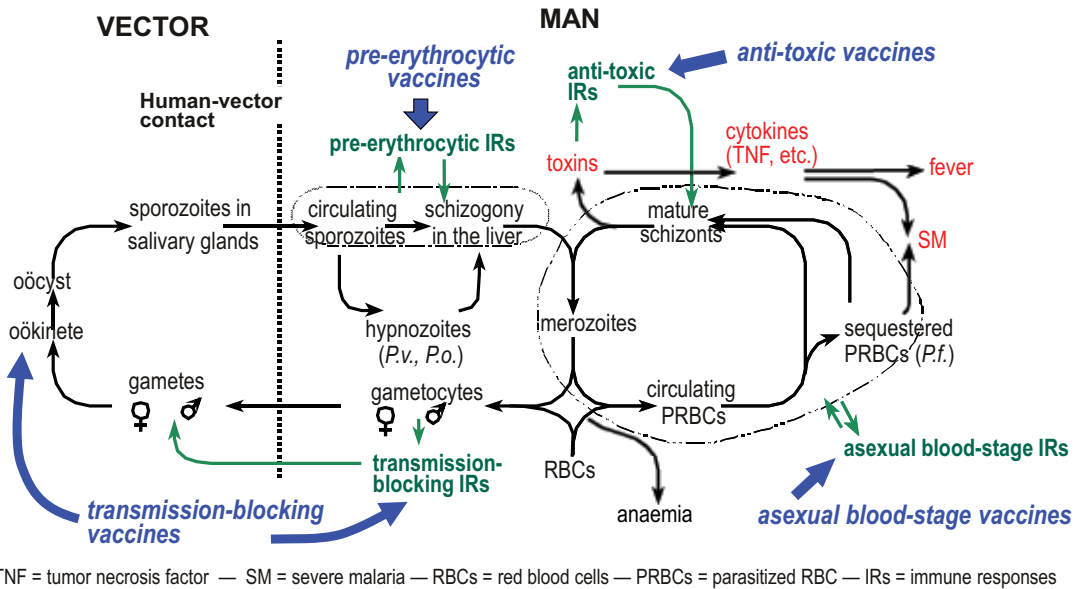
Figure 9.4   Parasite life-cycle, pathogenesis, natural immune response (IRs) and potential vaccines

Note: Transmission-blocking vaccines may contain, in addition to antigens expressed by gametocytes (naturally exposed to the host's immune system), some antigens expressed only after fertilization, thus not naturally exposed to the host's immune system.

9.4   The parasite's life-cycle and antimalarial drugs

Exercise 9.4

Figure 9.5 is the same as Figure 9.1, plus points of impact of the main antimalarial drugs.
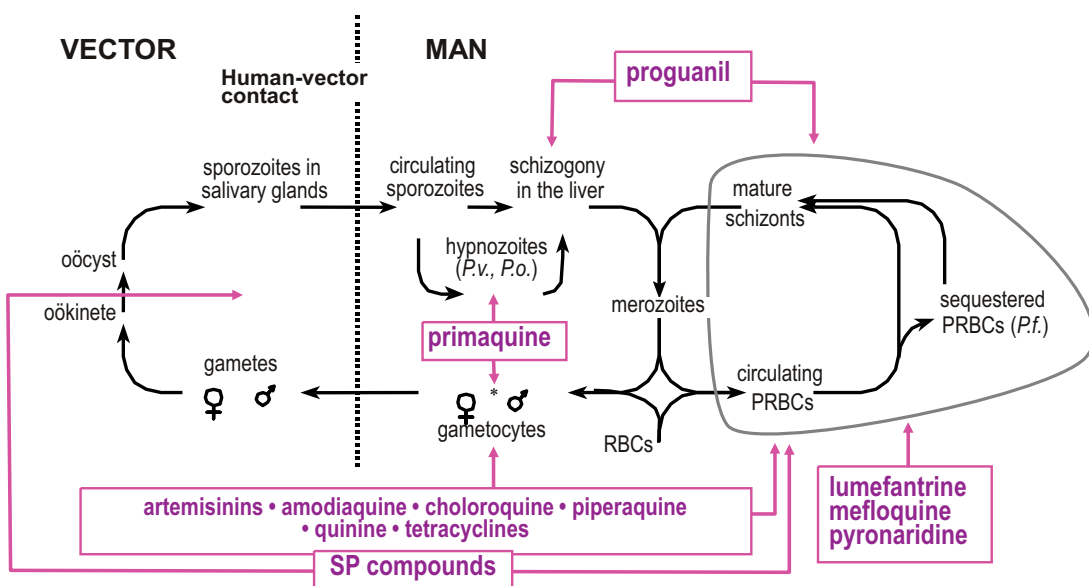
SP compounds = sulfadoxine-pyrimethamine, sulfalene-pyrimethamine
* except gametocytes of *P. falciparum*

Figure 9.5   Parasite life-cycle and antimalarial drugs

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9.5 Epidemiological measurements

Exercise 9.5

a. Figure 9.6 is the same as Figure 9.1, plus measurement methods.
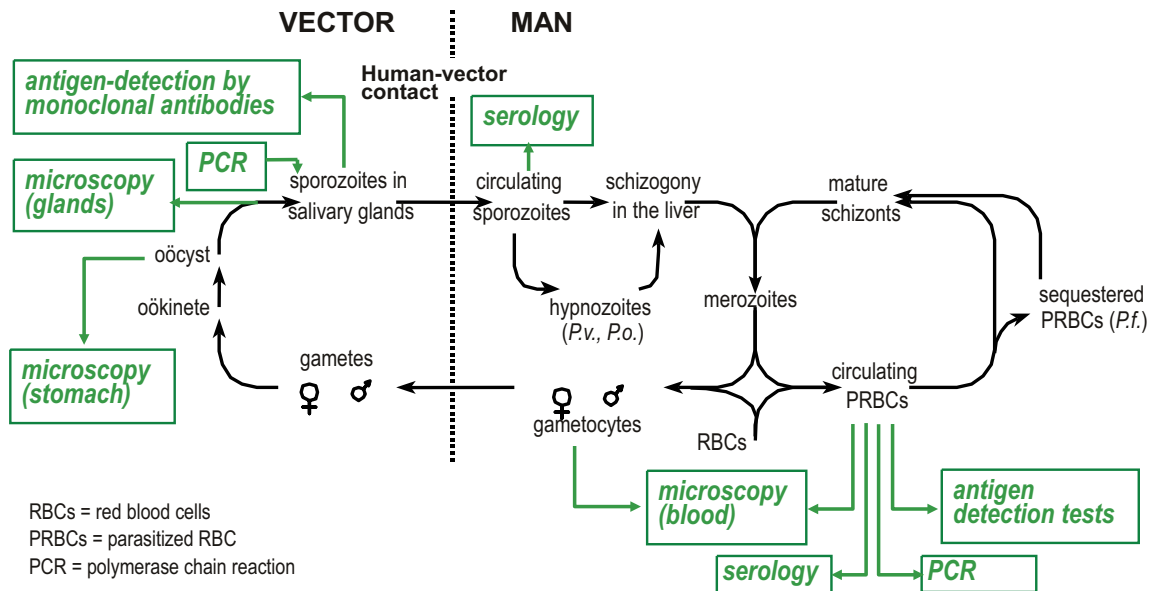
Figure 9.6 **Parasite life-cycle and** possible epidemiological measurements

b. The field test for diagnosis of malaria are microscopy and rapid diagnostic test (RDT). While polymerase chain reaction (PCR) tests are not yet adapted for routine disease surveillance, new methods for routine PCR-based surveillance of malaria infections are being deployed for research and field studies.

c. Sensitivity and specificity are the criteria for assessing the performance of diagnostic tests (Learning Unit 6).

For microscopic examination, sensitivity and specificity are directly related to the time available to read the blood film and to the level of competence of the microscopists. WHO considers minimum competency levels for peripheral level microscopists examining thick films as the following: 90% sensitivity, 80% specificity, 95% P. falciparum *species detection and 80% accuracy in parasite density determination.[1]*

Based on the results of the WHO Malaria RDT Product Testing Programme, several commercially available RDTs can consistently detect low parasite density infections (200 parasites/ μl) with corresponding low false positive and invalid rates.[2]

*PCR tests have higher sensitivities than light microscopy and RDT in detecting sub-microscopic infections, especially infections of less common species (*P. malariae, P. ovale, *and* P. knowlesi*), and mixed infections.*

[1]. WHO (2008). *Malaria microscopy Quality Assurance Manual. Version 1.* Geneva, World Health Organization. http://www.who.int/malaria/publications/atoz/mmicroscopy_qam/en/index.html.

[2]. WHO (2012). Malaria rapid diagnostic test performance: results of WHO product testing of malaria RDTs: Round 4, Geneva, World Health Organization. http://www.who.int/malaria/publications/rapid_diagnostic/en/index.html

LEARNING UNIT **10**

The life-cycle of the vector
and factors that influence it in relation
to malaria transmission

Learning Objectives:
by the end, participants should be able to...

■ Describe the life-cycle of the malaria vectors

■ Describe the factors affecting the vector's life-cycle in
relation to malaria transmission (including vector control)

■ Relate vector collection methods to the vector's life-cycle,
and entomological data to their epidemiological interpretation

The tutor should prepare photocopies in advance and use PowerPoint presentations the of Figures 10.1 to 10.3.

Answers

10.1 The vector's life-cycle

Exercise 10.1

The participants should work in small groups. Each participant should draw a diagram of the life-cycle of the malaria vector. After this has been completed, Figure 10.1 can be handed out to all participants. Time should then be allowed for comparison of the version produced by the groups with Figure 10.1 and to discuss any major differences. The tutor and facilitators should then invite questions and respond accordingly.

The tutor should point out that Figure 10.1 is very much simplified; in particular:

▶ it assumes gonotrophic concordance (one oviposition per blood-meal throughout), whereas in reality the first oviposition often requires two blood-meals;

▶ it ignores split blood-meals, including those split between human and animal;

▶ it ignores movement between indoors and outdoors resting within the same gonotrophic cycle.

These simplifications are not important for the present exercise.
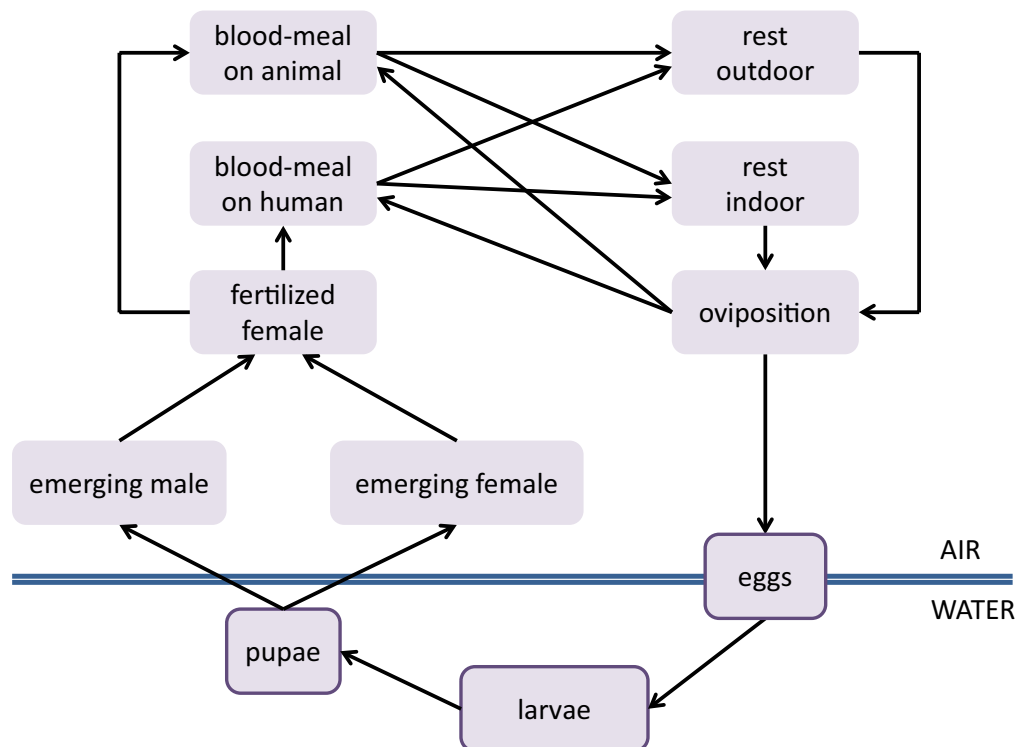
Figure 10.1 Schematic representation of the malaria vector's life-cycle

10.2 Factors affecting the vector's life-cycle in relation to malaria transmission, including vector control

Exercise 10.2

Ask the participants to list the factors that have a direct effect on the vector's life-cycle. The expected outcome from this exercise is outlined below.

1. Numerical factors

Time factors (durations) are all temperature-dependent; the following are typical of the main African vectors at high temperature.

► From egg to emerging adult: 7 days at 31 °C (20 days at 20 °C)

► From one blood-meal to the next (or from one oviposition to the next): 2–3 days

► Expectation of life of the adult female: 5–7 days[1]

Number of eggs: 100–200 per oviposition, i.e. every 2 – 3 days at 31 °C (partly compensated by high larval mortality)

2. Vector behaviour

This is determined by genetic factors, environmental factors and opportunity):

► choice of host (anthropophily, zoophily)

► choice of feeding place (endophagy, exophagy)

► choice of resting place (endophily, exophily)

► choice of oviposition place

3. Vector-parasite interactions

There may be differences in the susceptibility of the vector to infection and the physiological ability to transmit plasmodia. Susceptibility may be higher for some vectors than others in the same geographic area. Some vectors may or may not be susceptible to a particular parasite strain; this is an important issue with respect to the susceptibility of vectors from north of the Sahara to *P. falciparum* from south of the Sahara.

The duration of sporogony is dependent on the microclimate, e.g. temperature of the adult resting place, as well as on the species of *Plasmodium*.

At a temperature of 25 °C, 12–14 days are required for *P. falciparum* (or about 4 feeding cycles), slightly less for *P. vivax* (11–12 days), and considerably longer for *P. malariae* and *P. ovale*; thus only a minority of vectors live long enough to transmit (a very small minority for *P. malariae* and *P. ovale*).

At lower temperatures, sporogony takes longer time. The duration of sporogony is highly sensitive to temperature. The minimum temperature below which sporogony cannot be completed is about **19 °C** for *P. falciparum*, and **16 °C** and for the other species.

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[1.] Average; the range of individual values is wide.

The requirement for relatively high temperatures for the completion of sporogony determines the geographic distribution, with respect to both latitude and altitude, of the transmission of the different species, as well as the seasonal distribution of transmission at cooler latitudes and altitudes.

The duration of sporogony thus increases in the following order: *P. vivax, P. falciparum, P. ovale,* and *P. malariae.*

The effect of infection on vector longevity is probably insignificant. Loss of infectivity is probably not important, although degeneration of sporozoites has been shown in hibernating vectors infected with *P. vivax* in northern Europe.

Probable density-dependent regulation in the vector:

- The sporozoite-load developed by a vector is less than proportional to the number of gametocytes picked up. This is due to crowding and the effect of transmission-blocking antibodies;

- The number of sporozoites inoculated is also less than proportional to the sporozoite-load, due to injection of a very small volume of saliva.

4. Broad biological differences between vector species relative to malaria transmission

The vector species may differ mainly with respect to:

▸ Longevity

▸ Behaviour

  ▸ feeding preferences

  ▸ resting sites

  ▸ oviposition sites (suitability of different types of surface water)

▸ Susceptibility to infection

5. Physical environment

Factors affecting vector production include rainfall, type of soil, slope of the land, irrigation systems, urbanization, pollution, forestation and deforestation, existence of borrow-pits, and presence or absence of shade. Many of these factors affect the types of surface water that will be available. Factors affecting vector survival include the use of insecticides in agriculture, presence of predators, sudden changes in climatic conditions, etc.

Factors affecting human-vector contact include the position of settlements, housing, sleeping habits (anophelines bite mostly at night) and the availability of animals, especially cattle, as alternative sources of blood.

10.3   Vector control measures and their points of impact

Exercise 10.3

Participants should receive a copy of Figure 10.1 and should indicate on this vector control measures and their points of impact. The outcome should be Figure 10.2.

The question in the *Guide for Participants* on the effect of different control measures on the transmission of malaria is designed to emphasise that, at every **feeding cycle, the vector passes through the feeding, resting and oviposition stages,** whereas it goes through all other stages (egg, larva, adult, mating) only once in a lifetime. Thus indoor residual spraying gives an opportunity to kill the vector after every blood-meal, i.e. 4–5 times before it can transmit *P. falciparum* assuming a sporogonic cycle of about 8–10 days.

Personal protection methods or the diversion of bites from humans to animals can interfere twice with transmission, first by reducing transmission from human to vector, second by reducing transmission from vector to human. The other control methods against the larval stages act only once in a vector's lifetime (aquatic stages).
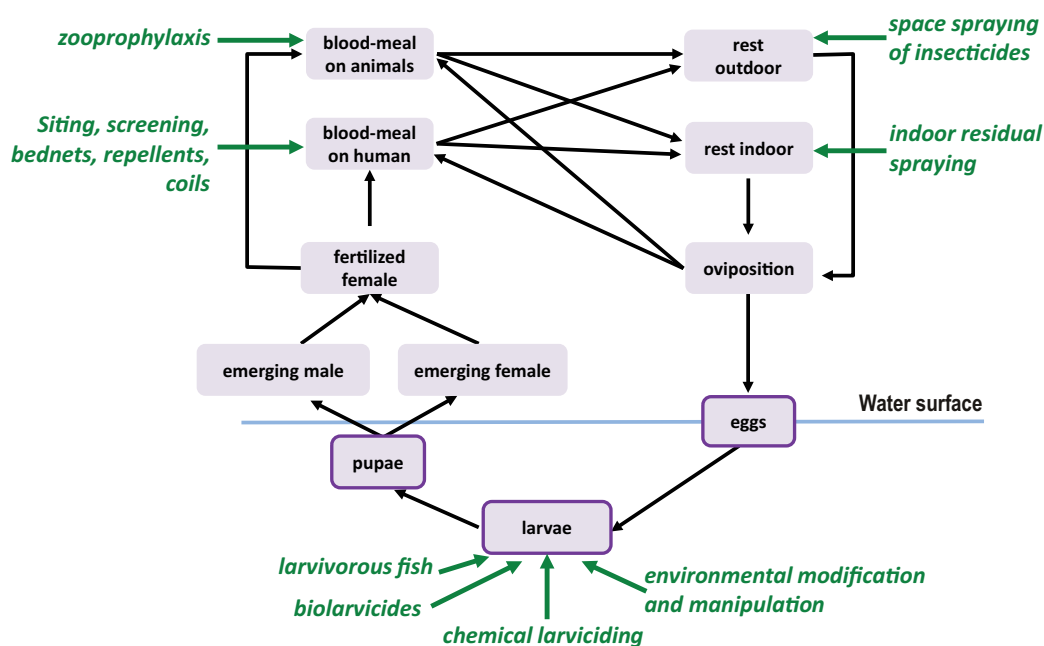
Figure 10.2 Schematic representation of the malaria vector's life-cycle, vector control methods

10.4   Efficacy of vector control measures

Exercise 10.4

The expected impact of residual spraying varies with the degree of uniformity of resting behaviour of the vector population. This can be illustrated by the following example. If:

i) half of the blood meals are followed by rest indoors

ii) rest indoors is lethal

iii) sporogony lasts for 4 gonotrophic cycles, i.e. there are 4 opportunities for exposure to the insecticide

Then:

i) If the resting behaviour is random in the vector population, half will escape the first opportunity of exposure, and half of those escape the second time, etc., so that the fraction that residual spraying fails to kill before completion of sporogony is $(0.5)4 = 0.0625$, i.e. 6.25%.

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ii) If this behaviour is not common to all members of the population, the expected impact is smaller, e.g. if half of the mosquitoes are totally exophilic and the other half totally endophilic, then half always escape exposure, so that the fraction that residual spraying fails to kill before completion of sporogony is 0.5, i.e. 50%.

The expected impact of diversion of bites to animals increases with the extent to which members of the vector population bite both humans and animals. This can be illustrated by the following example.

If half of the blood-meals are diverted to animals, then:

i) If the biting behaviour is completely random, the vector population acquires only half as many infections as before, and each infective vector infects only half as many persons as before, so that transmission is only: 0.5 / 2 = 0.25 of what it was previously.

ii) If behaviour is not random, the expected impact is smaller, e.g. if half of the mosquitoes are totally diverted to animals, and the other half not at all, the vector population acquires only half as many infections as before, but each infective vector infects as many persons as before, so that transmission is 0.5 of what is was previously.

There is evidence for the *A. gambiae* complex, the major vector group in Africa south of the Sahara, that both resting behaviour and biting behaviour vary within species and within local populations, and that the variations are at least partly genetically determined.

10.5 Measurement methods

Exercise 10.5

At this stage the course focuses on a review of existing measurement methods; the selection of methods to be included in a control programme is considered elsewhere.

(1) In natural or artificial shelters
(2) By hand (alive) or pyrethrum spray collection (dead)
(3) Two relatively common method to be added: exit traps and light traps
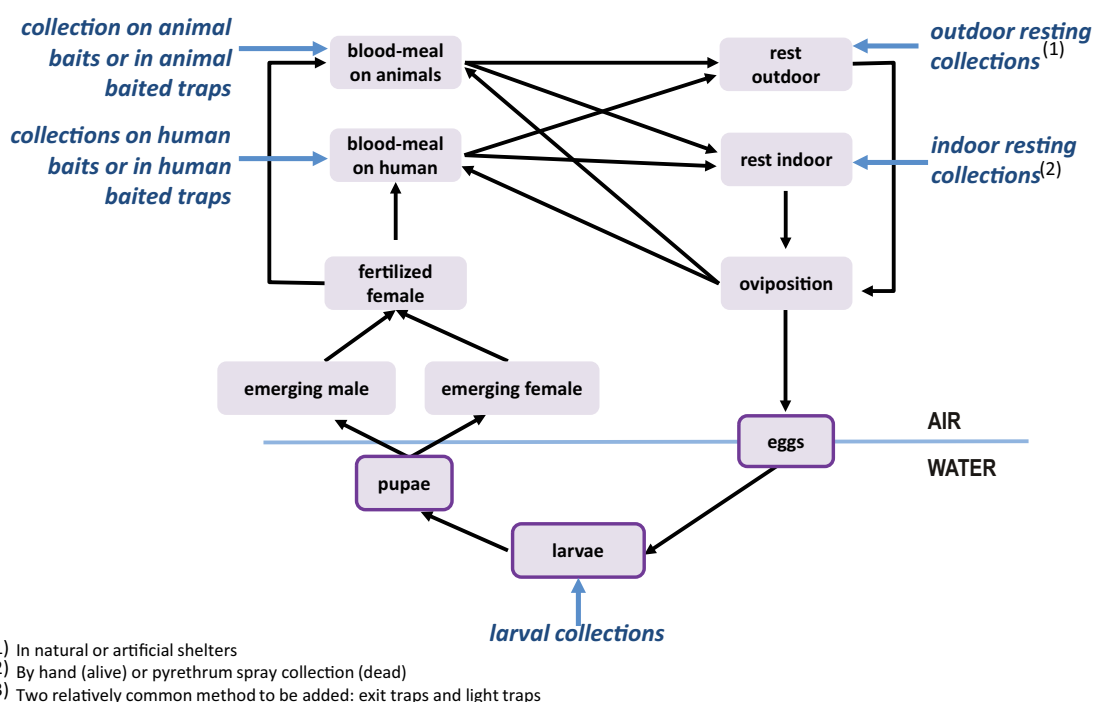
Figure 10.3 Schematic representation of the malaria vector's life-cycle and main vector collection methods[3]

10.6   Interpretation of entomological data

Answers to the three problems of epidemiological interpretation of entomological data

10.6.1   Representativeness

Exercise 10.6

Representativeness of entomological measurements

a. No, all the collection methods in Figure 10.3 measure density and behaviour at the same time.

b. Measurements of density are therefore only indicators of trend.

c. It matters for measuring impact of vector control if the control measure(s) affect both density and behaviour, as is the case with insecticide-treated mosquito nets, or with a residual insecticide which also has a repellent effect.

10.6.2   Ratio between sample size and population size

Exercise 10.7

The ratio between sample size and population size:

a. Entomological sampling fractions are usually very small.

b. In the example, in addition to the numbers given (20 female mosquitoes, 2 person-nights) we need to know:

i)   size of the village's human population

ii) fraction of the vector population feeding per night

iii) fraction of blood-meals taken on humans.

c. Let village population = 800; fraction of vectors feeding per night = 1/3; fraction of blood-meals taken on humans = ¼; the estimated vector population is (20/2) ✗ 800 ✗ 3 ✗ 4 = 96 000; the sampling fraction is 20/96 000 = 0.0002; it can also be calculated directly from the sampling scheme (i.e. before the collection), as follows: 2/(800 ✗ 3 ✗ 4) = 0.0002.

d. It is indeed common to find new cases of human infection without finding infected vectors. Suppose case detection identifies 75% of the actual new cases (i.e. sampling fraction = 0.75). If collection on human baits is conducted every 14 nights, the entomological sampling fraction calculated above must be further divided by 14, giving 0.000015. The ratio between the two sampling fractions is (0.75/0.000015) = 50 000, i.e. case detection is very much more sensitive than the detection of infected vectors (even though it misses 25% of the new cases of infection). Any other plausible numerical example will reach a similar conclusion. The finding of new human cases without finding infected vectors is therefore easy to explain.

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10.6.3 Calculating survival from age-composition

Exercise 10.8

a. *Age composition of adult female vectors at a point in time is determined by*

   i. *the number of females emerging per day over a period equal to the maximum life expectancy*

   ii. *survival*

b. *If survival is calculated from age composition at a point in time, it is assumed that emergence has been constant, over a period equal to the maximum life expectancy.*

c. *If survival is calculated from average age composition over a period of time, it is assumed that survival is constant over that period.*

LEARNING UNIT **11**

Natural history of malaria in the human host and factors that affect it

Learning Objectives:
by the end, participants should be able to...

◼ Describe the natural history of malaria in the human host

◼ Describe the factors that have an effect on the natural history of malaria in the human host, including immunity and malaria control measures

◼ Describe the role of improved diagnosis and treatment services at intermediate and peripheral levels in reducing morbidity and mortality due to malaria

The tutor should prepare photocopies in advance and use the PowerPoint presentations of the figures 11.1 to 11.6.

Answers

11.1 Natural history of malaria in the human host

Exercise 11.1

Working in small groups, each participant should carry out the tasks outlined in the *Guide for Participants*. Some guidance should be given in approaching this exercise in a logical manner such as considering infection, disease, recovery, death, and immunity, and the relationships involved.

About 30–40 minutes should be allowed for this exercise, giving the groups the time to discuss the results on their own; each group should then present its results and discuss the findings, especially any marked differences between their diagram, table, and answers to questions and those of this *Guide for Tutors*, i.e. Figure 11.1.
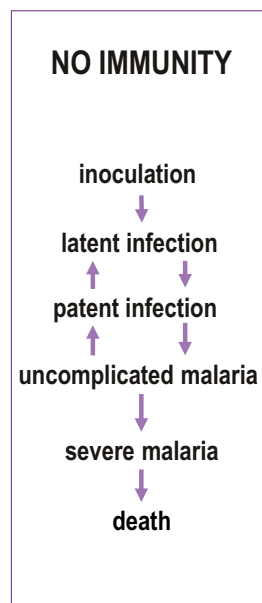
Figure 11.1 Natural history of malaria in human: six malaria states

Exercise 11.2

a. *Progression from one state to another can be very fast. In particular the intervals from onset of symptoms to development of severe malaria, and from onset of severe malaria to death are commonly very short, from a few hours to a few days.*

b. *The implications for case-management are therefore obvious:*

   i. *If a simple treatment of uncomplicated malaria can prevent its evolution into severe malaria, the time in which this intervention is effective is very short;*

   ii. *Immediate treatment of severe malaria is a major survival factor, indicating the administration of an interim treatment, by injection or suppository, before transportation to a more appropriate service for further management;*

c. In relation to the time of inoculation, the risk of disease tends to be concentrated in the first few weeks after appearance of the infection. The risk of severe malaria is even greater in the first few days after appearance of the infection.

Exercise 11.3

The classes of factors that might affect the outcome of an inoculation are summarized in Table 11.1.

Table 11.1   Classes of factors that might affect the outcome of an inoculation

1. The inoculum's intrinsic factors

• Quantity (the number of sporozoites inoculated)
• Quality (the kind of sporozoites inoculated)
       i. Differences of "virulence" among parasites
      ii. Differences of "virulence" within a parasite species, or within a local population
         of a parasite species

2. The human host's intrinsic factors
• Mutations that decrease or increase the host's susceptibility • Acquired immunity, active and passive • Other human biological factor
3. Interaction between parasite diversity and host diversity

11.2   The inoculum's intrinsic factors

Exercise 11.4

1. Number of sporozoites inoculated

a. An infected anopheline mosquito usually inoculates few sporozoites, perhaps about 10 on average, rarely up to 100.

b. The number of sporozointes has been estimated by letting an infected vector salivate on a glass slide or in a small vial of liquid nutrient, or by letting the vector feed on blood in vitro, through an animal skin.

c. Increasing the number of sporozoites inoculated slightly shortens the incubation period, but has little or no effect on parasitaemia or disease.

2. Differences of "virulence" among parasite species

a. P. falciparum causes severe malaria via sequestration. Within the 48-hour asexual blood stage cycle, the mature forms change the surface properties of infected red blood cells, causing them to stick to blood vessels. This leads to obstruction of the microcirculation and results in dysfunction of multiple organs (e.g. brain leading to cerebral malaria; kidneys leading to acute renal failure, etc.).

b. P. vivax malaria can also be fatal in case of rupture of the spleen, but this is extremely rare. Death due to *P. malariae* is also rare, and results from chronic renal insufficiency.

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P. falciparum invades red blood cells of all ages, whereas *P. vivax* tends to invade reticulocytes and *P. malariae* only relatively old red blood cells. This explains why *P. falciparum* reaches higher levels of parasitaemia than the other species. Another major pathogenic factor in malaria due to *P. falciparum* is the sequestration of parasites in vital organs, including the brain.

3. Differences of "virulence" within a parasite species or local parasite population

a. Differences of virulence within a species are suggested by old observations from an era when malariotherapy was used to treat neurosyphilis: e.g. *P. falciparum* from Italy was found more pathogenic than *P. falciparum* from India.

Differences of virulence within a local population of a species are suggested by points *(i)* and *(ii) in the Guide for Participants.* The example works out as follows:

Before superinfection, this child's circulating population of parasitized RBCs is: $2 \times 10^6 \times 10^3 = 2 \times 10^9$; each mature liver schizont releases 30 000 merozoites (see Learning Unit 10); suppose each of these merozoites successfully invades a RBC; the number of parasitized RBCs added by superinfection is: $20 \times 30\ 000 = 6 \times 10^5$, and the ratio of added parasitized RBCs to pre-existing parasitized RBCs is $(6 \times 10^5) / (2 \times 10^9) = 3 / 10^4$, i.e. very small.

Therefore, in order to cause disease (uncomplicated malaria or severe malaria) the added parasites must be *different*. However, in addition to intrinsic parasite diversity, its interaction with host diversity is probably important (see below).

11.3 The human host's intrinsic factors

11.3.1 Genetic traits and susceptibility

Exercise 11.5

Hemoglobin S (sickle cell): the heterozygotes have a high degree of protection against the lethal effect of falciparum malaria

Duffy-negative erythrocytes: individuals with erythrocytes lacking the Duffy blood group antigen (Fya Fyb) are resistant to *P. vivax* infection. Protection is absolute and specific. Persons throughout much of Africa have duffy negative erythrocytes.

G6PD deficiency: probably impedes the development of the parasite in erythrocytes and restricts parasitaemia.

Other haemoglobinopathies: HbC in Africa and HbE in Asia seem to protect against *P. falciparum* infection but this requires further investigation.

An example of a genetic factor that increases the human host's susceptibility: people with malaria who are homozygous for a gene that enhances TNF production have an increased risk of developing cerebral malaria.

11.3.2   **Acquired immunity (active)**

Exercise 11.6

a. Acquisition, loss, and effects of active immunity

Active immunity increases after each new appearance of parasites in the blood (infection, relapse or superinfection).

Immunity decreases gradually after the parasites disappear from the blood.

Immunity does not prevent infection, but in case of infection it decreases the risk of illness and in case of disease it decreases the risk of progression to severe disease and death.

Acquired immunity to malaria is species-specific. It induces an accelerated clearance of asexual parasites from the blood, probably combined with partial protective immunity against pre-erythrocytic stages. The acquisition of active immunity is already involved in recovery from the first infection. Subsequent infections tend to increase the level of immunity, while in the absence of inoculation the level tends to decrease.

Loss of immunity results from removal from exposure, as shown by the occurrence of clinical, even severe, malaria in previously immune adults returning from a stay of 1–2 years in a non-endemic area. Upon returning to an endemic area they will typically need 1–2 years to regain their immunity, depending on intensity of transmission and protection measures used.

b. Diagram

Figure 11.2 summarizes in a diagram the expected effects of gradual development of active immunity. The diagram correctly suggests that successive inoculations become progressively less pathogenic and less dangerous. There is no contradiction with the statement about some children developing severe malaria only after many previous inoculations: on a population basis, the fractions developing uncomplicated malaria or severe malaria decreases with successive
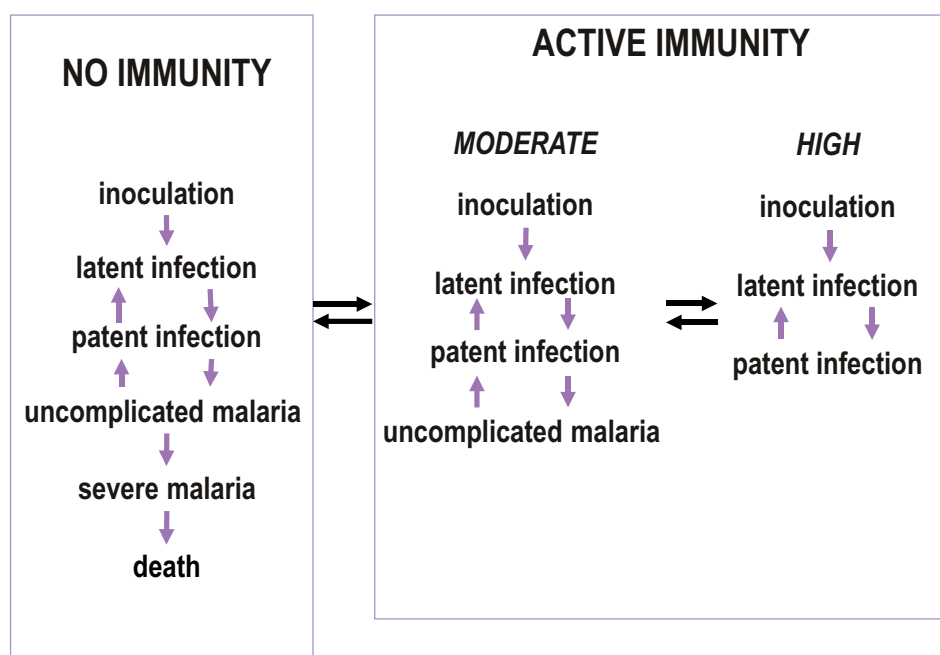
Figure 11.2 Natural history of malaria in human: the effect of acquired immunity, active and passive

inoculations; on an individual basis, the probability of developing uncomplicated malaria or severe malaria decreases with successive inoculations, but the actual outcome of an inoculation may also depend on host and parasite diversity and their interaction (see below).

c. Expected effects of different malaria control measures

Antimalarial drugs prevent or delay the acquisition of immunity, but the treatment of cases prevents and reduces mortality at the same time.

Future vaccines against asexual blood-stages might mimic natural immunity, which protects against disease and death more than against infection; but the vaccines should arrive at that result without the morbidity and mortality associated with the development of natural immunity.

Future anti-gamete vaccines will have no direct benefit on the host; they will have an indirect effect through the reduction of transmission in the community.

11.3.3   Acquired immunity (passive)

Exercise 11.7

a. Passive immunity is conferred through maternal antibodies in areas of relatively intense transmission.

b. Such immunity is partial and transient, and is probably lost by the age of 6 months or even sooner. The effects of passive immunity are also illustrated diagrammatically in Figure 11.3.
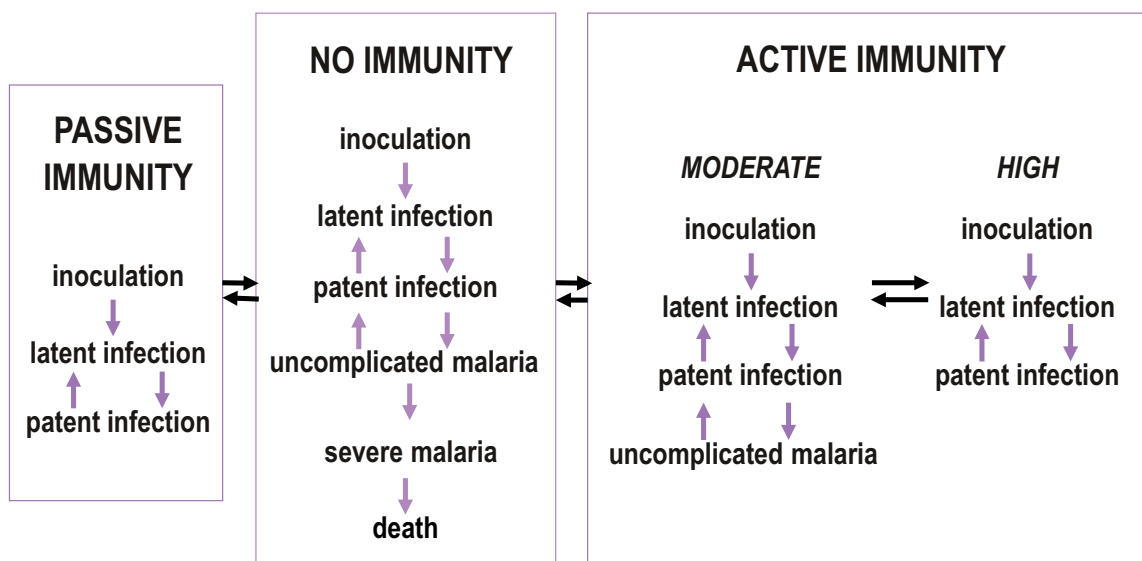
Figure 11.3 Natural history of malaria in human: the effect of passive immunity

11.4   Other human biological factors

Exercise 11.8

Discuss how pathogenesis is affected by:

a. Pregnancy
Pregnant women, especially primigravidae, show increased susceptibility to *P. falciparum* malaria, manifested by increased prevalence and density of parasites, anaemia, risk of

abortion, stillbirth and decreased birth weight. The main pathogenic mechanism is parasite sequestration in the placenta. Malaria experience during one pregnancy has a protective effect during subsequent pregnancies.

b. Nutritional status

Malaria has a negative effect on nutritional status by reducing food intake and increasing metabolism, and malnutrition could increase the case fatality rate of malaria by impairing general resistance. On the other hand the correction of severe malnutrition may cause latent *P. falciparum* to flare up.

c. Age per se (i.e. separately from its association with immunity)

Age per se affects susceptibility to the two main forms of severe malaria, cerebral malaria and severe malaria anaemia. Cerebral malaria is exceptional below 2 years of age, even under the most intense transmission. Infants, on the other hand, are particularly susceptible to severe malarial anaemia.

11.5   Interaction between parasite diversity and host diversity

Exercise 11.9

a. i. *many antigens*

   ii. *much antigenic diversity*

b. i. *no*

   ii. *yes*

c. *It is possible that any* P. falciparum *parasite could be dangerous for some hosts, if the host's immune repertoire covers too small a part of the parasite's antigenic repertoire.*

11.6   Age-specific distribution of malaria

Exercise 11.10

a. *Where there is relatively intense transmission, the age-specific distributions of acute malaria morbidity will appear more or less as in Figure 11.4 (see next page).*

b. *If the intensity of transmission increases, the peaks (maxima) occur earlier (at a younger age) and the subsequent decreases are steeper; if the intensity of transmission decreases, the opposite occurs.*

In fact, exposure to vectors increases with age; if the average exposure is high, its increase with age is probably not very important.

As the intensity of transmission increases, the source of infection, clinical malaria, severe malaria and malaria mortality become concentrated in younger age-groups (this concentration is greatest for severe malaria and malaria mortality). With respect to the source of infection, the size of the adult population partly compensates for the low infectivity of adult individuals. If the intensity of transmission decreases, e.g. under the impact of vector control, uncomplicated malaria and severe malaria may become more common in older age groups.

> ▶ **A. Low endemicity** – A person may attain adolescence before infection is acquired and may escape altogether.

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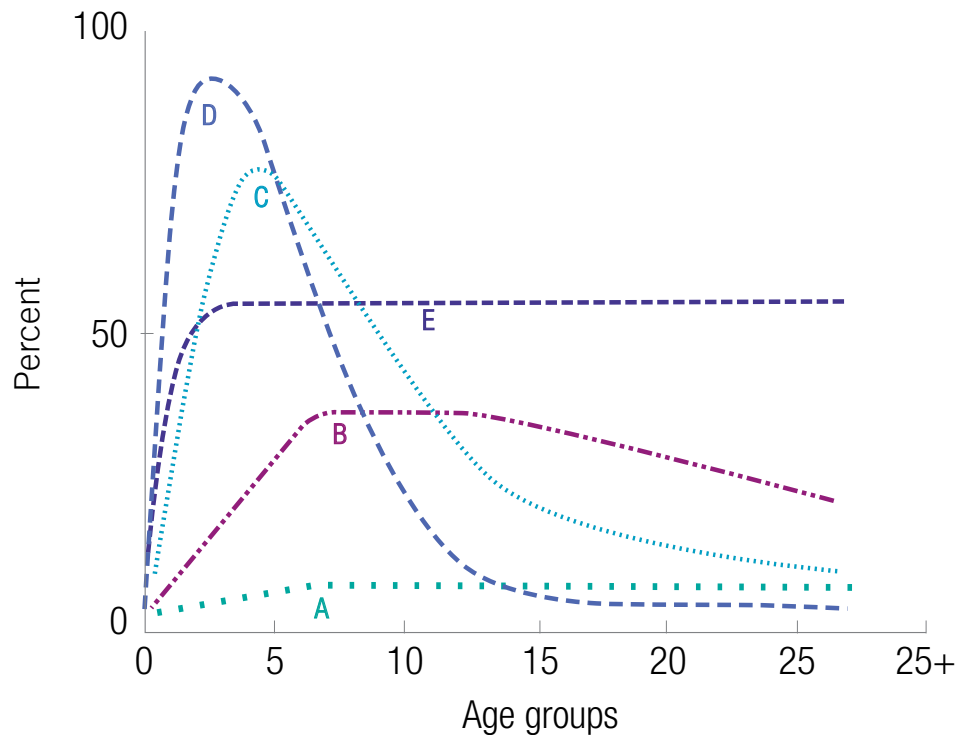
Figure 11.4 Diagram illustrating concept of incidence of acute malaria infections with transmission at different endemic levels in stable indigenous populations

> ▸ **B. Moderate endemicity** – Maximum incidence occurs in childhood and adolescence, though still not unusual for adult life to be attained before acquiring infection.

> ▸ **C. High endemicity** – By late infancy or early childhood practically all are infected. Little acute illness in adolescents and still less in adults.

> ▸ **D. Hyperendemicity** – Most individuals acquire infection in early infancy, but acute manifestations are less frequent in childhood and are unusual in adults.

> ▸ **E. Epidemic** – epidemics can only occur in populations where malaria was either previously absent or persisted at low or moderate endemic level. They are characterized by a high incidence at all age periods.

c. *Figure 11.4 outlines the classical picture of age-specific distribution of malaria morbidity at different levels of endemicity and in epidemic malaria, as described by Boyd in 1949. Immunity is the main factor affecting the age-specific variations of infection and disease.*

11.7   Malaria mortality

Exercise 11.11

a. *The risk of dying is almost certainly greater among children suffering from pneumonia **plus** uncomplicated malaria than among children suffering from pneumonia alone, and likewise for several other diseases. Generally, the addition of malaria is likely to increase the CFR of a number of diseases.*

Figure 11.5 is a diagram of the events leading to direct and indirect malaria mortality.
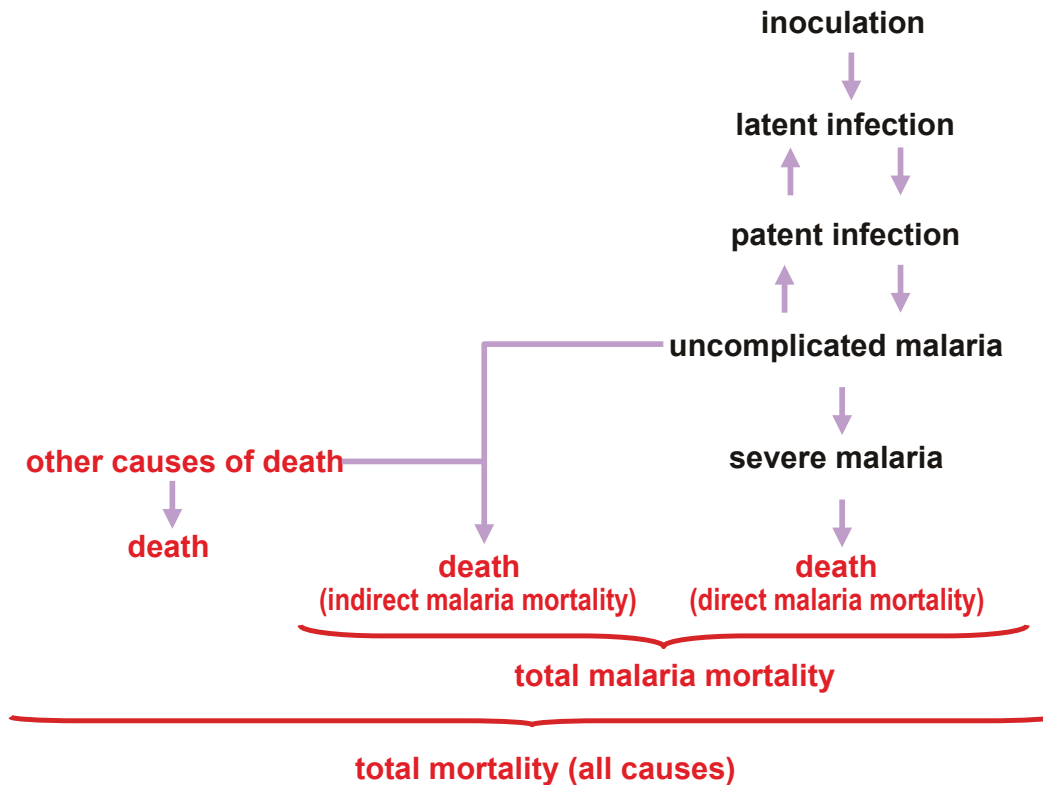
Figure 11.5 Malaria and mortality

The relative magnitude of direct and indirect malaria mortality is of practical importance: it affects what can be expected from the reduction of transmission.

b. *Two kinds of data may allow estimation of the relative magnitude of direct and indirect malaria mortality:*

  i. *Measurements of malaria-specific mortality from death certificates or from "verbal autopsies"[1] or of the incidence of severe malaria as an alternative indication in a population well covered by an adequate hospital service;*

  ii. *Measurement of the reduction in mortality from all causes following the removal, or near removal, of malaria by residual spraying.*

The second kind of measurement must correspond to all malaria mortality (direct and indirect), while the first kind of measurement is more likely to reflect direct malaria mortality; the difference might thus represent indirect malaria mortality.

c. *The data actually available may not be as clear cut as one might wish, but they do suggest that total malaria mortality, both direct and indirect, can be 2–3 times greater than direct malaria mortality alone.[2]*

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[1.] "Verbal autopsy" assigns a cause to a death on the basis of a standardized interview of close relatives and/or carers

[2.] Payne D., Grab B., Fontaine R. E. and Hempel J. H. G. (1976). Impact of control measures on malaria transmission and general mortality. *Bulletin of the World Health Organization*; 54(4): 369–377

Two other points could come up in the discussion:

- *The high (total) malaria mortality implicit in the high HbS gene frequency observed in some populations also suggests a large indirect malaria mortality.*

- *The usual way to define and measure cause-specific mortality assumes that every death has one cause and one cause only, which is unlikely to be true in all cases.*

LEARNING UNIT **12**

Intensity of malaria transmission

Learning Objectives:
by the end, participants should be able to...

■ Define the major parameters of intensity of transmission which are used in malaria epidemiology

■ Identify the relationships between the vectorial capacity, the basic reproduction rate, the inoculation rate, and the incidence and prevalence of malaria infection

■ Describe the expected impact of mass drug administration and/or vector control activities on malaria transmission at different levels of endemicity

■ Distinguish what models can or cannot contribute to the planning of malaria control

■ Indicate the epidemiological methods for measuring malaria morbidity and mortality and how information can be collected

■ Describe how the relationship between vectorial capacity and other concepts of the intensity of malaria influence the selection of control methods in different epidemiological situations

The tutor should prepare photocopies in advance and use PowerPoint presentations of figures 12.1 to 12.4, and of Table 12.1. A copy of Table 12.1 is to be given to the participants after completion of this Unit.

This Unit will require careful preparation and should be given more time than the other Units, unless the tutor decides to select only some parts which fit the scope of a particular course. Some of the participants may not be familiar with the mathematical formulae, so it is important that these are introduced step-by-step and that practical examples are given. The numerical exercises will help the participants to become familiar with the models and to understand how the formulae can be used to describe the determinants of malaria transmission.

Answers

12.1 Intensity of transmission

Exercise 12.1

Incidence rate

The incidence rate is number of new infections occurring in a given population unit, e.g. per thousand, in a given time period, e.g. one year. Note that the traditional API (annual parasite index) is an incidence rate.

Prevalence rate

The prevalence rate is the number of existing cases, new and old, in a defined population during a specified period (period prevalence) or at a given point in time (point prevalence). It is expressed as number of cases per X (e.g. 100 000) population. Note that the SPR (slide positivity rate) is a prevalence rate among *suspected cases*.

Entomological inoculation rate

The entomological inoculation rate is the number of mosquito bites (inoculations) containing sporozoites received by the population unit in a given period of time. It is often expressed as the total number of infective bites per person per day, sometimes as the number of infective bites during a whole transmission season or a whole year.

12.2 Vectorial capacity and basic reproduction rate

Exercise 12.2

a. *Primary and secondary cases*

   i. *Primary case is the person who first contracted malaria infection in a community.*

   ii. *Secondary cases are the persons who became infected by mosquitoes which had acquired the parasite from the primary case.*

b. *If a malaria patient has gametocytes in the blood for 14 days only (i.e. he/she could potentially transmit the infection), and from whom 5 new cases are added to the community every day, at the end of 14 days: 14×5 = 70 new cases would have been added to the community.*

c. *In this example the vectorial capacity value is 5 and the basic reproduction rate value is 70.*

Some important points:

Revise the following materials by going through Q & A's with the participants.

It must be remembered that the concept of vectorial capacity in malaria was first introduced by Ronald Ross, and the duration of disease *without treatment* was considered in the initial concepts. Falciparum malaria patients who survive can retain the parasite in the blood for 1–1.5 years without treatment, and for 2–5 years in vivax malaria patients. After this period the parasite will be cleared from the blood, but during this period the patients do *not* have gametocytes in their blood, and so they are not infective.

Derivation of a formula for vectorial capacity (C)

Exercise 12.3

▶ **Stage 1:** the number of female mosquitoes that feed on humans daily depends on *(i)* the number of female mosquitoes per person (vector intensity) which is represented by *m*, and *(ii)* the number of blood ingestions per mosquito in a day, which is represented by *a*.

▶ **Stage 2** and also **Stage 5**: in these stages the infection should be transmitted from human to mosquito and vice versa, the *efficiency* of the system intervenes, and this efficiency is incomplete. *Efficiency* of the malaria transmission system is represented by *b*.

▶ **Stage 3:** the number of mosquitoes that have ingested blood and are capable of passing through the sporogony cycle depends on: *(i)* the mosquito's survival which represented by *p*, and *(ii)* the length of the sporogony cycle which is represented by *n*. For example if *p* is considered to be 0.9 and the length of the sporogony cycle (which is influenced by factor such as temperature, humidity, parasite species and mosquito's species) to be 8 days, the 90% of the mosquitoes that have received the gametocytes will live and 10% will die on the first day. On the second day, 90% of the surviving 90% will live and 10% of them will die (i.e. 9% of the initial number). This process continues until the 8th day. Hence the percentage of mosquitoes that go through the sporogony cycle will be as follows:

$$0.9 \times 0.9 \times 0.9 \times 0.9 \times 0.9 \times 0.9 \times 0.9 \times 0.9 = 0.43$$

i.e. the possibility of a mosquito becoming infective is equal to *p* to the power of *n*, or p^n

▶ **Stage 4:** the important point is that the mosquitoes that become infective stay alive for a few days until they transmit the disease by biting the next hosts. The life period of the mosquito can be calculated from *p* which is survival. On this basis the number of days the mosquito stays alive is:

$$1 / -\log_e p$$

Although the exact expectation of life is expressed the formula above, the following approximation is used because it is more easily understood by people who are not very familiar with mathematical principles:

$$1 / 1 - p$$

In stage 4, in addition to the mosquito's survival, the number of blood feeds on humans per mosquito per day (represented by *a*) becomes important and has to be added to the formula *for the second time.*

On the basis of the above, vectorial capacity (C) must be the product of the five stages; they can be expressed in terms of the individual factors as follows:

Stage 1 = (m) x (a) = ma

Stage 2 x Stage 5 = b

Stage 3 = p^n

Stage 4 = $\left[\dfrac{1}{(1-p)} \right] a = \left[\dfrac{a}{(1-p)} \right]$

Considering the exact expression of Stage 5 = $\dfrac{a}{(-\log_e p)}$

$$C = m \cdot a \cdot b \cdot p^n \cdot a \cdot (1/1-p)$$

Number of mosquitoes per person

Number of bites per mosquito in a day

Number of days the mosquito stays alive

The system's efficiency in transmitting infection

A fraction of mosquitoes that go through the sporogony cycle
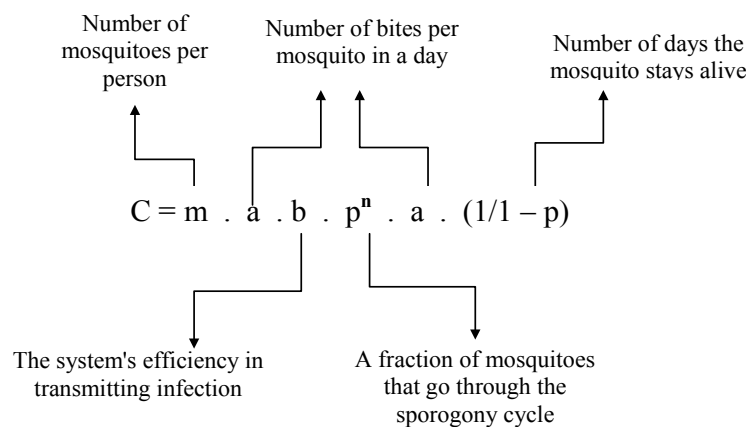
Multiplication gives: $C = \dfrac{m\, a^2 b\, p^n}{1-p}$

Considering the exact expression for $1 / 1 - p$ in stage 5, the above formula is expressed as:

$$C = \dfrac{m\, a^2 b\, p^n}{-\log_e p}$$

Table 12.1 summarizes factors determining the vectorial capacity of a mosquito population and the basic reproduction rate of malaria.

Relationship between vectorial capacity and basic reproduction rate

Exercise 12.4

a. *According to the definition, the following relationship should be established:*

Basic reproduction rate = vectorial capacity × number of days the person is infective

b. *Representing basic reproduction rate with Ro and vectorial capacity with C, the formula will be written as follows:*

R_o = C × *number of days the case is infective*

Table 12.1 Factors determining the vectorial capacity of a mosquito population and the basic reproduction rate of malaria[1] (after Black)

Factor	Definition of index	Common name of index	Method of obtaining the index	Macdonald's (1957) expressions
1	Bites perperson per night by vector population	Human-biting rate	Night-biting captures on human baits, e.g. 10 bites per person	ma
2	Bites per mosquito per night Proportion of bites on humans ("human blood index")	Human-biting habit	Composed of: **(i)** the feeding frequency based on the observed gonotrophic cycle in nature, e.g. 0.4 where the female oviposits and feeds once in 2.5 days on an average; and **(ii)** the human blood index, assessed by the precipitin test applied to daytime resting samples, e.g. 0.5: a = 0.4 x 0.5 = 0.2	a
3	Probability of vector's survival through the sporogonic period of the parasite		Based on age-grading or proportion parous, and knowledge of gonotrophic cycle duration, e.g. 0.6 days[a]	p^n
4	Life expectancy of female vectors			$\dfrac{a}{-\log_e}\, p$
5	Expected inoculations of humans per infective case per day	Vectorial capacity of vector population	Multiplication of factors 1 x 2 x 3 x 4. e.g. 10 x 0.2 x 0.6 = 1.2 When this value descends below 0.01, basic reproduction rate is 1 for *P. falciparum*	$\dfrac{m\,a^2 b\,p^n}{-\log_e p}$
To obtain the basic reproduction rate:				
6	Proportion of vector females developing parasite normally following ingestion of gametes	Mosquito's receptivity (susceptibility) to infection	Only assessable by infections of captive samples on malaria cases, e.g. 0.9	b
7	Days of infectivity per case (i.e. reciprocal of proportion of cases recovering in one day)	Reciprocal of recovery rate	Longitudinal observations of local cases of malaria in the absence of transmission, e.g. 100 days	$\dfrac{1}{r}$
8	Expected new infections per case in the absence of immunity	Basic reproduction rate of parasite	Multiplication of factors 5 x 6 x 7, e.g. 1.2 x 0.9 x 100 = 108	$\dfrac{m\,a^2 b\,p^n}{-r\,(\log_e p)}$

a To compute the factors from the proportion parous it is necessary to know also the mean difference in age between the nulliparous and the youngest parous females in the sample, and the sporogonic period of the parasite. Graphs are available to enable the field worker, who has observed these parameters, to read off from his/her data the proportion surviving one day, the expectation of infective life and the expectation of life.

Note: e is the base of natural logarithms (2.718).

[1.] Black RH. (1968). *Manual of epidemiology and epidemiological services in malaria programmes.* Geneva, World Health Organization.

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c and *d. In fact the number of days the person has been ill is equal to the inverse of the patients recovery rate (or 1/patients recovery rate). Recovery rate is shown by 'r'. If r is added to the formula above, the formula becomes the following:*

$$R_0 = C \cdot \frac{1}{r}$$

or

$$R_0 = \frac{C}{r}$$

The basic reproduction rate is obtained by multiplying the number of infective days by the vectorial capacity value.

The "number of days the person is infective" has an inverse relationship with recovery rate. As previously noted, if recovery rate is represented as *r*, the basic reproduction rate represented by R_0 will be: $C \times 1 / r$

Derivation of a formula for basic reproduction rate (R_0)

Exercise 12.5

Based on the above relationship between vectorial capacity and basic reproduction rate, the following formula can be derived for R_0:

$$R_0 = \frac{C}{r} = \frac{m \, a^2 b \, p^n}{r \, (1 - p)}$$

i.e. the basic reproduction rate is equal to vectorial capacity divided by recovery rate *r*. Recovery rate is the fraction of patients who recover and lose infectivity daily. Using the exact expressions for stage 4, the formula becomes:

$$R_0 = \frac{m \, a^2 b \, p^n}{r \, (- \log_e p)}$$

12.3 Vectorial capacity, basic reproduction rate, and control of transmission

Exercise 12.6

a. The following control measures can affect the various components of the vectorial capacity

Control measures	Factors affected (among *m, a, p, n, 1/r*)[a]
Residual spraying	reduces *m* and *p*, it may reduce *a*
Space spraying	reduces *m*
Source reduction	reduces *m*
Larviciding	reduces *m*
Reduction of human-vector contact	reduces *a*
Insecticide-treated mosquito nets	reduces *m, a*, and *p*
Treatment of cases	increases *r* (decreases 1 / *r*)

[a] *m* = vector density in relation to human; *a* = vector's biting rate on humans; *p* = survival of the vector; *n* = duration of sporogony cycle; 1 / *r* = duration of infectivity (in humans)

b. *Reduction of m reduces C (or R_o) in the same proportion*

Reduction of $(1 / r)$ reduces R_o in the same proportion

Reduction of a is amplified by squaring a in the formula

Reduction of p is amplified much more by putting p to the nth (where n is duration of sporogony cycle) power, i.e. 8th to 10th power for *P. falciparum* at high temperature, in addition to the roughly proportional reduction of the longevity $1 / (1 - p)$

c. *Solution of the numerical example*

m	a	p	n	C (approx)	C (exact)
10	0.5	0.8	10	1.34	
5	0.5	0.8	10	0.67	
10	0.25	0.8	10	0.335	
10	0.5	0.4	10	0.0004	

d. *With regard to the relative efficacy of different control measures, residual spraying appears much more effective than any other measure, and reduction of human-vector contact appears more effective than other control measures, with the exception of residual spraying.*

12.3.1   Identification of simplifying assumptions

Exercise 12.7

Uniform vector behaviour has been assumed; this maximizes the expected effects of residual spraying and of reduction of human-vector contact, as shown in Learning Unit 11.

The comparison between equal proportional reductions of various factors influencing the vectorial capacity does not correspond directly to an operational option; other factors are neglected, including:

▶ Cost

▶ Effectiveness of control measures in reducing the factors affecting the vectorial capacity

▶ Quality of operations, and its maintenance

▶ Acceptability, and its maintenance

▶ Insecticide resistance

So far the discussion is concerned with malarial infection and its transmission; it cannot be assumed that the impact of control measures on malarial morbidity and mortality is directly proportional to their impact on infection and transmission.

12.3.2   Measurement of intensity

Exercise 12.8

The following comments can be made about the actual measurement of the five parameters of intensity of transmission:

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a. *Incidence of infection can be measured by:*

i. Case detection i.e. detection of fever cases, from which a blood slide is then taken, if new infections are generally symptomatic. This may be true at low transmission, but is definitely not true at high transmission; cost is low if one relies on cases detected by the curative services, high if one aims at ascertainment (outside curative services).

ii. Longitudinal follow-up of a cohort of negatives, e.g. newborns, or children given a curative treatment; the estimate obtained in infants is usually termed 'infant conversion rate'.

iii. Fitting of a catalytic model to an age-specific prevalence curve among infants; the estimate is usually termed 'force of infection'; the prevalence of parasitaemia may be supplemented by prevalence of specific IgM, which is evidence of post-natal infection as IgM does not cross the placenta.

i. and *ii.* are only applicable on a sample base, and usually restricted to research projects.

b. *Prevalence of infection can be measured by sample survey; technical feasibility and reliability depend on representativeness of sampling and quality of parasitologic examination; cost is moderate as long as prevalence is relatively high.*

c. *Entomological inoculation rate can be measured by the human-biting rate (number bites/person/ night) and the sporozoite rate; it is technically feasible, but reliable only with relatively intensive sampling in time and space, which makes it expensive.*

d. *In principle the vectorial capacity can be measured:*

ma can be measured by collections on human baits

a can be calculated by dividing the proportion of blood meals taken on human by the interval between consecutive blood meals: the proportion is measured by the precipitin test (serological method used for identification of mosquito blood meals); the interval can be measured by various methods.

P can be calculated from the temperature and the known relationship between n and temperature.

The measurement of R_o requires in addition a value for r and $(1 / r)$. Values can be found in the literature but they are not very satisfactory.

In practice measurements of C and R_o are expensive and not reliable.

However, these concepts can be useful, even in the absence of actual measurements, for understanding certain principles of the epidemiology and control of malaria.

12.3.3 Relationship between prevalence and incidence

Exercise 12.9

a. *Encourage an interactive discussion on the relationship between prevalence and incidence*

b. *Prevalence (of a phenomenon) is determined by its incidence and its duration*

$$P = I \times D \text{ or } I = P / D$$

where: **P** = prevalence

I = incidence

D = duration

c. Example using the formula P = I x D

If the incidence rate is 200 per thousand or 0.20 per year, and the duration of a case is 2 months or (2 / 12) or a year, the expressed prevalence is 0.20 x (2 / 12) = 0.033 or 3.3%.

Note that *I* and *D* have to be expressed in the same time unit.

12.3.4 Qualitative relation between the different dimensions of intensity of malarial infection and its transmission

Exercise 12.10

The vectorial capacity and the prevalence rate together determine the entomological inoculation rate. This determines the incidence rate, which in turn determines the immunity level, and this, together with the basic (non-immune) recovery rate, determines the actual recovery rate, i.e. the actual duration of infection. The incidence rate and the actual recovery rate together determine the prevalence rate, whilst the vectorial capacity and the basic recovery together define the basic reproduction rate.

In Figure 12.1, infection and infectivity are distinguished.
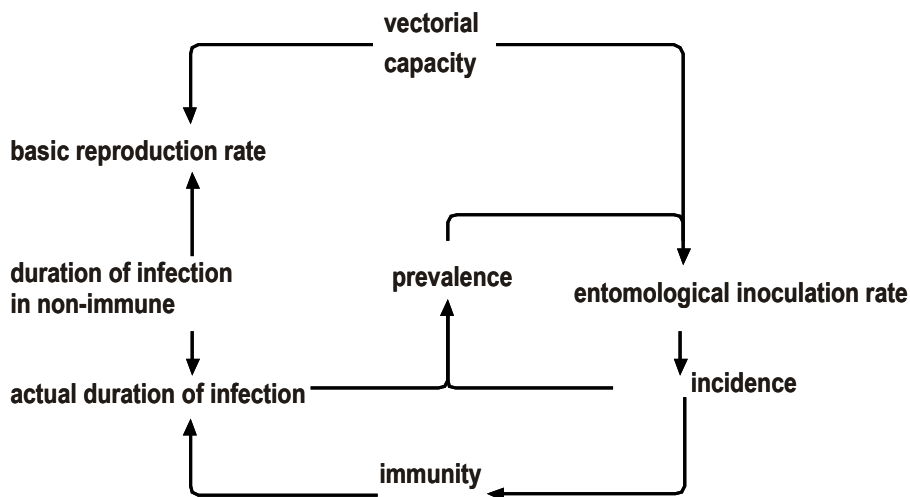
Figure 12.1 Relationships among measures of intensity

12.3.5 Quantitative relationship between prevalence and vectorial capacity

Exercise 12.11

$$y(t + 1) = y(t) + y(t)\ C\ [1 - y(t)] - r\ y(t) \qquad \text{FORMULA 1}$$

a. Discussion on **formula 1** *and its components:*

where: *y* is a fraction of the community that is infected with malaria

1 − y = a fraction of the community that is healthy

C = vectorial capacity (by the unit of time)

r = recovery rate (by the unit of time)

(t) represents the events that take place at time '*t*'

(t +1) represents the events that take place at a unit of time after the time '*t*'

Prevalence is represented by '*y*' in the formula '*y(t)*' representing the prevalence of disease at the time of '*t*' and '*y(t+1)*' representing the prevalence of disease at the time later than '*t*' (e.g. one day after '*t*'). In this formula '*r*' is recovery rate and '*C*' is vectorial capacity. The prevalence of disease at the time of '*y(t + 1)*' is a function of: *(i)* prevalence of the disease at present, i.e. '*y(t)*', *(ii)* the number of cases that are added to this group, which is obtained by multiplying vectorial capacity by the prevalence of the fraction of the community that are ill, and *(iii)* the number of cases that recover and reduce prevalence, which is the third line of the formula and is obtained by multiplying recovery rate by prevalence of disease at the time of '*t*'.

$$y = 1 - \frac{r}{C}$$

b. *Figure 12.2 shows the relationship between disease prevalence and vectorial capacity. The graph represents the formula 2 above with two different values of r (recovery rate).*
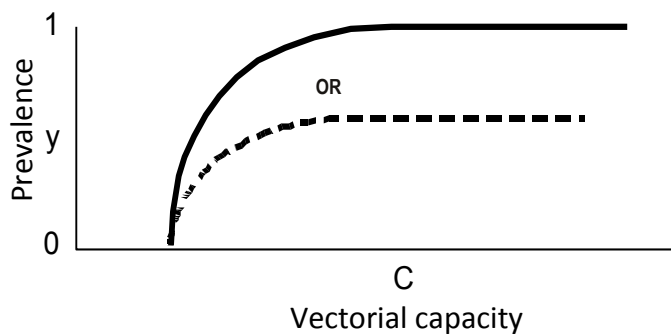
Figure 12.2 Graph for the formula $y = 1 - r/c$

Formula 2, which can be used for calculating prevalence (*y*) as a function of vectorial capacity, is derived from **formula 1** in its state of equilibrium. Therefore if in the graph, prevalence neither rises (epidemic) nor declines (elimination process), then '*y(t+1)*' will be equal to '*y(t)*' and could be removed from both sides of the formula; and if the formula for '*y(t)*' is solved with the remaining lines, **formula 2** is obtained.

c. *Following are the changes in y for each unit change in C, assuming r=0.5:*

C	*y*
0.5	0
1.5	0.67
2.5	0.8

If C=0.25, *y* will be zero.

d. In order to save time in class the tutor could prepare the graphs and tables in MS-Excel beforehand. In the class, it would then only be necessary to change the values in the table to study the effects of changes on the graph.

e. Points to be learnt from Figure 12.2: it is evident in the graph that, with a rise in vectorial capacity, the prevalence also rises, and after a sharp rise it reaches the upper end near value 1. In other words, regardless of the recovery rate, with a rise in vectorial capacity, a state will be reached in which most residents of an area are infected. This condition will occur even if the recovery rate is 100% (i.e. if r = 1).

The points above are significant for understanding the role of vectorial capacity and its influence in the prevalence rate of an area, and explain many of the problems faced in malaria-prone regions of Africa and South-East Asia where highly efficient vectors are present. If the biological, human, and infrastructure circumstances are such that they favour the maintenance of high vectorial capacity in a malaria-prone area, endemicity is likely to remain *stable* in that area, because the area is always at the plateau part of the curve. On the other hand, by reducing the vectorial capacity, the prevalence of malaria in the region will be transferred to the sharp slope of the curve, a state wherein the slightest change in vectorial capacity (e.g. following rainfall or an increase in the anopheline mosquito's larvae nests) will greatly increase the prevalence of malaria in the area. In such regions malaria is in an *unstable* state and they are constantly prone to periodic outbreaks.

*f. Another important point in the graph is the point of intersection of the graph with the X axis (the vectorial capacity axis). This is actually a point where C has become equal to r. The fact that at the point of intersection vectorial capacity is not equal to zero implies that in order to eliminate malaria in a region, vectorial capacity does not necessarily have to reach zero. In other words, elimination of malaria in a region is not dependent on complete elimination of the **Anopheles** mosquito. Below a certain level of vectorial capacity, malaria will be eliminated, even though the **Anopheles** mosquito still resides in that region. This critical value of vectorial capacity below which elimination takes place is traditionally represented by C^*.*

The above holds true for the uprising slope of the curve (Fig. 12.2) as long as '*r*' is smaller than 'C'. If '*r*' is equal to 'C' prevalence will remain constant, and if '*r*' is greater than 'C' this means that more people recover from the disease in comparison with those who are infected. Therefore the disease will move towards elimination.

g. Basic reproduction rate (R_o) was derived from the following formula.

$$R_o = C \, / \, r$$

*If R_o is added to **formula 2** the following will be obtained:*

$$y = 1 - \frac{1}{R_o}$$

If a graph of malaria is drawn as was done for figure 12.2, a graph similar to Figure 12.2 will be obtained, but this time R_o will replace C and the endemic level reaches zero for $R_o = 1$ (intuitively, malaria can be endemic only if the basic reproduction rate is greater than one). When $R_o = 1$ the disease is in a stable state and does not increase or decrease. And when its value is less than 1 the

disease will move towards elimination. For malaria, the definition of basic reproduction rate is used with a slight modification, as in graph 5 when $R_o = 1$, y (representing prevalence) becomes zero. In this case malaria endemicity becomes zero in the region.

h.

R_0	y
0.5	–1
1	0
2	0.5

i. **8** x 2 x 2 x 2 = 64

   8 x 0.5 x 0.5 x 0.5 = 1

12.3.6   The value of the vectorial capacity below which malaria transmission cannot be maintained

Exercise 12.12

a. At the critical level **y** = 0, *and so*

$$1 - \frac{r}{C^*} \text{ must be zero, i.e. } \boldsymbol{C^* = r}$$

From this it can be concluded that the critical vectorial capacity is lower for longer lasting infections, and that it is lower for *P. vivax* than for *P. falciparum*, because the recovery rate (**r**) for *P. vivax* is lower than for *P. falciparum*.

b. The critical value of the vector density can be derived from the formula:

$$\boldsymbol{C^*} = \frac{\boldsymbol{m^* a^2\, p^n}}{1 - \boldsymbol{p}} = r \qquad \text{from which}$$

$$\boldsymbol{m^*} = \frac{\boldsymbol{r\,(1 - p)}}{\boldsymbol{a^2\, p^n}}$$

Considering the exact expression for $1/1–p$ in stage 5, the above formula is expressed as:

$$\boldsymbol{m^*} = \frac{(-r \log_e p)}{\boldsymbol{a^2\, p^n}}$$

*c. The critical value of the vector density (**m***) for the given values will be calculated as:*

	r	*n*	*a*	*p*	*m** approximate formula	*m** exact formula
Efficient vector	0.01	10	0.5	0.9	0.0015	0.012
Inefficient vector	0.01	10	0.1	0.5	512	710

d. The expected relationship among the possible measures of "intensity" is shown in the graph in Figure 12.3. The graph, based on the Garki model,[1] is meant to show the approximate shape of the relationships, not their exact numerical values.
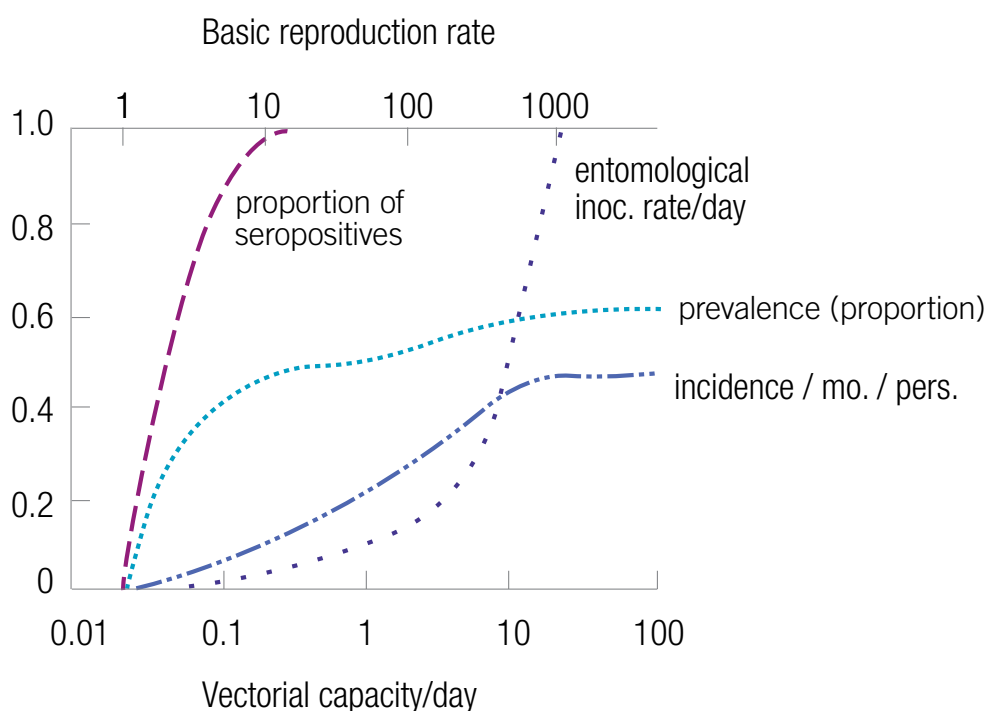
Figure 12.3 The relationship between vectorial capacity, basic reproduction rate, entomological inoculation rate, incidence of infection, prevalence of patent parasitaemia and prevalence of seropositivity in *P. falciparum*

e. With respect to the diagnosis of malaria situations, it is desirable to know how close a situation is to the threshold of either **C** *or* **R$_o$**.

A crude *indirect estimation* of *C* or *R$_o$* may be possible as follows: *close to the threshold,* parasitological and serological measurement (prevalence, incidence) are sensitive and informative, and instability is likely to be obvious, while entomological measurements (entomological inoculation rate, vectorial capacity) are insensitive; *far above the threshold,* the reverse holds true: entomological measurements are sensitive and informative, parasitological and serological, measurements are insensitive, and stability is likely to be obvious. Recent studies measuring anti-sporozoite antibody titres suggest that these are likely to become a good indicator of the entomological inoculation rate, more stable and less costly than the direct measurement.

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[1.] Molineaux L. and Gramiccia G. (1980). *The Garki Project.* Geneva, World Health Organization.

12.3.7 Effects of a reduction in prevalence or in vectorial capacity

Exercise 12.13

This exercise shows two other major insights given by Ross's model, i.e. the expected impact of a reduction in prevalence or in vectorial capacity. The correct answers to questions *(a)* and *(b)* are:

a. *Prevalence is expected to return to its original level, unless the reservoir has been reduced to zero.*

b. *The prevalence will decrease towards a new equilibrium value – not zero – unless the vectorial capacity has been reduced below its threshold level; the rate of decrease is not constant but progressively slowing down. The decline will not continue at its initial rate.*

The tutor should leave the groups to reach their own conclusions without directing them towards any specific resolution. Their results will be compared with figure 12.4.
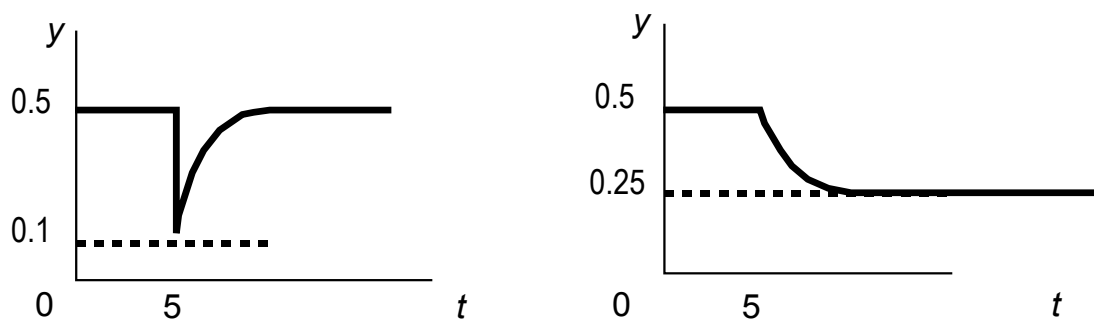
Figure 12.4 Effects of a reduction in prevalence or in vectorial capacity

12.3.8 Is there a place for models in planning malaria control?

Exercise 12.14

a. *Statements i to iv are all correct. However:*

Knowledge of facts is – and will remain – incomplete, and planning always involves some kind of model. The model may be intuitive and implicit, rather than mathematical and explicit, but it is there, and it is preferable to make it explicit, so that it can be considered critically.

Questioning the assumptions and numerical values which underlie the projections is an integral part of modelling. Once the model is explicit, the assumptions and the numerical values can be varied to evaluate how sensitive the conclusions are to such variation, i.e. a sensitivity analysis can be conducted. For example as seen above (see also Learning Unit 11), the calculated impact of residual spraying is very sensitive to the assumption made about the distribution or resting behaviour among the vector population.

b. *Models should probably not be used to make **absolute** predictions about the future, only **relative** predictions to **compare, or eventually rank, the outcomes of the small number of operationally realistic options.***

12.4 Measuring the burden of malaria

Exercise 12.15

a. Of the 5 measures of intensity, only incidence and prevalence are applicable to malaria in terms of disease.

b. The burden of malaria is due to its effect on people's health (morbidity, mortality), health services and economy (direct and indirect effect).

c. Other applicable parameters:

    i. incidence of severe malaria,

    ii. average duration of episodes of malarial illness,

    iii. absenteeism from school or work.

d. Malaria-specific mortality rate = the number of malaria deaths in a time period (usually one year) in a population unit (usually 100 000)

Malaria case fatality rate (CFR) = the number of malaria deaths in a time period, divided by the number of malaria cases in the same period; the ratio is usually multiplied by 100, to express the CFR as a percentage.

LEARNING UNIT **13**

Overview of stages in malaria programme phases

Learning Objectives:
by the end, participants should be able to...

◼ Compare and contrast the concepts of malaria control, elimination and eradication

◼ Describe the different objectives for each phase of the malaria programme

The tutor should prepare photocopies and a PowerPoint file of Figures 13.1–13.6 provided.

Answers

13.1   Phases of a malaria programme

Exercise 13.1

a. *Definitions of control, elimination and eradication:*

Malaria control: reduction of the disease burden to a level at which it is no longer a public health problem.

Malaria elimination: reduction to zero of the incidence of locally contracted infection by a specific human malaria parasites in a defined geographical area as a result of deliberate efforts. Continued intervention measures to prevent re-establishment are required.[1]

Malaria eradication: permanent reduction to zero of the worldwide incidence of human malaria as a result of deliberate efforts. Intervention measures are no longer needed once eradication has been established.[1]

When health facility data that are representative of the entire target area/country indicate that the monthly test positivity rate among febril patients with suspected malaria is constantly below 5% through out the year, , hence malaria case-load is considered 'manageable' enough to allow the intensive follow-up of individual cases as required in an elimination programme. At that point, the country could start reorienting its malaria control programme towards elimination entering the 'pre-elimination phase'. When malaria distribution becomes increasingly focal and the incidence rate declines progressively to below 1 per 1000 population at risk , the programme could move to the elimination phase with necessary programme adaptations.

b. *The malaria transmission types (1, 2,3 and 4) have been matched with the appropriate malaria control programme (a, b, c and d).*

1. Areas where transmission has been reduced to <1 case/1000 population per year	b. Elimination
2. Areas where transmission has been reduced to 5% SPR fever cases in health facilities	c. Pre-elimination
3. Areas where transmission has been interrupted	d. Prevention of re-introduction
4. High- and moderate-transmission	a. Control

c. *The continuum of malaria programme stages is shown in figure 13.1, provide it to the participants after they have completed their own figure. Discuss the differences.*

[1.] WHO (2012). *Disease surveillance for malaria elimination: am operational manual.* Geneva, World Health organization. http://www.who.int/malaria/surveillance_monitoring/operationalmanuals/en/index.html
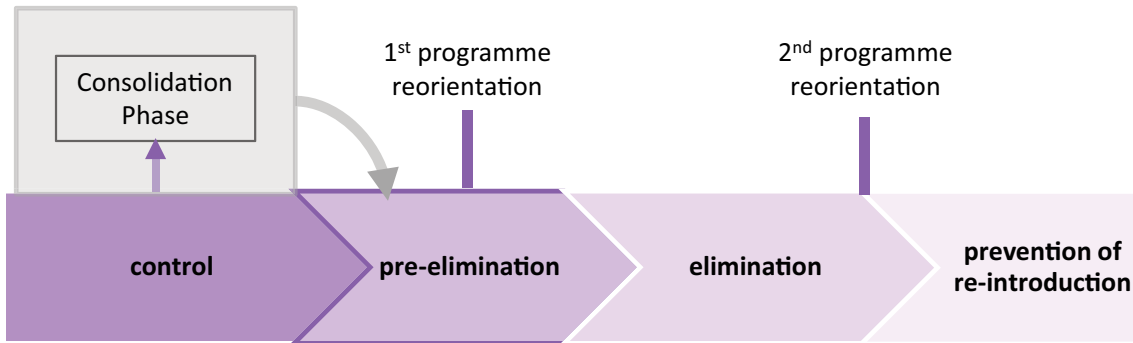
Figure 13.1 Malaria programme phases on the path to malaria elimination[1]

13.2 Transition from malaria control to elimination

Exercise 13.2

a. *Malaria programme phases and programme goals are shown in figure 13.2, provide it to the participants after they have completed their own figure. Discuss the differences.*
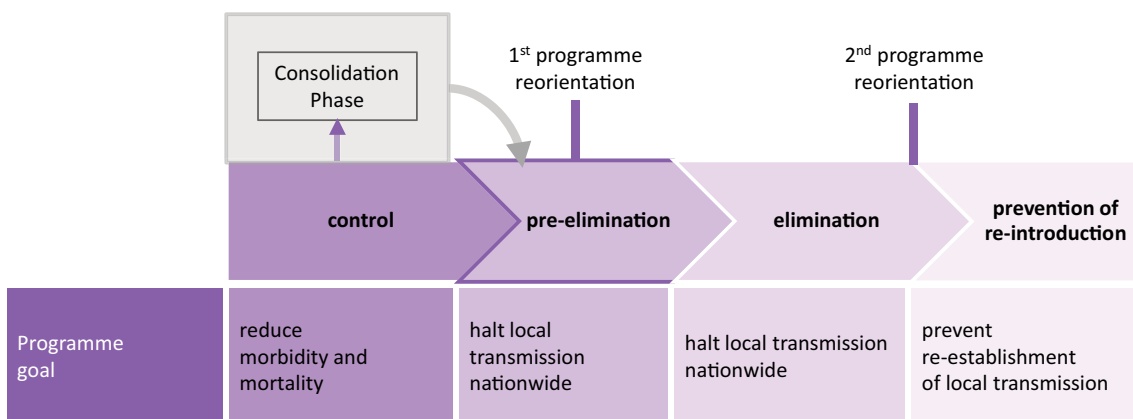
Figure 13.2 Malaria programme phases and respective main programme goals

b. *Malaria programme phases, epidemiological and transmission objectives have been added to the figure 13.2 to create figure 13.3, to be provided by the tutor.*

c. *The areas of operations for the different phases are:*

  i.   *Control phase: the problem of malaria involves the whole country or region,*

  ii. *Pre-elimination phase: the units of intervention are the foci of malaria.*

  iii. *Elimination phase: the units of intervention are the foci and the individual cases (locally acquired and imported).*

  iv. *Prevention of re-introduction phase: the focus is on imported cases.*

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1. WHO (2007). *Malaria elimination: a field manual for low and moderate endemic countries*. Geneva, World Health Organization. http://www.who.int/malaria/publications/atoz/9789241596084/en/index.html

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	control	pre-elimination	elimination	prevention of re-introduction
Programme goal	reduce morbidity and mortality	halt local transmission nationwide	halt local transmission nationwide	prevent re-establishment of local transmission
Epidemiological objectives	reduce burden of malaria	reduce number of active foci to zero; reduce number of locally acquired cases to zero	reduce number of active foci to zero; reduce number of locally acquired cases to zero	prevent introduced cases and indigenous cases secondary to introduced cases
Transmission objectives	reduce transmission intensity	reduce onward transmission from existing foci	reduce onward transmission from existing foci	reduce onward transmission from imported cases

Figure 13.3 Malaria programme phases and respective programme, epidemiological and transmission objectives

d. A flow chart illustrating the classification of malaria cases by origin of infection is shown in figure 13.4, to be provided by the tutor.
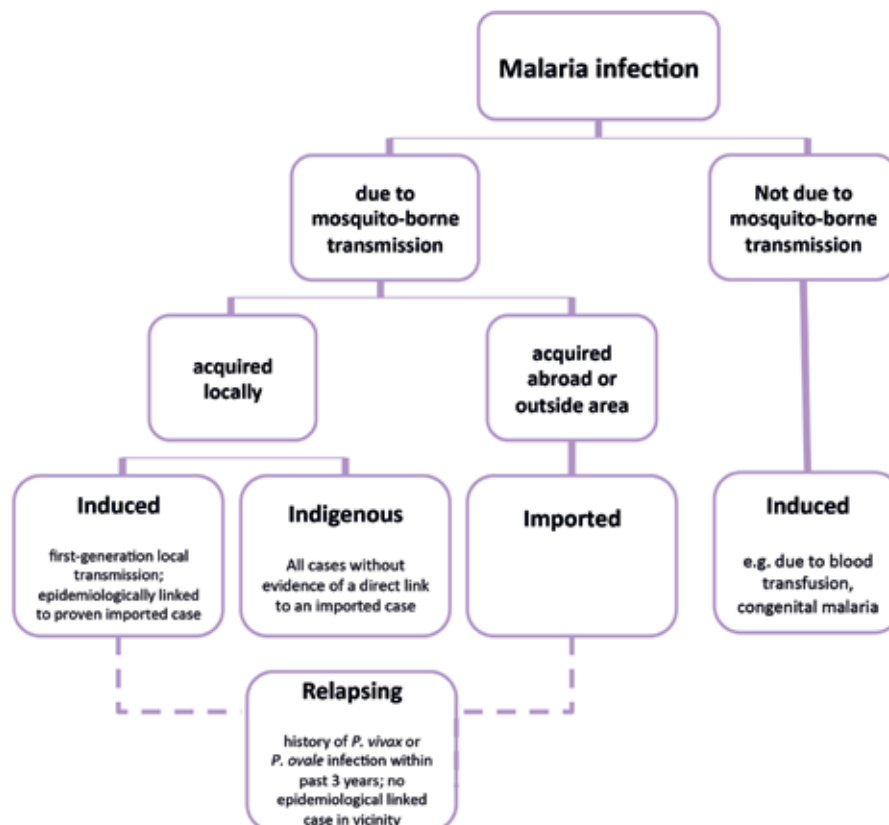
Figure 13.4 Classification of malaria cases by origin of infection

e. In most instances sufficient information is not available to differentiate between relapsing, introduced and indigenous cases, therefore these 3 categories are usually grouped together in one category which is called "autochthonous", that is, cases due to local transmission by mosquitoes.

f. The most important data sources for measuring progress towards reaching a milestone are shown in figure 13.5, to be provided by the tutor.
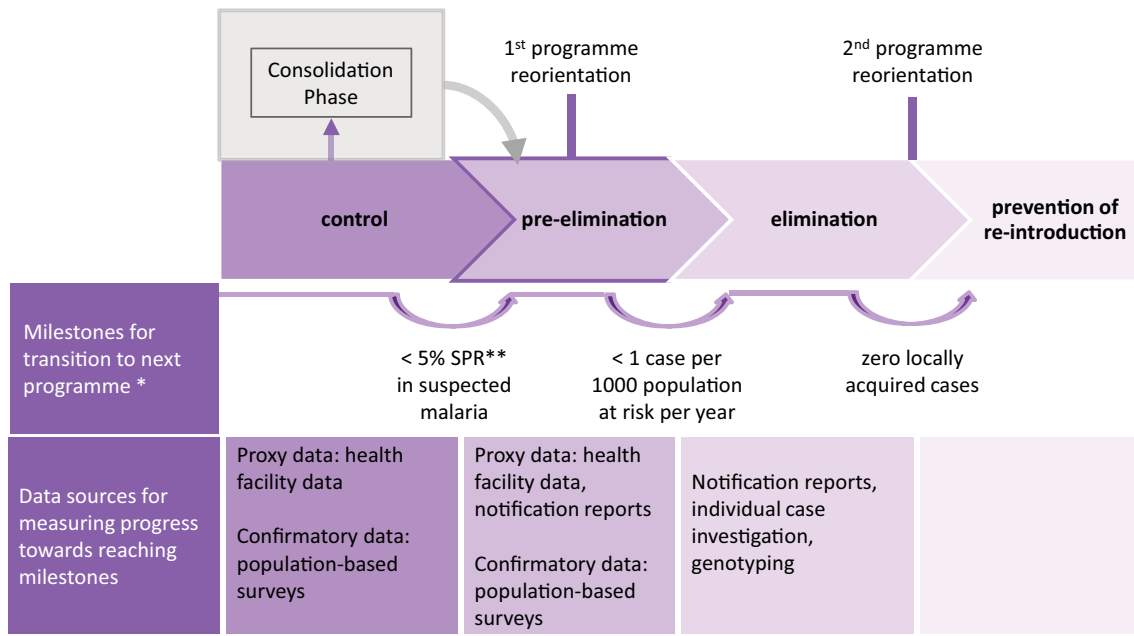
Figure 13.5 Malaria programme phases and respective milestones for programme and data sources

*   These milestones are indicative only: in practice, the transitions will depend on the malaria burden that a programme can realistically handle

**Slide or rapid diagnostic test positivity rate.

Health facility and population-based survey data can be helpful in malaria control and pre-elimination programmes where either the whole region or foci are affected by malaria. But during the elimination phase, where local transmission is no longer an issue, individual case definition and genotyping and notification reports are of greater significance.

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LEARNING UNIT **14**

Surveillance system

Learning Objectives:
by the end, participants should be able to...

- Define the term *surveillance*

- List the uses of the surveillance system

- Give examples of a surveillance system's objectives

- Explain the connection between the objectives of a surveillance system and its ability to detect cases

In introducing the Unit, the tutor should provide a general overview, taking particular care to provide examples and concepts that may be misunderstood. Plenty of time should be allowed for discussion and for the participants to carry out the exercises.

Exercises on surveillance

Divide the participants in groups of 6 to 8. Allow the groups to read the information and to work for about 25 minutes, then spend the rest of the time discussing their findings in plenary. Be sure to allow adequate time to discuss Exercise 7.2 (possible solutions) – it is easy to find problems, but it is often more difficult to come up with practical solutions.

Answers

Exercise 14.1

Several problems can be identified in this surveillance system, including the following:

▶ **Data collection**

　▶ Data being collected on too many diseases.

　▶ A relatively complicated form with 3 age and 2 sex categories and 43 diseases; this means that each month there are $3 \times 2 \times 43 = 258$ boxes to be filled in on each form, and even more if the results are to be totaled for both sexes and for all age-groups.

　▶ Guidelines not available.

　▶ No reference manual for use by health personnel.

　▶ Lack of supervision and lack of checking for data quality.

▶ **Data analysis**

　▶ Not timely; old data are unlikely to be useful for planning.

　▶ Data represented in an unusable fashion as a series of complex tables with no interpretation.

▶ **Use of information**

　▶ Data not being used at any level.

　▶ Data not being used for planning or for detecting outbreaks.

▶ **Relevance**

　▶ Considerable reporting delays at all levels within the system making the data analysis potentially irrelevant

▶ **Feedback**

　▶ No feedback to those who collect data; this leads to demotivation of staff.

　▶ Delayed feedback to higher levels, to such an extent that data are not likely to be of much use.

Exercise 14.2

The answers to this question will depend on the problems selected. In general, the system could benefit from:

- a simplification of the forms (fewer diseases and fewer categories)

- better training in simple analysis of data at peripheral level (including measures such as the development of a reference manual) and also using those data for decision-making at the local level

- better supervision of data collectors with an emphasis on feedback to enable them see the usefulness of their efforts

- more rapid turnaround of the data at all levels

- development of a reader-friendly report that offers graphic presentation of key diseases and simple interpretative text

- others

Encourage participants to relate their findings and proposed solutions to their own situation.

LEARNING UNIT **15**

Indicators for monitoring and evaluation of malaria control programmes

Learning Objectives:
by the end, participants should be able to...

■ Describe the importance of monitoring and evaluation

■ Explain the difference between monitoring and evaluation indicators

■ Give suitable examples of input, process, output, coverage and impact indicators

■ Explain the relation of indicators with objectives of the malaria control programme, and also their internal relationships

The tutor should provide participants with copies of Tables 15.1 and 15.2 during this session.

Answers

Exercise 15.1

a. *For a programme or project to achieve its goals, **inputs** such as money and staff time must result in **outputs** such as new or improved services, trained staff, persons reached with services, etc. These outputs are the result of specific **processes**, such as training for staff, which should be included as key **activities** aimed at achieving the outputs. If these outputs are well designed and reach the populations for which they were intended, the programme or project is likely to have positive **effects** or **outcomes**, for example increased use of ITNs. These positive short-term outcomes should lead to changes in the longer-term **impact** of programmes, measured in fewer new cases of malaria and lower burden of disease.*

b. *1. Incidence rate*

2. Prevalence rate

3. Entomological inoculation rate

4. Vectorial capacity

5. Basic reproduction rate

c. *No, these indicators are not sufficient to measure the programme's input and impact. To evaluate the impact, mortality and case fatality rate should be monitored as well.*

d. *These measurements help to understand the epidemiology of malaria. Periodic measurements of such indicators help changes in malaria transmission and impact of interventions over time. However, measurements such as vectorial capacity and basic reproduction rate are difficult and costly to conduct routinely.*

Exercise 15.2

a. ***Input** indicators measure the level of resources available for use by the programme or intervention, e.g. funding to procure ITNs.*

*   ***Process** indicators help check that a programme or intervention is implemented as planned, e.g. verifying that ITNs have been purchased and are ready for distribution.*

*   ***Output** indicators generally measure benchmarks of programme-level performance, such as the number of ITNs distributed to a particular target population.*

*   ***Outcome** indicators measure medium-term population-level targets, e.g. level of ITN ownership and/or usage by a target population, attributable to an ITN programme or intervention.*

*   ***Impact** indicators generally refer to measuring progress in achieving long-term **objectives**, e.g. reducing malaria-related morbidity and mortality by 75% by 2015.*

Input, process, and output indicators assess or monitor programme performance while outcome and impact are mainly used for evaluation. Output and outcome can also measure coverage of interventions. However, some impact indicators such incidence or number of cases measured in a relatively short period can be used to monitor performance, e.g. monitoring of epidemic containment efforts.

b. Yes. More information is needed for project management at district level for example than is needed at national or international levels. The number of indicators reported should decrease substantially from the sub-national to the national and international levels.

Indicators selected for monitoring will be different depending on the reporting level within the health system and the epidemiological situation of the country. At the national and sub-national levels, where efforts to implement interventions are functional, monitoring of programme inputs (human resources, financing), processes (procurements and supplies, training) and outputs (services delivered by programmes) is also needed for understanding the complete picture of programme activities in order to improve performance. At the global and regional/inter-country levels, the monitoring efforts focus on understanding and standardizing population-based coverage indicators for recommended interventions.

Exercise 15.3

a. Table 15.1 shows some of the malaria indicators and the purpose of each indicator as either monitoring performance or impact evaluation.

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Table 15.1   Some of the malaria indicators and their targets

	Indicator	Target	Purpose
1	Confirmed malaria cases (microscopy or RDT), per 1000 persons per year	Reduction in cases by 75% by 2015 compared to 2000	Impact evaluation
2	Inpatient malaria death per 1000 persons per year	Reduction in deaths by 75% by 2015 compared to 2000	
3	All-cause deaths in < 5 children per 1000 <5 children per year (*for high-transmission areas*)	Reduction of global malaria deaths to near zero by end 2015	
4	Proportion of individuals who slept under an ITN/LLIN the previous night	100%	Coverage evaluation
5	Proportion of population at risk protected by IRS in the last 12 months	No specific target set	
6	*In moderate to high transmission areas:* Proportion of women who received three doses or more of intermittent preventive treatment (IPT) during their last pregnancy	100%	
7	Proportion of suspected malaria cases that receive parasitological test	100%	
8	Proportion of confirmed malaria cases that received first-line antimalarial treatment according to national policy	100%	Monitoring evaluation
9	Proportion of health facilities without stock-outs of first-line antimalarial medicines, ITNs and diagnostics, by month	100%	
10	Percent of districts reporting monthly numbers of suspected malaria cases, number of cases receiving a diagnostic test and number of confirmed malaria cases	No specific target	

b. *In regions where malaria transmission is moderate to high, the main control methods used are a combination of the following interventions:*

1. *Prompt diagnostic testing and effective treatment of confirmed cases.*

2. *Insecticide-treated mosquito nets (ITNs) or provision of Insecticide Residual Spraying (IRS).*

3. *Intermittent preventive treatment (IPT) during pregnancy (IPTp) – only recommended for sub-Saharan Africa*

c. *Table 15.2 shows indicators for each category and corresponding interventions.*

Table 15.2   Indicators according to the steps of Monitoring and Evaluation

Intervention	Monitoring Performance		Evaluation	
	Input/Process	Output	Outcome (coverage)	Impact
Insecticide Residual Spraying (IRS)	Insecticides and sprayer pumps provided for services	Rooms and house structures sprayed with insecticide among those targeted (programme data)	Households living in areas with more than 80% coverage of house structures with IRS	Confirmed malaria cases Inpatient malaria cases Inpatient malaria death Parasitaemia Anemia (especially in high transmission areas) Malaria-specific deaths Deaths in children aged < 5 years from all causes (in high transmission)
Insecticide-treated nets (ITNs)	Number of ITNs provided for distribution	Ownership of ITN distributed in populations at risk	ITN use in all persons, or children aged <5 years, or pregnant women	
			Coverage of all persons at risk with an ITN	
Case management	Health facilities without stock-outs of first-line antimalarial medicines, mosquito nets and diagnostics, by month	Malaria test positivity rate (SPR) or Test Positivity Rate (TPR) Percentage of out-patient suspected malaria cases that undergo laboratory diagnosis Percentage of out-patient cases that received appropriate antimalarial treatment	Appropriate antimalarial treatment of children aged <5 years	
Intermittent preventive treatment (IPT) (only in moderate to high transmission settings in sub-Saharan Africa)	Supply of drug SP for IPTp (SP compound)	Percent of pregnant women who received 3 or more doses of IPTp in the ANC (surveillance)	Percentage of pregnant women in population who received 3 or more doses of IPTp (survey)	

d. *Practically, these indicators assess the overall results of a programme and do not assess each intervention's impact on the burden of malaria separately; hence they have been placed in one cell. Ideally, if one intervention is applied alone in a given population and given time, then impact can be attributed to that particular intervention. However, in reality, more than one intervention (e.g. treatment and ITNs) would be employed concomitantly and hence is difficult to quantify the impact of single intervention.*

Exercise 15.4

a. No. In practice, different programme phases implement different strategies for malaria control based on programme type. Consequently different indicators are adopted.

b. The participants might consider additional indicators, which is justifiable. The point is that there is a standard list of indicators which allow comparison between national programmes, and their measurement is necessary in all countries. In addition to these indicators each country may choose to measure more indicators, but these will not have an international application.

LEARNING UNIT **16**

Data collection methods

Learning Objectives:
by the end, participants should be able to...

■ Name different sources of data collection related to the main indicators of malaria

■ Specify which source is important for each group of indicators (performance, coverage and impact)

■ From a numerator and denominator of an indicator, explain from which source it should be calculated and why that source is chosen.

■ Name the main types of surveys that can estimate coverage indicators at a national level

Answers

16.1   Sources of information

Table 16.1 is a modified form of Table 15.2 in Learning Unit 15, with one additional column.

Exercise 16.1

Table 16.1   Indicators for each Monitoring and Evaluation category and corresponding interventions

| Intervention | Monitoring Performance | | Evaluation | | |
| | Input/Process | Output | Outcome (coverage) | Impact | |
				Morbidity	Mortality
Insecticide Residual Spraying (IRS)	Insecticides and spray pumps provided for services	Rooms and house structures sprayed with insecticide among those targeted (programme data)	Households living in areas with more than 80% coverage of house structures with IRS	Confirmed malaria cases Inpatient malaria cases	Inpatient malaria deaths Malaria-specific deaths All-cause deaths in < 5 children (in high transmission)
Insecticide-treated nets (ITNs)	Number of ITNs provided for distribution	Ownership of ITN distributed in populations at risk	ITN use in all persons, or children aged <5 years, or pregnant women		
			Coverage of all persons at risk with an ITN		
Case management	Health facilities without stock-outs of first-line antimalarial medicines, mosquito nets and diagnostics, by month	Slide positivity rate (SPR) or Test Positivity Rate (TPR) Percentage of out-patient suspected malaria cases that undergo laboratory diagnosis Percentage of out-patient cases that received appropriate antimalarial treatment	Appropriate anti-malarial treatment of children aged <5 years		
Intermittent preventive treatment (IPT) (only in moderate to high trans-mission areas)	Supply of SP for IPTp	Percent of pregnant women who received 3 or more doses of IPTp in the ANC (Surveillance)	Percentage of pregnant women in population who received 3 or more doses of IPTp (survey)		

b. *Indicator for morbidity: malaria incidence rate in the population at risk.*

▶ *Numerator:* Number of confirmed malaria cases in given time period (by month or year) in a given geographical area

▶ *Denominator:* Total population at risk in the given time period (by month or year) in a given geographical area.

The objective is to measure the impact trends in the general population so that they can be comparable and interpretable over time. Example: 450 cases per 1000 (0.45) in 2000 compared to 100 cases per 10 000 (0.1) in 2009.

Indicator for mortality: malaria mortality in the population at risk.

▶ *Numerator:* Number of malaria deaths in the given time period (by month or year in a given geographical area).

▶ *Denominator:* Total population at risk in the given time period (by month or year) in a given geographical area. The objective is to measure the impact trends in general population so that they can be comparable and interpretable over time. Example: 45 deaths per 1000 (0.045) in 2000 compared to 10 deaths per 10 000 (0.01) in 2009.

Such impact indicators are attributed to a mixture of interventions unless there is clear evidence of timing and scale of a single intervention. For example, if treatment alone may be the only intervention employed in a given area for several years and then other vector control interventions are added later in a known period, the changes in impact indicator may be attributable to the vector control interventions (after excluding other potential confounders).

After participants' thorough discussion, refer the participants to Annex 1 in the *Guide for Participants*. This annex provides the numerators and denominators for current indicators for malaria control.

c. *For morbidity, the sources of the data elements for the numerator include public health facilities, private sectors/clinics, and even communities (where information is appropriately documented). The type of facilities may be hospitals, health centres, clinics or health posts, etc. depending on the local situation.*

In reality the fraction of reporting is incomplete and some sectors, e.g. the private sector, are often not included in the national reporting system. The other factor affecting completeness is that many of the lower administration levels or facilities may not report on time. Therefore, the reported malaria cases in the health facilities are usually an underestimation of the actual burden. However, if the percentage of the health facilities not reporting is known, then the reporting fraction can be adjusted.

For *mortality*, data for the numerators are obtained through public health facilities, private sectors/clinics, and even communities (where information is appropriately documented).

Ideally, the best source for mortality would be the registry of all deaths, including those which occur at health facilities and those that occur outside health facilities. However, in countries where the health information system and/or death registry have not been fully developed, health facility data still has to be used as above, with correction for reporting fractions. Verbal autopsy is used to a limited extent in some countries to specify the cause of death in surveys, i.e. after a death, the probable specific cause is sought through structured interviews of family members and care givers. However this is often subject to recall bias and may also not reflect recent changes in malaria transmission.

Exercise 16.2

a. *There may be partners other than the Ministry of Health delivering services in different countries, such as NGOs. A significant proportion of health care is delivered through the private sector. NGOs also distribute ITNs/LLINs in many countries. However IRS is carried out by the Ministry of Health.*

b. *Regarding coverage, since service is delivered through different channels, the sources of data collection can also differ. In countries where these services are not delivered by a single source, the data related to coverage must be collected through surveys. This holds true for diagnosis and treatment of cases and ITN/LLIN distribution. Since IRS is implemented by the public sector, then the data can be collected through the malaria control programme. For IPTp the antenatal care registries and reporting systems are important source of data.*

Concerning data related to performance, these are usually collected in the Health Information System.

For information from the data collection sources for indicators, the following summarized Table 16.2 can be considered. However, these sources may differ in different countries.

c. *Table 16.2 provides the data collection sources for the indicators of the corresponding interventions.*

Table 16.2   Summary of the data collection sources for indicators of the anti-malaria interventions (IRS, ITN, treatment and IPT)

Intervention	Performance (Input/process)	Outcome (coverage)	Impact	
			Morbidity	Mortality
Insecticide Residual Spraying (IRS)	Health Information system routine or logistic data	Routine data from national malaria control programme	Routine surveillance system Survey	Ruotine surveillance system Verbal autopsy survey
Insecticide-treated nets (ITNs)		Routine data from national malaria control programme, Household survey		
Diagnosis and treatment		Ruotine surveillance system Household survey		
Intermittent preventive treatment (IPT) in moderate to high transmission areas in sub-Saharan Africa		Ruotine surveillance system		

16.2   Surveillance and survey

Exercise 16.3

a. *Surveillance is an ongoing system for collection of information which produces, gathers and analyses data, transmits the data to those who need it for decision-making and action, at minimal cost for the malaria control programme. Surveys are useful to obtain population-based estimates e.g. LLIN ownership and use (to minimize bias).*

In areas with high transmission where the surveillance system is dysfunctional, surveys can also give approximate values on disease burden and coverage of interventions. However, surveys are costly, time consuming and provide only a point estimate of the indicator. In low transmission settings, surveys become less informative whereas surveillance becomes the backbone of the control and elimination efforts. Therefore the principal source of data for monitoring trends of disease incidence in countries should be the surveillance system (of course adjusting for reporting completeness and other factors) whereas surveys are primarily used for estimating coverage.

In the absence of a functional surveillance system, surveys may be considered as a temporary measure and source of information to obtain point estimates of indicators.

Table 16.3   Applications of surveys and surveillance in malaria programmes

Programme phase	Surveillance		Survey	
	Objective	Question to be answered	Indicators/data elements	Question to be answered	Indicators/data elements (e.g. use LLIN as intervention)
Control	• Assess malaria burden • Coverage of interventions	• Trends of disease incidence • Supply of commodities	• Confirmed malaria cases, inpatient malaria cases, malaria deaths • Stock of medicines and diagnostics	• Evaluation of coverage of interventions • Knowledge and behaviour • Population based prevalence	• LLIN ownership and use • KAP (knowledge, Attitude and Practice) • Parasitaemia, anaemia (in high transmission), mortality (through verbal autopsy)
Pre-elimination	• Assess malaria burden • Coverage of interventions (in focal areas)	Trends of disease incidence in different geographical strata	• Foci and individual based surveillance • Foci and Case investigation (including detection of epidemics) • Notification through general health services	• Population-based prevalence survey • Coverage of interventions (in focal areas)	
Elimination	Assessing interruption of transmission	Occurrence of local transmission	• Imported and indigenous cases • Foci and individual based surveillance • Foci and Case investigation (including detection of epidemics) • Notification through public and private sectors services	No survey required	Parasitaemia
Prevention of reintroduction	Monitor re-introduction of cases	Occurrence of any transmission	• Vigilance through general health services • Investigation of any suspected case	No survey required	

b. Table 16.3 summarizes the comparison between surveys and surveillance in terms of their applications including objectives, question they answer, data elements, etc.

c. The most essential surveillance data for all malaria situations, from high to low transmission areas, are suspected, tested, confirmed outpatient[1] and inpatient cases and deaths disaggregated, if possible by age. For practical reasons malaria data (particularly in high transmission countries) are often stratified by age category of <5 and >5 years old. In countries with both P. vivax *and* P. falciparum, *confirmed cases need to be reported by parasite species.*

In countries with sustained ability to test all suspected cases, number of suspected cases as a separate data element may not be needed (since suspected = tested). However, the criteria for suspected malaria should be kept constant.

Data required from a malaria surveillance system follows from the core indicators for malaria control detailed in Annex 1. Surveillance data are drawn from information recorded in patient registers. Information to be collected in patient registers for malaria surveillance should include:

1. Personal identification: name and surname, date, address, pregnancy status.

2. Laboratory test results: RDT result (positive or negative), microscopic examination result (positive or negative), diagnosed species (*P. falciparum, P. vivax,* mixed, *P. malariae, P. ovale*), or not tested.

3. Outpatient diagnosis: uncomplicated and/or severe, probable or confirmed. Is the patient receiving re-treatment?

4. Outpatient treatment: which treatment has been advised and has the drug been administered?

5. Admitted patients: diagnosis, treatment outcome (transfused, cured, sequelae, or deceased).

d. This depends on the country's malaria control programme. In countries in the control phase with a considerable number of cases per year (difficult to monitor individual cases), both inpatient and outpatient data should be reported, primarily in aggregate form.

As control improves and countries reach near pre-elimination, the number of malaria cases seen in facilities declines and hence emphasis should shift from aggregate data to case-based, first for inpatient malaria cases and deaths, and then for all outpatient confirmed malaria cases.

Case-based data (data for each individual – on a line list or paper form for each case) provides quality data to evaluate programme performance, identify areas with relatively high transmission (foci), and detailed information on clustering of cases and reasons for failure of preventive interventions in certain areas (that become a source of cases).

In the elimination phase: *(i)* confirmed case data are recorded on separate case forms and carefully studied, *(ii) f*ield investigation is done on all confirmed cases to gather additional information such as on receptivity, vector breeding sites (foci), measure size of foci, and *(iii)* classification of the source of infection is done for all confirmed cases.

Exercise 16.4

a. Table 16.4 shows surveillance in different transmission levels and malaria programme phases (control and elimination)

[1.] Classification of case definitions was given in Learning Unit 7.

**Table 16.4   Malaria surveillance in different transmission settings and programme phases
(control and elimination)[1]**

Characteristics	Guide for responses[a]	Control phase		Elimination phase
		High & moderate transmission	Low transmission	Very low transmission
Incidence				
Cases and deaths	Common, less common, sporadic	common	less common	sporadic
Temporal variation	Limited, variable	limited	variable, risk of epidemic	imported cases maybe high of total
Geographical variation	Limited, heterogeneous, focal	limited	heterogenic	focal
Fevers (proportion due to malaria)	Large, small, very small	large	small	very small
Health facility attendance (proportion due to malaria)	High, low	high	low	
Vectors	Efficient, inefficient	efficient	controlled efficient/ inefficient	controlled efficient/ inefficient
Programme objectives	Mortality reduction, case reduction, eliminate transmission	reduce mortality and cases	reduce cases	interrupt transmission
Surveillance system				
Resources	Low expenditure per head, resources to investigate cases			
Data recording	Aggregate numbers, lists of inpatient and deaths, lists of all cases, case details	aggregate numbers	aggregate numbers Lists of inpatients and deaths to lists of all cases	case details
Investigation	Inpatient cases, all cases, individual cases	inpatient cases	inpatient cases to all cases	individual cases

[a]   Second column of Table 16.4 contains possible responses which the participants should use to fill columns 3, 4 and 5.

16.3   Core analyses

Exercise 16.5

Description of the surveillance graphs

Graph 1: This graph shows trends in the numbers of confirmed malaria cases per 1000 population, malaria inpatients per 10 000 population and deaths per 100 000 population. It may be necessary to experiment with the size of the reference population (1000, 10 000 or 100 000) so that the lines fit conveniently on the same graph (or they may be plotted on a second axis or separate graphs). These indicators are basic measures of morbidity and mortality that reflect the success of control programmes and indicate demand for treatment in the public sector. There has been a reduction in the numbers of malaria cases, inpatients and deaths in recent months, particularly at the beginning of 2012.

[1.]   WHO (2012). Disease surveillance for malaria control: operational manual. Geneva, World Health Organization. http://www. who.int/malaria/publications/atoz/9789241503341/en/index.html

Graph 2: This graph shows the positivity rate with slides and/or RDTs, the percentage of inpatients with a discharge diagnosis of malaria and the percentage of inpatient deaths due to malaria. These measures are affected less by fluctuations in reporting rate and total patient attendance and sometimes more reliably indicate the direction of change in malaria morbidity and mortality. Changes in test positivity rates and proportionate malaria cases or deaths (proportion of all-cause cases or deaths) do not, however, reflect the percentage change in malaria cases or incidence, as the number of malaria cases is part of the denominator. In areas where the percentage of deaths due to malaria is small and fluctuates erratically, it may not be useful to plot the percentage of deaths due to malaria. The slide positivity rate and percentages of inpatients and deaths due to malaria do not appear to follow the downward trend in the number of malaria cases (apart from a dip in early 2012).

Graph 3: This graph shows the total number of outpatients per 1000 population, the total number of inpatients per 10 000 population and the number of deaths per 100 000 population. It may be necessary to experiment with the size of the reference population (1000, 10 000 or 100 000) so that the lines fit conveniently on the same graph (or they may be plotted on a second axis or separate graphs). These indicators provide information on overall use of health facilities, which can influence observed trends in malaria. This chart will also be useful for interpreting other disease-specific data that are collected and analysed regularly. The graph shows lower outpatient attendance and admissions overall.

Graph 4: This graph shows the annual blood examination rate, which reflects total diagnostic activity in a population. This can influence observed trends in malaria and is therefore important contextual information. The graph shows a reduced rate of diagnostic testing.

Graph 5: This graph shows the percentage of suspected malaria cases receiving a diagnostic test and the percentage of health facilities submitting reports each month. The target for both indicators should be 100%. This can provide information on the extent of parasitological diagnosis and the completeness of reporting, both of which can influence observed trends in malaria. There is a lower reporting rate in recent months.

Graphs 6: This graph shows the percentage of cases due to *P. falciparum*. Such information is required for countries in which *P. vivax* and *P. falciparum* are present.

Interpretation of the graphs 1 to 6

There has been a reduction in the numbers of malaria cases, inpatients and deaths in recent months, particularly at the beginning of 2012 (graph 1). This decrease appears to be related to lower outpatient attendance and admissions overall (graph 3) and a reduced rate of diagnostic testing (graph 4), which could also be due to lower reporting rates in recent months (graph 5). The slide positivity rate and percentages of inpatients and deaths due to malaria do not appear to follow the downward trend in the number of malaria cases (apart from a dip in early 2012) (graph 2). Similarly, there has been no marked changed in the percentage of cases due to *P. falciparum* (graph 6).

Hence, there appears to be no real decrease in the number of malaria cases; the apparent decrease is due to less reporting in recent months. Such a pattern, in which data are incomplete for the most recent months, is common in many reporting systems and suggests that effort is needed to improve the timeliness of reporting (otherwise, the reporting rates are reasonably

good at > 90%). There is also scope to increase the percentage of patients with suspected cases receiving a diagnostic test, and it might be necessary to determine why this has decreased in the most recent months (perhaps due to the selection of health facilities reporting).

Exercise 16.6

a. In low-transmission countries, the distribution of malaria is usually patchy. As transmission is reduced in areas with high transmission and efficient vectors remain, vulnerability to epidemics increases. With time, immunity declines, rendering communities even more susceptible to the damaging effects of epidemics.

Low-incidence settings have several characteristics that impact on surveillance system design:

1. fewer cases than high-transmission areas

2. more emphasis on outpatient uncomplicated cases

3. increased proportion of the burden in older age groups: as transmission declines, percentage (but not the rate) of cases that are ≥5 years of age increases; an age shift to older ages is a good indicator of decreasing transmission of malaria

4. malaria does not occur nationwide and becomes focal within districts

5. proportion of fevers in children that are due to malaria becomes small

6. orientation of surveillance in relation to national elimination target

In some low-transmission areas, *P. vivax* may become more prevalent (if both *P. falciparum* and *P. vivax* were present) as *P. falciparum* declines. *P. falciparum* generally disappears more quickly than *P. vivax*.

If less efficient vectors are present, the risk of sudden, massive outbreaks may be lower.

Some low-incidence countries have better health systems.

b. Parameters of surveillance:

1. Analysis of aggregate data by health facility catchment area (this may have already started at the end of the high/moderate-transmission phase), instead of analysis only by district.

2. Intensified analysis and response to all inpatient malaria cases and deaths (shift to case-based surveillance for inpatient cases/deaths should have already taken place). Inpatient malaria cases and deaths represent severe outcomes that become rare events.

3. Shift from outpatient aggregate data to outpatient case-based, line-listed reporting of all confirmed cases. Case-based data permits health facility and district staff to conduct village-level analysis and allows better characterization of malaria foci.

4. Addressing treatment and surveillance gaps by adding additional sites for treatment and/or surveillance (additional treatment and surveillance sites, private sector involvement, and possibly active surveillance).

5. National feedback bulletin: adding sub-district mapping to identify foci and more focus on listing and characterizing of foci.

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16.4 Expected impact of improved diagnosis and treatment of malarial illness

Exercise 16.7

a. *The expected impact of changes in variables following improvement in diagnosis and treatment are shown in Table 16.5.*

Table 16.5   Expected impact of improved diagnosis and treatment of malarial illness

Variables	Expected change	
	In reality	Reported information
Incidence of infection	→ (stable)	→ (stable)
Prevalence of infection	*	→ (stable)
Incidence of disease	↘ (slight decrease)	↗ then → (increase then stable)
Prevalence of disease	↘ (decrease)	Not measured
Incidence of severe malaria	↘ (decrease)	** ↗↘ (increase then decrease)
Death rate (all causes)	↘ (decrease)	↗↘ (increase then decrease)
Malaria mortality	↘ (decrease)	** ↗↘ (increase then decrease)
Case fatality rate of malaria	↘ (decrease)	***
Case fatality rate of severe malaria	↘ (decrease)	***

*   Since the area has intense transmission, this variable does not change significantly.
**   Paradoxical effect: initial increases by better detection
*** Difficult to foresee, because both numerators and denominators will change

b. *Objectives:*

   i) epidemiological objectives are the maximum reduction of:

   ► malaria mortality,

   ► incidence of severe malaria

   ii) operational objectives are the correct management of:

   ► all malaria illness

   ► all therapeutic failures

Exercise 16.8

a. *No*

b. *Yes. The main sources of error are:*

By increase: to consider as "malarial illness" all cases of unexplained fever or all cases of sub-clinical parasitaemia.

By decrease: the services are not accessible to all, or are not utilized by all those to whom they are accessible.

c. Yes to all three questions

d. No to both questions

e. It would involve the investment of considerable resources, and that is neither necessary nor possible.

f. No, they cannot be counted together. Examples of important differences:

  ▸ The species of *Plasmodium*

  ▸ The severity of disease

  ▸ Diagnostic criteria, e.g. microscopic examination

  ▸ The level of the service making the diagnosis

g. Malaria-associated mortality has been classified into direct and indirect mortality. Direct malarial deaths are deaths resulting from malaria alone. Indirect malarial deaths result from malaria and an associated disease. Verbal autopsy and death registry cannot reflect the true status of malaria-associated mortality.

Sensitivity and specificity for verbal autopsy were estimated to be 46% and 89% respectively in comparison with hospital-derived diagnosis.[1] The low sensitivity of verbal autobsy in detecting malaria-associated mortality may mask the real success of the malaria control programmes.

There are limitations with each of the potential measurements of the malaria mortality and changes in it. In most malaria-endemic areas, most deaths occur outside of any system of death registration linked with health facility and laboratory confirmation. Verbal autopsy methods can be used to categorize a death as caused by malaria, but with low sensitivity. And, it is widely recognized that malaria is a contributing cause of many deaths for which the principal cause may be categorized as another condition.

h. Facility data have been most useful with regard to understanding trends of severe disease and case fatality rates among inpatients. Although data available from health facilities are potentially useful for monitoring time trends in the number of cases and deaths, these data have also limitations for inferring trends for programme evaluation and impact assessments.

In principle, these data should be representative of all health facilities, but in practice not all facilities and districts report. Reporting from health facilities to districts and from districts to the Ministry of Health varies in its completeness and timeliness and often does not include private and nongovernmental facilities. As a result reported malaria burden represents only a fraction of the malaria burden in the population, since in areas where the malaria burden is greatest, many malaria patients either do not seek treatment or are treated outside the formal health sector.

i. Due to current limitations in information collected from routine information systems and the cost of household surveys, sentinel sites may be important source for malaria monitoring in some settings; they are often used for early warning and detection of malaria epidemics, and to monitor changes in antimalarial drug and insecticide resistance.

U16

[1.] Snow RW et al. (1992). Childhood deaths in Africa: Uses and limitations of verbal autopsies. *Lancet,* 340: 351–5.

16.5   Surveys

Exercise 16.9

If necessary, the tutor may allow the participants to do this exercise and report it after checking references on the internet.

The participants are expected to see surveys as complementary and not as a substitute for routine surveillance.

LEARNING UNIT **17**

Burden of malaria

Learning Objectives:
by the end, participants should be able to...

■ Explain how an estimate of malaria morbidity and mortality can be obtained from the surveillance system

■ Explain the need for indicators of disease burden

■ Describe the difference between inequity and inequality

17.1   Malaria morbidity

Answers

Exercise 17.1

a. By dividing by 20% it is clear that the number should be multiplied by 5.

b. 1. Not all patients do consult health-care centres for treatment.

> *2. Some consult the public sector; private clinics usually do not provide their patient statistics to the national health information system, and not all public health-care centres submit their reports.*

> *3. Patients are often not diagnosed correctly for malaria.*

c. Distribute copies of Figure 17.1 to the participants and discuss possible differences.
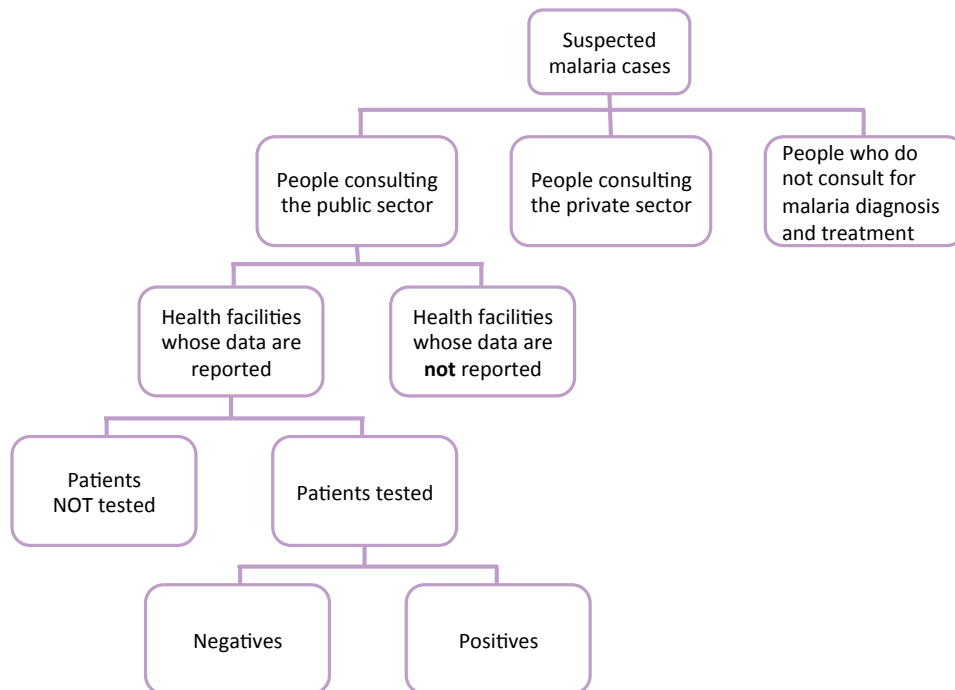
Figure 17.1 Data reported in a malaria surveillance system

d. Provide copies of Figure 17.2 to participants and discuss possible differences.
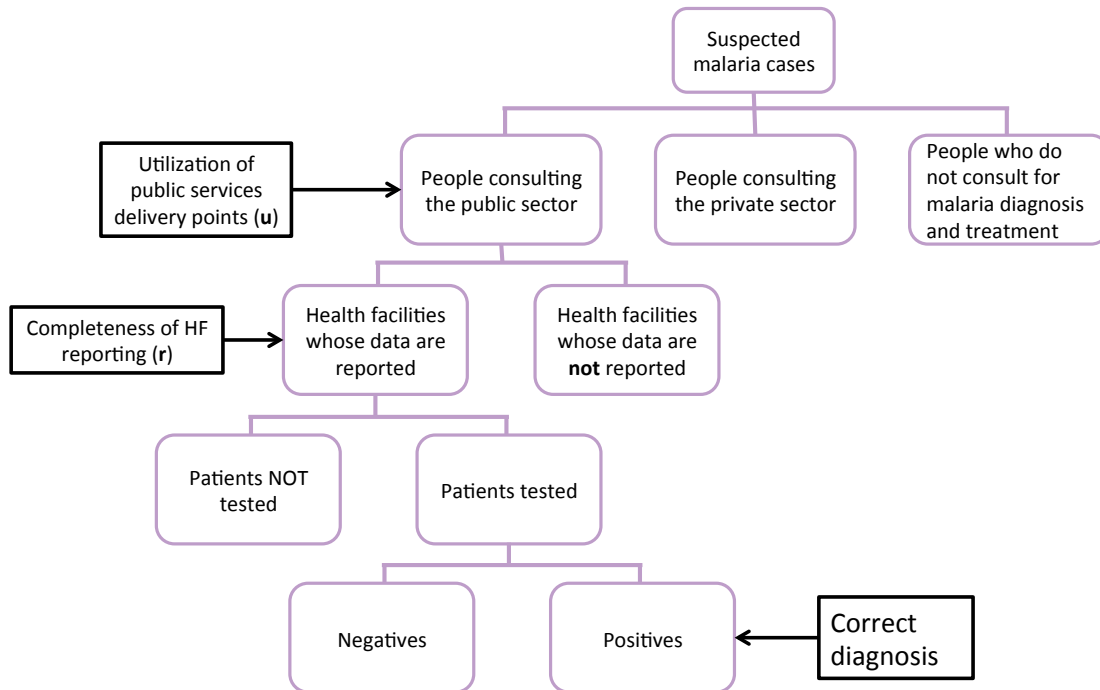
Figure 17.2 Factors affecting the malaria surveillance system sensitivity

e. Data on factors affecting the surveillance system sensitivity can be obtained from:

▸ Utilization of public service delivery points (u)

This can be obtained from the survey data. In DHS and MICS studies that have been conducted in different countries, there was a question asking if fever was present in children <5 years of age in the past two weeks and where they had consulted.

▸ Completeness of health facilities reports (r)

This can be obtained after studying the notification forms received at different levels of the surveillance system from health delivery units, i.e. if the data are to be delivered monthly, how many have arrived of the total expected monthly reports.

Exercise 17.2

a. The steps to correct diagnosis are shown in Figure 17.3, to be distributed to the participants.
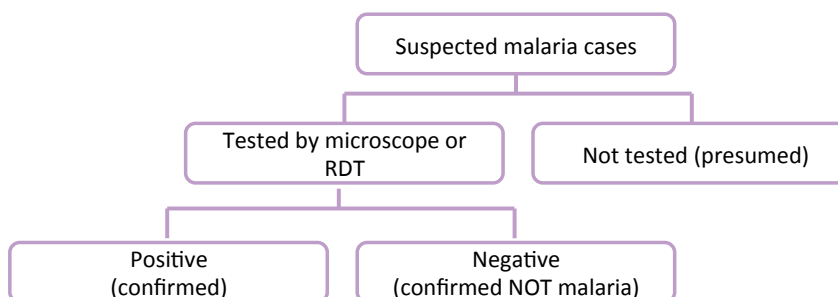
Figure 17.3 Relationship between presumed, unconfirmed and confirmed malaria

b. *Data needed:*

- Reported number of confirmed cases in a year (**C**)
- SPR/TPR (slide or test positivity rate): the proportion of slides/tests examined that are positive for malaria parasites.
- Reported number of not tested (probable or unconfirmed malaria) cases in a year: cases suspected of being malaria but not tested or confirmed (U); and recorded as malaria.

c. *All three can be found in the notification. In countries where parasitological examination for all suspected cases is not available, SPR/TPR can be derived from a selection of facilities that undertake parasitological confirmation.*

d. *Variables*

- *Variables that are directly related:*

   C: (reported confirmed cases in a year)

   SPR/TPR (slide/test positivity rate): the proportion of the slides/tests that are positive for malaria parasites.

   U (number of probable or unconfirmed in a year): the cases suspected of being malaria but not tested or confirmed.

- *Variables that are indirectly related:*

   u (utilization of public service delivery points): the proportion of the population with suspected malaria that used health facilities covered by the surveillance system

   r (completeness of health facilities reports): number of outpatient health-facility reports received divided by the expected number of facility reports

Therefore the overall formula to estimate the total malaria cases (M) will be as follows:

$$M = \frac{C + (SPR \times U)}{r \times u}$$

Provide the above formula to all participants on a flipchart or board.

e. *The tutor should ask the participants to state briefly their responses, and discuss the general points emerging.*

17.2 Malaria mortality indicator

Exercise 17.3

a. *The principal sources for data regarding malaria deaths include health facility records and registers and death certificates.*

b. *Total malaria cases* × P. falciparum *rate = expected number of* P. falciparum *cases*

   2 820 000 × 50% = 1 410 000 = expected number of *P. falciparum* cases

   Expected number of *P. falciparum* cases × CFR = expected malaria deaths

   1 160 000 × 0.09% = 1269 expected malaria deaths

LEARNING UNIT **18**

Introduction to malaria epidemics

PART 4

Learning Objectives:
by the end, participants should be able to...

■ Define a malaria epidemic

■ Identify contributing/triggering factors

The tutor should explain to the participants that the questions in this Unit are designed to make them think about malaria epidemics and epidemic control as it pertains to their own country or place of work. In working through this process, and with the help of the tutor, they will have a better understanding. Participants should be encouraged to answer the questions as precisely and briefly as possible preferably in working groups.

At the end of the session the tutor should review the answers given and identify any specific areas which are the cause of common difficulties and which will need special emphasis in the Units that follow.

In plenary session, the tutor should open a discussion between the participants to compare experiences of the individual countries/participants and discuss the differences.

Answers

18.1   Definition of a malaria epidemic

Exercise 18.1

a. *Participants may answer as Yes or No depending on their respective involvement in epidemics.*

b. *Malaria epidemic: it is generally accepted that an increase in morbidity well beyond the normal occurrence is the main feature of epidemics. However, the definition of "normal" occurrence can only be defined for a particular population in a specific area and time. In some settings malaria epidemics could be considered as a disturbance of a previously existing epidemiological equilibrium.[1] Epidemics generating a small number of cases are usually called outbreaks.[2]*

c. *Based on the form of presentation of epidemic, following are the major epidemic types:*

   i. *True epidemics – infrequent/cyclical outbreaks in relatively non-immune populations related to climatic anomalies (mainly arid and semi-arid zones). Examples: Eastern Kenya, Ethiopia, Somalia, Sahelian countries, etc.*

   ii. *Increased seasonal transmission – variable but relatively predictable transmission influenced by variations inin climatic factors. Population living in highlands (above an altitude depending on the distance from Equator) or in Sahelian/Southern African region. Examples: Kenya, Botswana.*

   iii. *Breakdown of control – where malaria has re-emerged due to interruption of control activities (not necessarily linked to a humanitarian emergency situation) with subsequent increase of transmission on an epidemic mode. Examples: Central Asian republics, Madagascar, etc.*

   iv. *Humanitarian emergencies – malaria transmission exacerbated by population movements and country political instability. May include (i) and (ii). Example: Burundi*

The situations *(i), (ii)* and *(iii)* indicated in the Figure 18.1 correspond to the types of epidemics discussed above.

[1.]   Najera (2001). Malaria control achievements, problems and strategies. *Parasitologia*, U3:1–89.

[2.]   To avoid any confusion, the term "epidemic" is used throughout this document.

Classification of major malaria epidemic types
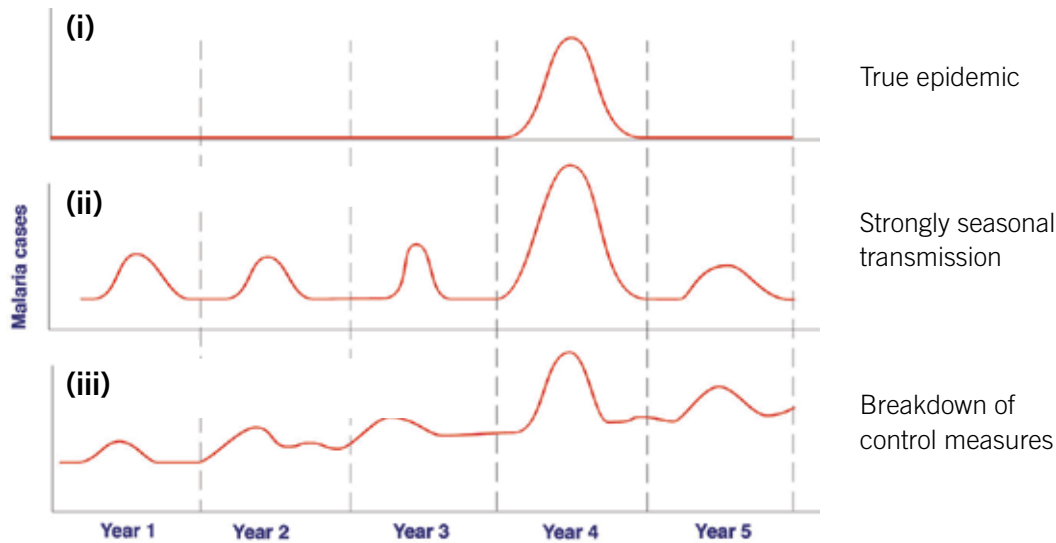
Figure 18.1 Major malaria epidemic types based on the form of presentation of epidemic

18.2   Population at risk of malaria in epidemic-prone regions

Exercise 18.2

a. *Epidemics occur in areas of unstable low transmission where the populations do not have adequate immunity to malaria.*

Epidemics occur when existing equilibrium between rate of infection and the herd immunity of a population in a given area is altered. If the rate of infection is stable, malaria epidemics do not generally occur in high transmission areas (other than when there is large migration of non-immunes to these areas) because the local populations develop partial immunity against the disease.

b. *The answer is No. Because, in populations with low immunity, malaria can affect all age groups.*

c. *Answers of participants may vary depending on where they come from; allow participants to present their situation and discuss the differences in the class.*

d. *The identification of the population at risk and associated precipitating factors is essential to effectively prevent or control malaria epidemics and prevent new epidemics in the future.*

e. *In summary, the following conditions make human populations vulnerable to malaria epidemics:*

  ▶ Migration of non-immunes to areas with high malaria transmission.

  ▶ Introduction of parasites and/or introduction of suitable vectors for malaria transmission to areas with constant low or no transmission, where populations do not achieve a high degree of immunity.

  ▶ Increasing population vulnerability after a long period of drought (and famine) followed by intensive rainfall and creation of suitable conditions for malaria transmission.

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f. Characteristics of epidemic-prone areas:

▶ They are normally less favourable for malaria transmission, but certain climatic, biological and/or epidemiological conditions could change, resulting in an increased transmission far beyond the typical pattern.

▶ Epidemic-affected areas are often at the fringes of endemic areas.

▶ They can also be areas undergoing rapid demographic changes. Movements of populations which are immunologically naive towards malarial infections, change malaria transmission and may cause epidemics.

Examples:

▶ Highland areas bordering endemic lowland areas and which may normally have low temperature which do not allow malaria transmission

▶ Hot, dry arid areas and desert fringes bordering endemic areas (e.g. river valley)

▶ Endemic areas receiving an influx of non-immune migrants

▶ Areas undergoing massive environmental changes such as deforestation, damming/ irrigation and flooding.

18.3 Indicators of transmission and monitoring epidemic risk

Exercise 18.3

a. Successful transmission of the malaria parasite by the vector has two main requirements:

i. There must be sufficient human/vector contact.

ii. The survival time of the vector must be long enough to complete the life-cycle of the parasite and allow the vector to become infective.

b. The basic reproduction rate (R_0) equation is

$$R_O = m\, a^2\, p^n\, /\, r - \log_\mathrm{e} p$$

This equation expresses the functional relationship between the various factors responsible for malaria transmission. However, the influence of immunity and other barriers to super-infection in the host are not accounted for in this equation.

Within the equation, the most important factors impacting human malaria transmission are duration of the sporogonic cycle, vector survival, and the average number of times a mosquito bites a human. Therefore, any parameters that may directly or indirectly affect any of these factors play an important role in determining the level of malaria transmission.

Another key concept in malaria transmission is *Entomological Inoculation Rate (EIR),* the number of infective bites per person per time. Based on the Ro, the direct and indirect factors responsible for malaria transmission can be defined. "Direct" factors appear in the equation, but these are frequently difficult or impossible to measure. The following is a list of direct factors that affect the level of transmission and are, in turn, affected by the corresponding indirect parameters.

c. The tutor should provide hints on the relationship of these two columns and ask the participants to complete the empty column individually.

> i. *The factors that influence the determinants are given below: compare with the answers given by the participants.*

> ii. *The indirect or influencing factors that affect the level of transmission are usually used as indicators to monitor the risk of malaria epidemics in a given region and are easy to measure. See Table 18.1.*

Table 18.1   Direct and indirect factors that contribute to occurrence of malaria epidemics

Determinants (direct)	Influencing factors (indirect)
Vector density	Rainfall, drought, incorrect maintenance of irrigation systems, changes in vector breeding habitats, breakdown in vector control efforts
Human biting	Housing, behaviour, disasters, socioeconomic factors, breakdown in vector control efforts, presence/absence of livestock (in case of zoophilic vectors)
Rate of gametocyte carriers	Population movements
Length of sporogony	Temperature
Daily survival rate of vectors	Temperature, humidity

d. The use of health statistics to differentiate endemic and epidemic prone areas

> ▶ Yes, health statistics are useful to differentiate between endemic and epidemic prone areas. Assuming that everybody has equal access to functioning health care facilities, epidemiological statistics on attendance rate reflect age distribution according to demographic data.

If health statistics from various sources (hospitals, health clinics, communities) are reasonably well collected and maintained with breakdown by age, months and place of residence over a certain period of time (1 year at least), they can be used to identify age groups which develop most disease, and to correlate them with usual place of residence.

In epidemic prone areas where immunity is low, all age groups are at risk. This means for example that in epidemic prone areas (and according to demographic census) approximately 20% of suspected malaria fever cases are expected to be detected in children aged <5 years and 80% in those ≥5 years old. If the majority of those attending most health facilities with fever are children under 5 and pregnant women, the region is probably endemic because in this transmission setting, infants and children are the most affected by the disease.

In epidemic prone areas the number of reported malaria cases tend to vary year to year.

18.4   Precipitating factors for malaria epidemics

Exercise 18.4

a. Factors which may cause an unexpected increase in transmission are numerous. They mainly operate by modifying the environment thereby increasing vectorial capacity. They can be classified as follows:

1. Human activity

> ▶ *Socioeconomic development activities* modifying the environment (directly linked to human activities) and leading to the temporary or permanent displacement of immune or non-

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immune people. As a result, secondary larval breeding sites are often created, vector density increases, behaviour of vectors may change and new vectors may adapt to the new conditions. People may also move into recently exploited areas where vectors are present. For example:

▶ Forest and jungle areas subjected to economic exploitation (Amazon region, South-East Asia)

▶ Large-scale agricultural projects or extensive cultivation of marshes particularly in highlands (irrigated rice fields, sugar cane cultivation) in Rwanda, Burundi, Tanzania (Usambara mountains), Madagascar, etc.

▶ Irrigation projects, dams (Sahel countries, etc.)

▶ Mining and logging activities (Brazil, Sahel countries, south and South-East Asian countries)

▶ Refugees making borrow-pits in resettlements (Pakistan)

▶ New roads better connecting endemic lowlands to highlands virtually free of malaria (Madagascar, Rwanda, Burundi, Algeria…)

▶ Fast-growing process of urbanization leading to new overcrowded settlements in periurban areas (Somalia, Mozambique). Urban malaria has also been described in some Asian countries (India, Bangladesh, Myanmar, Indonesia, Nepal, Maldives, Sri Lanka and Thailand). *A. stephensi* was considered as the main vector (resistant to DDT) in big cities, and *A. culicifacies* in the periphery. In cities, the following factors have been identified to increase the risk of malaria transmission: *(i)* changes in topography and socioeconomic conditions due to the expansion of the cities, as well as to rapid industrial growth, *(ii)* increasing movement of population from rural areas to find jobs, *(iii)* poor housing settlements with borrow pits, water accumulation and ponds, open drainage with blocked drains, uncovered overhead tanks…, *(iv)* (unauthorized) temporary dwellingswithout vector barriers, *(v)* inadequate or outdated sewerage and drainage systems, etc.

▶ Low economic status, overcrowding, and deprivation also contribute to the malaria transmission.

▶ *Overpopulation* leading to the increase of population pressure on the available agricultural land, for example:

▶ Extensive cultivation of natural marshes in highlands (Rwanda, Burundi, eastern DRC, India, etc.),

▶ Population movements exploiting natural resources, changing the microclimate for the insect fauna and driving wild animal population away (India).

▶ *War and socio-political disturbances* leading to:

▶ Large population movements contributing to modification of the environment (large refugee camps),

▶ Resettlement of non-immune people in malarious areas (Rwanda),

▶ Deterioration of the public health system including breakdown of surveillance and malaria control activities (e.g. Rwanda and neighbouring countries, Sudan).

2. Natural disasters

- Natural disasters and other disturbances can lead to unexpected environmental modifications and population movements (e.g. cyclones in Madagascar, hurricanes in Caribbean countries…).

- Climatic changes leading to more rapid development of infective stages of *Plasmodium* in adult mosquitoes and development of aquatic stages of vectors (Rwanda, United Republic of Tanzania …). High temperature and high humidity may prolong the survival of most vectors. Rainfall greatly influences breeding sites. The impact of rainfall depends on local evaporation rates, soil percolation rates, slope of the ground and proximity of large water bodies and rivers, and irrigation system.

3. Breakdown of health services

▶ Defects or breakdowns in epidemiological surveillance (irregular monthly reports, faulty examination of slides…) leading to abnormalities being neglected (Madagascar, India, Grenada, Namibia, etc.)

▶ *Deterioration of health services* (including malaria control activities).

For example:

▶ Where malaria is no longer a public health concern, there may be shortage of insecticide and/or inadequate and/or poor spray coverage. The increasing reluctance of householders to accept some malaria control activities such as indoor spraying has been documented in many countries and may have played a role in malaria epidemics (e.g. Sri Lanka, Sudan, Turkey, India, Sudan, South Africa, Madagascar). In some countries increased *Plasmodium* resistance to antimalarial drugs and increased vector resistance to insecticides has led to malaria epidemics. (KwaZulu Natal, South Africa).

▶ Insufficient primary care coverage influencing rapid access to essential drugs and appropriate treatment of severe cases.

▶ Weaknesses in disease management such as: *(i)* lack of antimalarials in health facilities, *(ii) P. falciparum* resistance to available drugs *(iii)* high cost of the available drugs in private sector.

▶ Inadequacies of the health information system including: *(i)* long delays in the analysis of routine monthly reports at district level, *(ii)* overburdened regional epidemiological section leading to delay in computing the data, *(iii)* irregular reporting and collection of irrelevant epidemiological data, *(iv)* insufficient coverage by the surveillance system.

The problems caused by epidemics may be compounded by factors related to poor health services, and insufficient knowledge of health workers and communities including: *(i)* lack of information on malarial disease, its diagnosis and treatment; *(ii)* severe cases (especially cerebral malaria) being treated by traditional healers and as a consequence, many deaths.

b. After listening to results or responses of participants, the tutor will provide them with copies of Table 18.2 for comparison and further discussion. The chart (Fig. 18.2) that shows the classification of the precipitating factors should also be provided.

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Table 18.2   Precipitating factors for malaria epidemics and their consequences

Cause	Potentially leading to:
1. Human activity	
Economic development activities (legal or not)	Modification/destruction of environment (ecological disturbances)
	High mobility of population (seasonal non-immune workers and/or migrants seeking new settlements)
	Displacement of populations by hydroelectric projects
Overpopulation	Population pressure on available agricultural land : cultivation of natural marshes in highlands, destruction of forest
War/civil disturbances	Large scale uncontrolled population movements Modification of the environment (large refugee camps) Lack or weaknesses of the PHC system including malaria control activities Poor housing conditions
Road construction/ improvement in transport facilities	Increased contact between lowlands and highlands or between endemic and non-endemic areas The increase of gametocytes carriers coming from endemic areas
Urbanization	"Urban and periurban malaria" New overcrowded settlements in periurban areas with new breeding sites for vectors
Global and local climate changes	Modification of vector-borne disease distribution and biology in altitude
2. Natural disasters	- Increased breeding sites - Population movements
Expected or unexpected meteorological events (heavy rainfall, unusual heavy flooding, cyclones, climatic changes...)	- Create secondary larval breeding-sites, - Increase density of vectors, - Change the behaviour of vector(s), - Modify the duration of the sporogonic cycle in vectors and aquatic stages of vectors
3. Break down of health services (degradation of preventive and curative health services)	Absence of drugs / inappropriate case management especially for severe cases
Deficient surveillance within the control services	Malaria interventions are interrupted while the environment is still favourable for malaria transmission
Malaria prevention activities are deteriorating (such as lack/shortage of insecticide and/or inadequate or poor spray coverage) Refusal of villagers of some spraying operations.	"Post-eradication" epidemics Persistence of malaria foci Decrease the coverage and/or quality of malaria control activities
Increasing resistance of vectors to insecticide and/or parasites to antimalarials.	Build-up an infective reservoir of mainly resistant vectors/ parasites
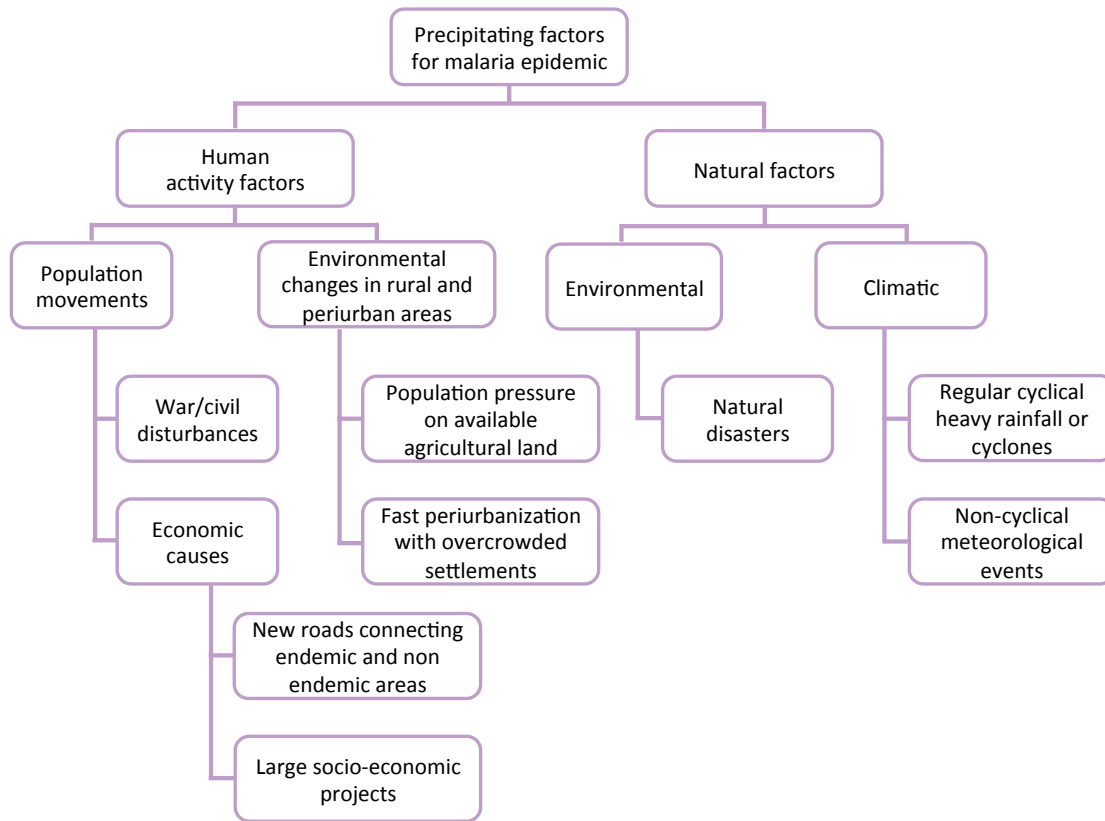
Figure 18.2 Classification of the precipitating factors for malaria epidemics

c. It is necessary to identify precipitating factors for malaria epidemics in order to select proper preventive and control options, and to plan early warning and preparedness mechanisms.

Essential past and current information requested to explore potential contributing factors for any malaria epidemics.

Allow participants to discuss the factors relevant to this section mentioned in the *Guide for Participants* and summarize.

d. The information could be obtained as follows:

▸ Epidemiological health records: at clinics, district or national level

▸ Meteorological stations: facilities at peripheral or/and national level

▸ Population movements/displacements: through local authorities, NGOs, humanitarian community, other survey reports

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LEARNING UNIT **19**

Early warning, detection, notification and verification of a malaria epidemic

Learning Objectives:
by the end, participants should be able to…

■ Describe the usual channels for notification

■ Explain the concept and rationale of an early warning and detection system

■ Describe how to identify/detect a malaria epidemic on a timely basis

■ Describe how to rapidly confirm a malaria epidemic

■ Describe urgent measures to contain the epidemic

Answers

19.1   System for early detection of malaria epidemics

Exercise 19.1

a. Allow participants to discuss their findings, then distribute copies of the diagram below for comparison. Discuss the discrepancies
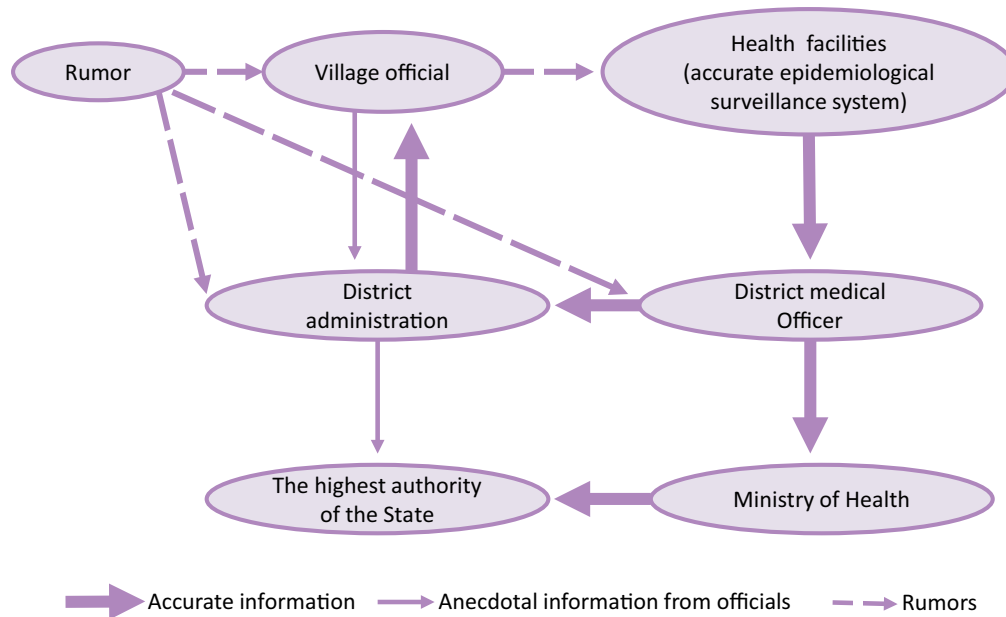
Figure 19.1 Information flow for unusual events from communities/villages

b. The rationale to set up a weekly-based early detection system for malaria epidemics

In most countries, the health information system routinely collects and reports health data on a monthly basis, sometimes on a quarterly basis. The interval for reporting to the higher level (for example from health care facilities to district management team) is at least 10 days and usually longer. Experience shows that malaria epidemics progress rapidly with an average duration of 3–4 months. *It is obvious that a monthly reporting system cannot detect an upsurge of suspected malaria cases at an early stage and, as a result, does not allow sufficient time to mobilize control resources in a timely manner.* For this reason Heads of State and Ministries of Health agreed in Abuja in 2000 to identify key Roll Back Malaria targets, including "to detect and control epidemics within 2 weeks of onset".

Note that other epidemic diseases like meningococcal meningitis, cholera, yellow fever, etc, are monitored on a weekly basis and that malaria should be part of the list of epidemic-prone disease in well defined epidemic-prone regions.

19.2   Methods for determining epidemic thresholds

Exercise 19.2

a. Epidemic threshold detection systems

Routinely, the malaria epidemic threshold is used for early detection within 2 weeks of onset of the epidemic. Attempts have been made by WHO and other institutions to identify epidemic thresholds which clearly define an epidemic against the previous trends of the disease. Such thresholds can be worked out in areas where historical *epidemiological data/pattern* exist for some years, and the population has remained stable. If this information is available, the following methods can be proposed to develop epidemic thresholds.

    i.   *Constant case count thresholds*

    ii.   *Mean + 2SD*

    iii.   *Median + upper 3rd quartile*

    iv.   *The cumulative sum (C-SUM) method*

    v.   *Incidence thresholds (meningitis as an example)*

These methods are described in detail in the sections below.

Many epidemics occur in situations where previous data is either not available, or unreliable due to significant contextual changes. In these circumstances, precise thresholds will be difficult to set up and in practice an epidemic situation is detected by:

   ▸ *The rapid and unexpected (noticed on a weekly basis) increase in numbers of cases*

   ▸ *A high case fatality rate (due to late specific treatment at community level)*

   ▸ *The fact that the existing health services are overwhelmed (e.g. shortage of health personnel and drugs).*

Method 1: Constant case count thresholds

In Botswana three alert thresholds based on both *unconfirmed and confirmed* malaria cases are used for malaria epidemic prediction at the district level. In this system, 400 absolute cases/ week in one district indicates an alert which should be acted upon at the district level, 800 cases/week indicates that the national authorities should be informed, and 1200 cases/ week indicates a national emergency. The simplicity of this method is reinforced by a data entry system in which the values of case numbers above the threshold are automatically highlighted in red, drawing the information to the attention of those reviewing the data. Botswana is unusual with respect to much of Africa because laboratory diagnosis is carried out for all suspected cases. This system seems appropriate to the district structure in Botswana, which is largely determined by population size (~100 000 persons per district).

In Viet Nam, in non-endemic areas, when the number of local *confirmed* malaria cases is over 10 within 2 weeks, an epidemic is declared.

Other methods based on statistical analysis of data

Setting epidemic thresholds is more commonly achieved by comparing the normal mean/ median number of cases of at least the 5 previous years with the current case numbers over a

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set time (preferably weekly than monthly-based due to the fast sharp increase of cases when an epidemic starts). Initially this may be from all reported malaria cases but subsequent analysis of only laboratory confirmed cases by thick blood film or RDT can define the real change in malaria cases.

Method 2: Mean + 2SD

This involves the calculation of the long-term mean of monthly reported malaria cases (derived from a minimum 5 year data set after excluding very abnormal years) and an epidemic threshold set at two times the standard deviation of the mean.

Experience from Madagascar, where this threshold method has been tested, indicates that it has high sensitivity, but low specificity and predictive value. Out of 69 epidemic alerts signalled by this system only 17 of these were reported within 30 days and only 5/69 were found, on further investigation, to represent a real increase in malaria cases. The main causes of false alerts being given were poor predictive value of presumptive diagnosis of malaria with only 12.1% of reported cases confirmed as malaria by microscopy.[1]

Method 3: Median + upper 3rd quartile

The recommended method for setting the epidemic threshold is to compute the monthly median value and the upper 3rd quartile from a time series of monthly data, generally over five years. Months in which cases exceed the 3rd quartile will be declared routinely as epidemic months. This method has the advantage over Method 2 in that results are less influenced by abnormal years and the values are easier to calculate without computing facilities. Again a minimum of 5 years data is required. However, if the historical data does not include any epidemic years, any value marginally exceeding those that have occurred could result in an epidemic being declared – even though the case numbers may be well within the normal range. In Uganda, historical malaria reported cases (3–5 years) from sentinel sites are used to define median and quartile values for malaria incidence on a monthly basis. Health workers in the health facilities considered sentinel sites are trained to plot malaria cases onto this graph on a weekly basis. When cases are in excess of the median a report is sent to the District Medical Officer (DMO) to provide an initial alert. If cases rise above the 3rd quartile, then an epidemic is declared and the local DMO, MoH and DMOs in other epidemic prone districts are notified immediately.

b. *Divide participants into small working groups to do the exercises i – iv related to the data given in* **Table 19.1** *below in the Guide for Participants.*

i. *In order to determine the median and quartiles, the data need to be re-arranged in ascending order for each month. This would be best done by entering the data in Excel by computer. When sorted in an ascending order, the second lowest number in the month is the 1st quartile and the second highest value is the 3rd quartile. The 2nd quartile, which is the middle of the mid-value throughout the 5 years observation of that month, is the median. Compare the results reached by the working groups with* **Table 19.1.**

[1.] Albonico M. et al. (1999). Control of epidemic malaria on the highlands of Madagascar. *Parassitologia* 41:373–6.

Table 19.1   1st quartile, median and 3rd quartile of malaria cases reported from Province X, 2001 to 2005

Year	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.
Lowest value	1198	1099	1784	1411	1449	1958	398	1902	1939	1490	1299	2223
1st quartile	1214	1322	2010	1597	1863	2018	1737	2424	3188	1842	2269	2267
median	1609	2219	2035	1880	2973	2200	2612	2815	4761	3395	2332	2321
3rd quartile	2597	2235	2619	2462	4927	2442	2822	4028	8658	5845	2588	2944
Highest value	2941	2449	2988	2977	5276	3534	2857	5159	9245	10158	4274	

ii. Allow participants to enter the data in Excel and sort the numbers in ascending order. Then ask them to plot the numbers on a graph.

In the absence of a computer, participants can do these exercises on paper and for graphs they can plot using graph paper or simple squared paper to construct a graph of the median and the 3rd quartile. The plotting should resemble figure 19.2.
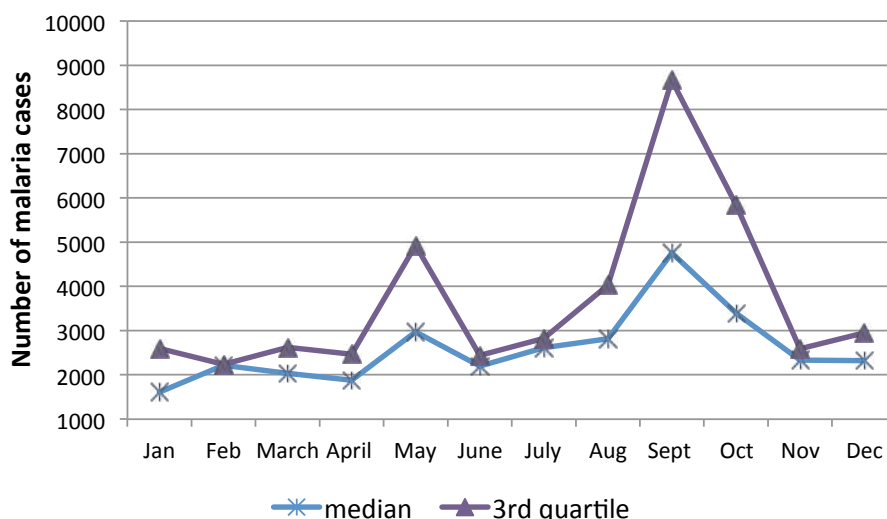
Figure 19.2 Median and 3rd quartile of data from Province A (2001–2005)

iii. The upper line – *the 3rd quartile* – indicates a level above which the possibility of *an epidemic* should be considered.

iv. After each group has presented its findings, compare with the following results. Add the row of figures for 2006 into the previously constructed table (2001–2005) and plot another graph to see the situation of the year that is being monitored.

Year	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.
2006	1364	2560	2817	1656	1958	2021	2255	3169	4897	9158		

The graph should resemble Figure 19.3
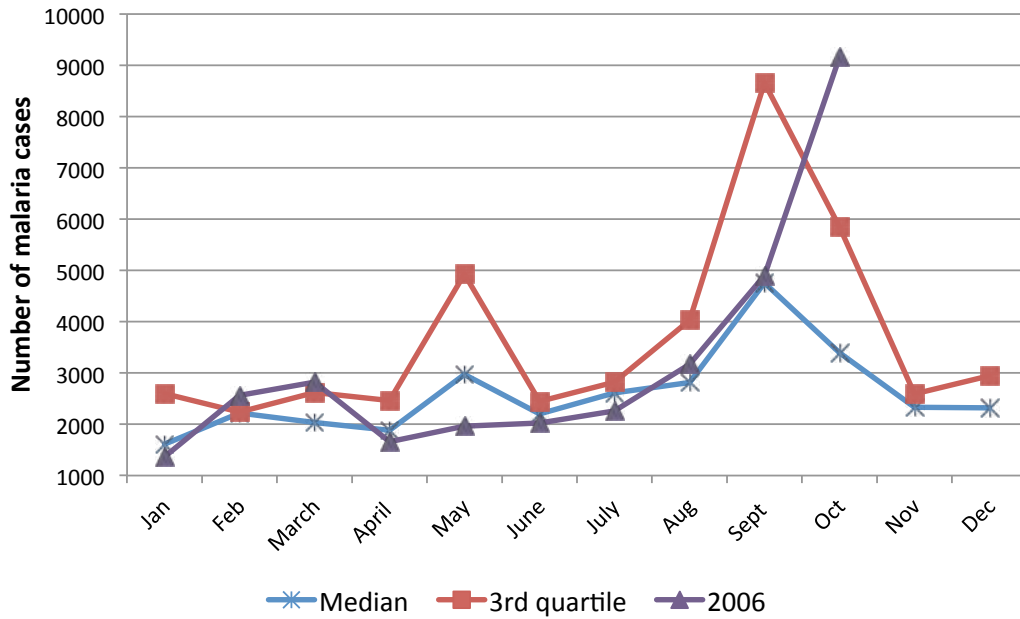
Figure 19.3 Graph comparing 2006 data with the mean and 3rd quartile of the 2001–2005, data of Province X

As the graph shows, the October value rises steeply above the 3rd quartile, signalling the possible beginning of an epidemic.

Exercise 19.3

a. As done in the previous exercise with data from the Province X, participants need to rearrange the data from Province Z in ascending order as shown in Table 19.2 in the Guide for Participants. They should show numbers in bold in the columns that contain median, 1st and 3rd quartiles. Compare the results reached by the participants with Table 19.2.

Table 19.2   Malaria morbidity data of Province Z, 1996-2004

Month	Week			1st Quartile		Median		3rd Quartile			2005 epidemic
Jan.	1	9	20	24	40	44	47	48	76	121	63
	2	6	8	29	37	39	45	50	65	83	41
	3	8	13	31	32	43	48	105	108	112	56
	4	1	15	35	46	49	52	88	96	130	69
Feb.	1	7	9	38	41	44	46	72	84	88	41
	2	4	14	23	31	41	48	58	76	100	45
	3	3	11	27	28	35	38	52	70	74	50
	4	8	14	41	43	49	68	70	97	98	39
Mar.	1	4	11	30	32	33	39	42	50	69	50
	2	3	10	24	25	39	45	66	77	80	52
	3	5	18	32	35	39	44	45	59	67	46
	4	8	9	9	33	34	45	49	63	83	38
Apr.	1	5	18	25	35	40	44	44	47	62	42
	2	6	14	23	25	36	44	45	48	76	30

Month	Week			1st Quartile		Median		3rd Quartile			2005 epidemic
	3	8	22	31	33	34	35	35	53	61	23
	4	18	19	27	42	42	54	57	60	60	36
May	1	9	15	24	35	43	44	53	77	106	36
	2	9	23	25	31	38	42	54	55	72	45
	3	5	23	27	33	34	37	69	80	95	44
	4	24	37	40	57	71	76	94	95	113	76
Jun.	1	21	25	31	52	54	74	81	93	113	44
	2	17	39	48	50	55	60	69	72	123	61
	3	15	23	40	51	58	67	69	116	157	64
	4	18	41	46	57	59	94	100	113	200	79
Jul.	1	19	29	29	55	60	62	94	110	184	93
	2	11	25	44	51	56	60	69	129	200	62
	3	15	24	31	40	53	63	92	123	129	68
	4	16	23	31	64	64	74	92	96	216	89
Aug.	1	9	23	29	39	41	77	86	89	112	81
	2	5	23	26	29	73	81	95	109	202	112
	3	13	28	41	55	60	90	99	154	156	132
	4	9	29	41	62	104	118	159	200	271	188
Sept.	1	13	19	75	79	80	84	93	128	136	162
	2	9	30	95	116	126	141	159	193	221	188
	3	11	26	108	109	127	137	149	181	259	258
	4	31	62	101	105	139	183	272	279	540	346
Oct.	1	23	27	28	85	100	161	165	190	302	350
	2	28	36	69	88	131	174	185	220	272	322
	3	23	33	68	83	100	123	159	170	181	343
	4	25	46	71	109	169	179	182	221	276	413
Nov.	1	19	30	42	85	103	104	122	139	230	487
	2	11	13	41	71	73	86	96	128	192	378
	3	18	23	32	51	58	74	79	100	153	383
	4	12	18	53	66	95	114	116	147	248	265
Dec.	1	11	17	45	50	62	69	93	108	143	106
	2	12	25	41	46	53	65	76	99	115	113
	3	7	12	33	41	50	53	55	67	114	163
	4	15	19	21	26	36	37	50	69	102	223

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b. *The graph plots for the Median, Upper and Lower Quartiles are indicated in Figure 19.4.*

c. *From the Figure 19.4 it can be concluded that the case load of 2005 clearly exceeds the 3rd Quartile during the last quarter, and , using this method the "epidemic alert could be given as early as week 30-31 at least 2 months before the epidemic peak.*
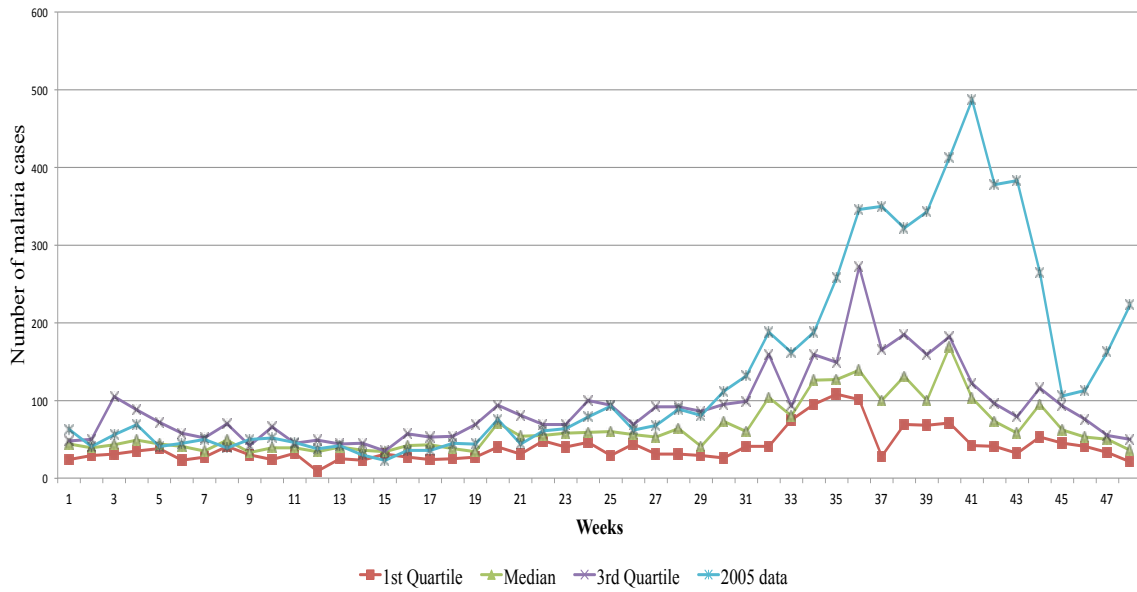
Figure 19.4 Median, 1st and 3rd quartiles of data 1996–2004 compared to 2005 epidemic in Province Z

Method 4: the cumulative sum (C-SUM) method

Exercise 19.4

The same example will be used to define the threshold using C-SUM method.

Table 19.3 Same data set as before, with the sum total of each month added

Year	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.
2001	1609	2235	2035	1597	4927	2442	2857	5159	9245	1490	1299	2267
2002	1214	1322	1784	1880	1863	1958	398	2815	4761	5845	2588	
2003	1198	1099	2010	1411	1449	2018	1737	1902	1939	1842	2332	2321
2004	2597	2219	2988	2977	5276	3534	2822	4028	3188	3395	2269	2223
2005	2941	2449	2619	2462	2973	2200	2612	2424	8658	10158	4274	2944
sum	**9559**	**9324**	**11436**	**10327**	**16488**	**12152**	**10426**	**16328**	**27791**	**22730**	**12762**	**9755**

a. *To calculate the C-SUM for January, add the sum for December, January and February for the 5 years of data, and divide the total by 15. Similarly the C-SUM for February is calculated by adding the sum of January, February and March and dividing by 15.*

The values for C-SUMs for each month are then as follows.

Year	Jan.	Feb.	Mar.	Apr.	May	Jun.	Jul.	Aug.	Sept.	Oct.	Nov.	Dec.
C-SUM	1902	2021	2072	2550	2598	2604	2594	3639	4457	4219	3016	2138

b. The values calculated above can be shown on a graph as in Figure 19.5.
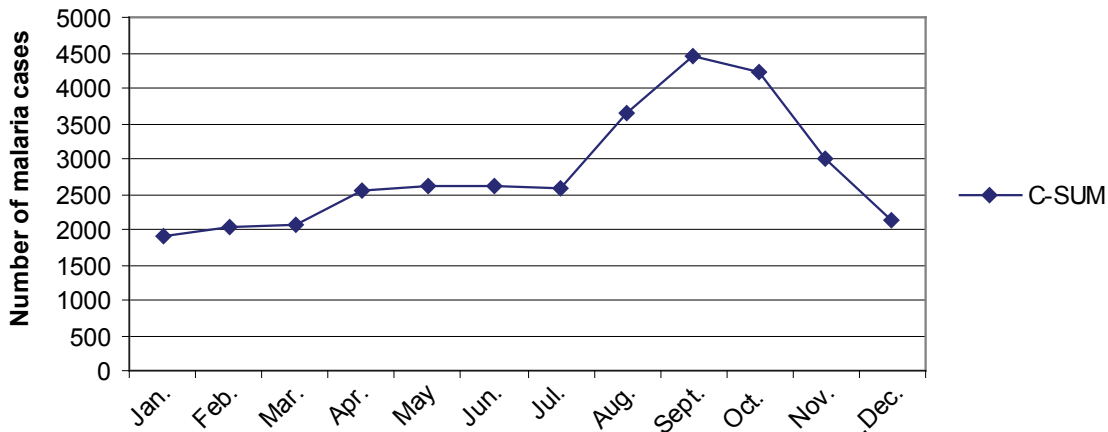

Figure 19.5 Cumulative sum of morbidity data 2004–2005, Province Z

The line represents the alert threshold for malaria epidemics.

c. If the data for 2006 are then added, the graph becomes Figure 19.6
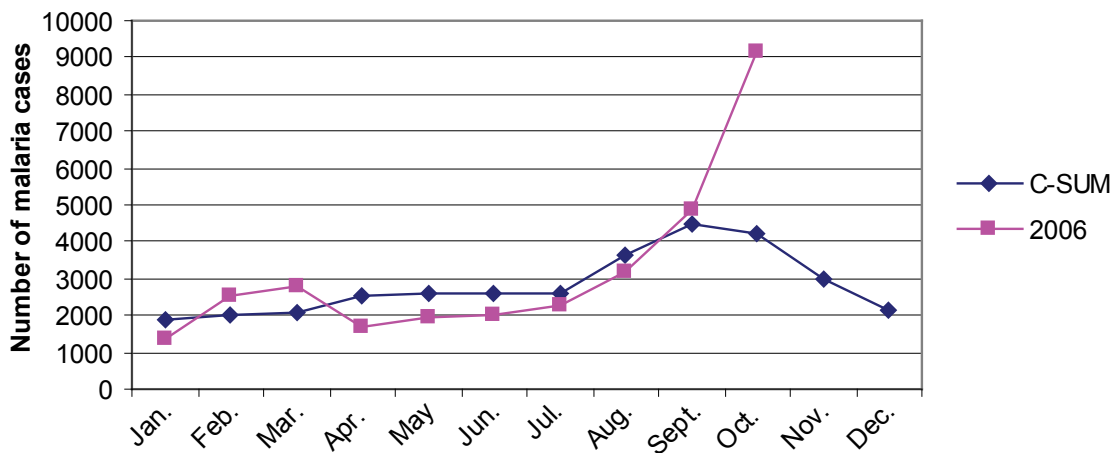

Figure 19.6 Comparaison of 2006 data with the cumulative sum of morbidity data 2004–2005, Province Z

It is easily seen that the numbers for October are far above the threshold, signalling an epidemic.

*d. All these methods use **monthly** data. By the time data are collected, reported and analysed it could be 4 weeks or more after the onset of an epidemic, entailing unacceptable delays to the investigation and response. Ideally data should be collected and analysed at the peripheral level on a weekly basis, and both the median+upper 3rd quartile and the cumulative methods described above can be adapted to weekly dat. However, few places have weekly data going back 5 years. The following method is suggested to use the thresholds developed from 5 years of monthly data and apply them to current weekly data.*

e. Advise participants to use graph paper with the C-SUM or quartile threshold clearly marked as above.

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As the weekly data are collected, mark the number as a column under the month in question. The next week, add the number to that of the first week, and extend the column to the new figure. Using a different colour for each week will make it clearer. Participants should do the same for the 3rd and 4th weeks. If the column is already at the threshold by the 2nd or 3rd week, it will be possible to raise the alert of an epidemic much sooner than waiting for the whole month's data (see Figure 19.7 for example of data manually plotted on graph paper).
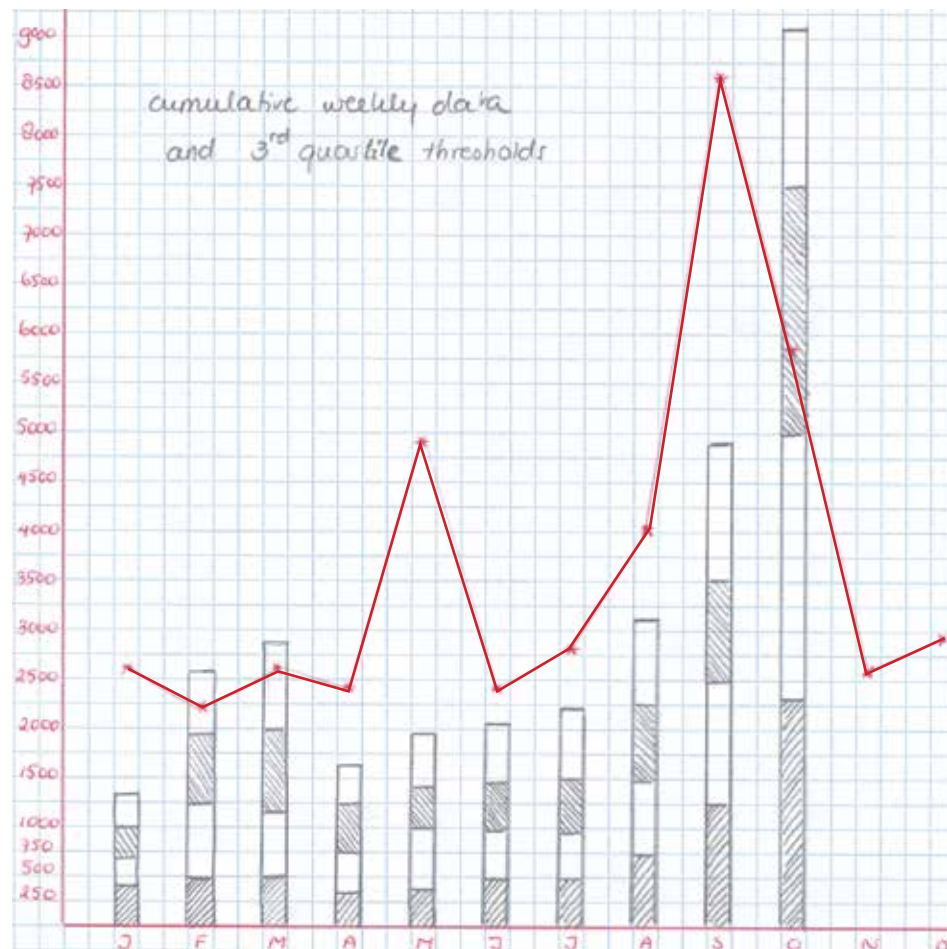

Figure 19.7 Manually prepared graph comparing C-SUM morbidity and weekly-based observations

Point out to participants to note that by the end of the second week in October the numbers had already exceeded the threshold, allowing the earlier investigation and declaration of an epidemic. Let participants compare their results with the diagram provided.

Method 5: Incidence thresholds (meningitis as an example)

Exercise 19.5

The concept of "alert threshold" and "epidemic threshold" are not generally applicable to malaria. The use of all reported malaria cases (including probable, not tested malaria cases) can provide "alert thresholds", which are less predictive of true malaria epidemics than when using confirmed positive malaria cases.

19.3   Early detection and overall management systems

Exercise 19.6

Measures/systems for early detection overall management systems at all levels:

▶ At peripheral level:

  i.   The weekly-based reporting system is expected to work at the peripheral level. Those working at community or primary health care level should detect and report any unusual events.

  ii. Peripheral health workers should be able to make a simple analysis of data they are collecting daily. Analysis should include plotting a weekly data on a graph, and rapid reporting to the health district management team in case of an unusual increase (see thresholds) of fever cases.

  iii. Quick verification procedures should also take place at the periphery by using either microscopy or or RDTs, to test all febrile suspected malaria cases.

▶ At district level:

  i.   District management team should be able to compile data from clinics and establish/ update thresholds based on past data analysis in health facilities/sentinel sites.

  ii. District teams should also be able to correlate epidemiological data with any other relevant warning indicators such as meteorological data, population movements or the environment that can influence malaria transmission.

▶ At national level:

  i.   The NMCP team should carefully analyse data and coordinated work with other sectors relevant in this area (e.g. metereology, agriculture, demographic).

  ii. Strengthening the capacity of health workers – to analyse data, ensure verification procedures, maintain emergency stocks and initiate urgent actions – is a key element of success.

Also explain to participants the following.

  i.   Proper analysis of past epidemiological data, if possible weekly data, is the first step to be done, preferably at district level, with the support of the NMCP.

  ii. Particular attention should be paid to data generated during past epidemics and correlation with specific determinants which could serve as potential warning indicators. In this process it may be necessary to go back to clinic records since most of the data are not available at national or district level, and rarely on a weekly basis.

  iii. Historical data from at least the past 5 years should be investigated; if possible, the period should include an epidemic year. From these data, it should be possible to define epidemic thresholds and develop an early warning system.

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19.4   Verification of malaria epidemics

Exercise 19.7

a. *The steps for verification of detected malaria epidemics at different levels are described as follows.*

> ### *At peripheral level:*
>
> i. *Rapid assessment to confirm: Malaria epidemics are often reported outside the health care system. The first task of a malaria control team or peripheral health team is to determine whether or not the cause of the unusual increase of fever cases is due to malaria.*
>
> ii. *Laboratory investigation: In addition to immediate laboratory investigation made by the peripheral health laboratory (see further), an expert team should also be mobilized comprising a medical officer, epidemiologist and trained staff to perform diagnostics for rapid assessment.*
>
> > - Rapid diagnostic tests are recommended for rapid confirmation of malaria diagnosis in the field.
> >
> > - If RDTs are not available, blood-film examination could be used for verifying epidemics, assuming sufficient slide reading capacity exists.
> >
> > - Entomological survey with larval and/or adult mosquito collection are also important to make a quick investigation of the cause, to determine whether vector control is necessary, and if so, what vector control measures are most appropriate.
>
> iii. *Notification: If the expert team confirms that a malaria epidemic is occurring, the district monitoring centre should notify the national malaria control programme immediately.*

b. *Assist the participants to prepare a flowchart similar to **Figure 19.8** for early detection, **verification** and notification of a malaria epidemic using routine clinical data, recorded weekly. The verification process starts at peripheral level by using either microscopy or RDTs.*

Local authorities, community health workers, and peripheral health workers are those in the front line of any unusual events. In general, "hot information" often originates outside the health sector and comes through administrative authorities and local media which may disseminate inaccurate information. It is important that health workers ensure regular communication with local and political authorities to avoid unnecessary panic, ensure quick verification of reports, and define and articulate early specific interventions with partners according to the preparedness plan of action. It is also important that peripheral health workers have the necessary equipment (like RDTs and emergency drugs in stock) to take early action without delays that might occur while waiting for district or central decision and support.

When an usual increase of malaria cases is detected in any peripheral health care facility, the first action is to verify in a sample of sick patients with fever, the proportion infected by either *P. falciparum* or by *P. vivax*. The proportion of confirmed malaria cases varies locally and depends on the epidemiological situation: an unusual increase over the expected for a specific areas indicates possible epidemic.

c. *In settings where parasitological confirmation is not available, it is necessary to monitor the proportion of confirmed malaria cases in a sample of cases with suspected malaria. In arid and semi-arid areas, the proportion of sick people with fever and blood parasites is expected to be low*
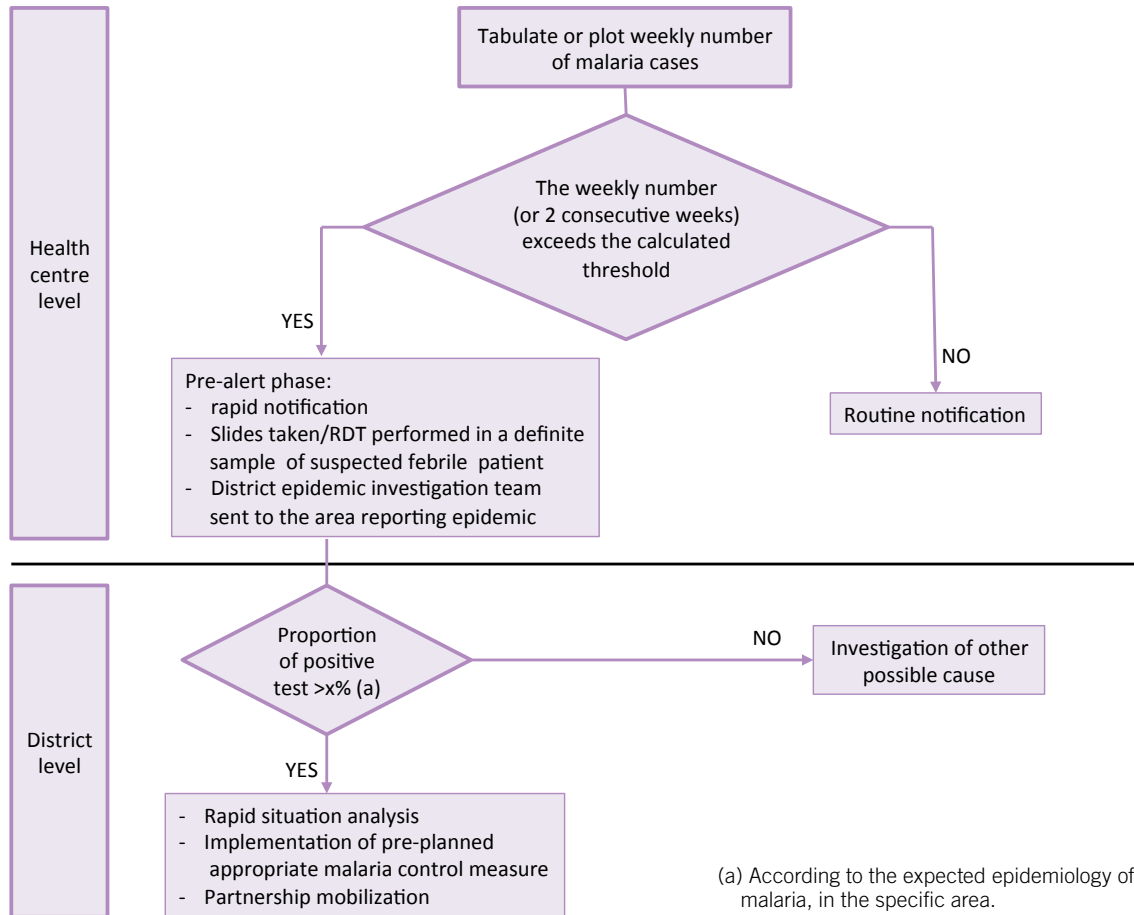
Figure 19.8 Flowchart for detection, verification and notification of malaria epidemics

(<5% to >50% during epidemics). In highlands or regions with short seasonal transmission, the test positivity (SPR or positive RDT rate) might be higher (30–40%) during normal transmission seasons and >70% during epidemics. Baseline data are essential to set up a threshold for positivity rate. It should be noted that in case of epidemics everyone, including those with minor symptoms, is encouraged to go quickly to a health facility; thus affecting the observed positivity rate.

19.5   Monitoring areas of epidemic risk

Exercise 19.8

Allow working groups enough time to analyse the model in Figure 19.9. Provide copies of the figure below to the participants for comparison and discussion.

a. In the example presented above:

- A long range weather forecasting (first warning) would be assumed (Flag 1). At this level the flag could be raised at the regional level after sea-surface temperatures suggest an impending El Niño/La Niña event.

- Early warning based on meteorological indicators: rainfall is monitored directly as part of an early warning system and if it is in excess Flag 2 is raised.

- Early detection: malaria cases are monitored at the individual facility level and if a defined threshold is exceeded (Flag 3) an epidemic is declared.
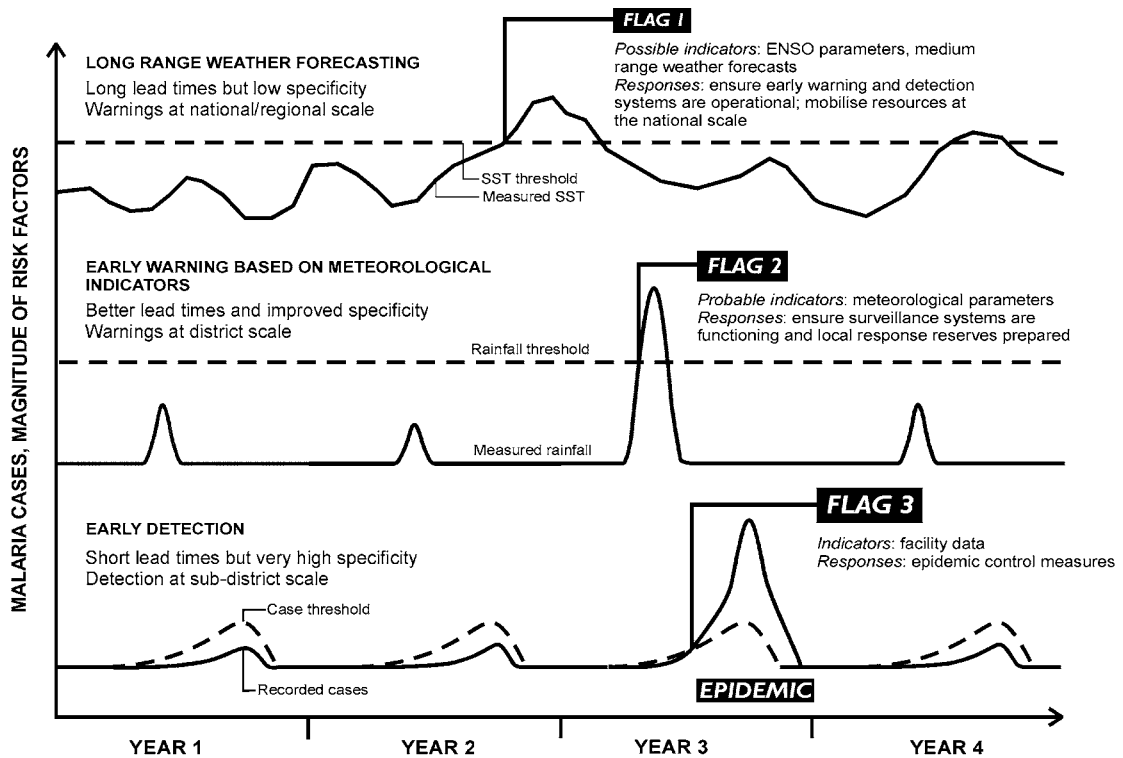
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Figure 19.9 Forecasting, early warning and early detection model, Anon,[1] 1999

b. Indicators and responses for each flag are indicated in the figure.

In general, risk factors which may be monitored routinely by health services in order to assess the likelihood of an epidemic occurring in the near future include:

► climate forecasts

► weather monitoring

► environmental vulnerability assessment

► morbidity surveillance

1. Anon (1999). *Developing new approaches for the surveillance and control of malaria epidemics in the highlands of East Africa.* Highland Malaria Project and Mapping Malaria Risk in Africa: Salt Rock, South Africa.

LEARNING UNIT **20**

Prevention and early response to confirmed malaria falciparum epidemics

Learning Objectives:
by the end, participants should be able to...

- Describe the main malaria epidemic control options

- Describe how to identify the most cost-effective malaria epidemic prevention and control options

Answers

20.1 Cost-effective interventions to control *P. falciparum* malaria epidemics

Exercise 20.1

a. *The most important cost-effective measures to control malaria epidemics, ranked according to their relative importance and/or cost-effectiveness, are as follows:*

   i. *Early diagnosis and effective treatment* for all non-immune people affected (severely or not) by the disease in communities. This will impact directly on mortality because sick people have easy access to efficient drugs.

   ii. *Early vector control measures* targeting adult mosquitoes transmitting malaria parasites. Well prepared and managed IRS of all houses quickly reduces transmission and significantly reduces morbidity and mortality rates. In an emergency context (e.g. refugee camps), insecticide space spraying with ultra-low-volume sprays, which has limited effect and duration, can be considered as a complementary measure to IRS.

   iii. Mass drug administration (MDA) to the entire population at risk. If it is well managed and used together with vector control measures, this is one of the most effective ways to rapidly reduce the parasite population.

Mass fever treatment may be a more acceptable and cost-effective variant of the previous strategy since it proactively targets only household members with fever suspected to be due to malaria. The essential measure to be set up at early stages of any *notified* malaria epidemic is: early diagnosis and effective treatment for both uncomplicated and severe cases.

b. *The guiding principle/s for a drug to have a significant effect on transmission during epidemics are: (i) the drug should have a gametocytocidal effect and (ii) the drug can easily be administered correctly and on a large scale.*

c. *No. Even good case management procedures have little effect on transmission using chloroquine and sulfadoxine-pyrimethamine as these are partially effective blood schizontocidal drugs and have no gametocytocidal effects. Artemisinin-based combinations together with primaquine, which are active against gametocytes, could have an effect on transmission if they are used on a large scale. In emergency situations, effective drugs must be provided free of charge.*

d. *In case of malaria epidemics in remote areas, access to health care by those who are sick is often the major problem. A possible solution could be the establishment of new health posts (mobile clinics) as well as the use of local collaborators in communities through rapid training and social mobilization. Particular attention must be paid to the management of severe cases with rapid referral to health facilities.*

Exercise 20.2

a. *After the small group discussions, allow the groups to present their arguments on vector control for epidemics in plenary and encourage exchange of views. For operational and biological reasons, vector control options may or may not be applicable in epidemics.*

Operationally, vector control options would be applicable if epidemic-prone districts are well prepared and emergency stocks are established and maintained.

Vector control measures can be effective, provided they are implemented in the early stages of an epidemic. Because of their complexities, vector control activities need to be well prepared in advance and staff adequately trained and supervised.

b. *Vector control options mainly target survival of adult mosquitoes, in order to have a direct impact on malaria transmission and hence on the malaria burden.*

c. *Indoor residual spraying (IRS) is effective when well-planned and conducted, and when the coverage rate is above 85% and the vector involved has an indoor resting habit.*

d. *Use of ITNs or re-treatment of existing mosquito nets is effective when the coverage is high (above 85%).*

e. *In complex emergency situations where refugee camps are set up, the use of pre-impregnated tents or prefabricated impregnated plastic sheets has a great impact.*

f. *Space spraying of insecticides (usually done regularly on a weekly basis) could be of benefit in particular conditions such as densely overcrowded populations in small shelters in acute emergency settlements.*

Exercise 20.3

Divide participants into working small groups and ask them to use the data given in Table 20.1 in the *Guide for Participant* and work on the exercise on different scenarios of early detection and interventions of epidemics, and the consequences if these are not done. If computers are not available, the participants can prepare paper graphs.

a. *From the data given in Table 20.1 in the Guide for Participants, let participants first present their findings and compare them with the graphs shown below.*

b. *The differences are:*

  ▸ *Figure (i)* represents a graph of column 2, a suddenly occurring fully blown epidemic with no detection and no intervention. It phases out naturally as the precipitating factors disappear or reduce.

  ▸ *Figure (ii)* represents a graph of column 3 as compared to column 2, an epidemic which is detected late and intervention uses expensive control measures. Considerable the number of cases that occurred due to delayed response.

  ▸ *Figure (iii)* represents a graph of column 4 as compared to column 2, an epidemic where there is some delay in detection and intervention, but relatively better than in Figure (ii).

  ▸ *Figure (iv)* represents a graph of column 5, an epidemic which has been averted due to earlier detection and better preparedness and response. This could result from better community awareness and/or better health service with trained health workers. Early application of control measures may have minimized the number of cases.
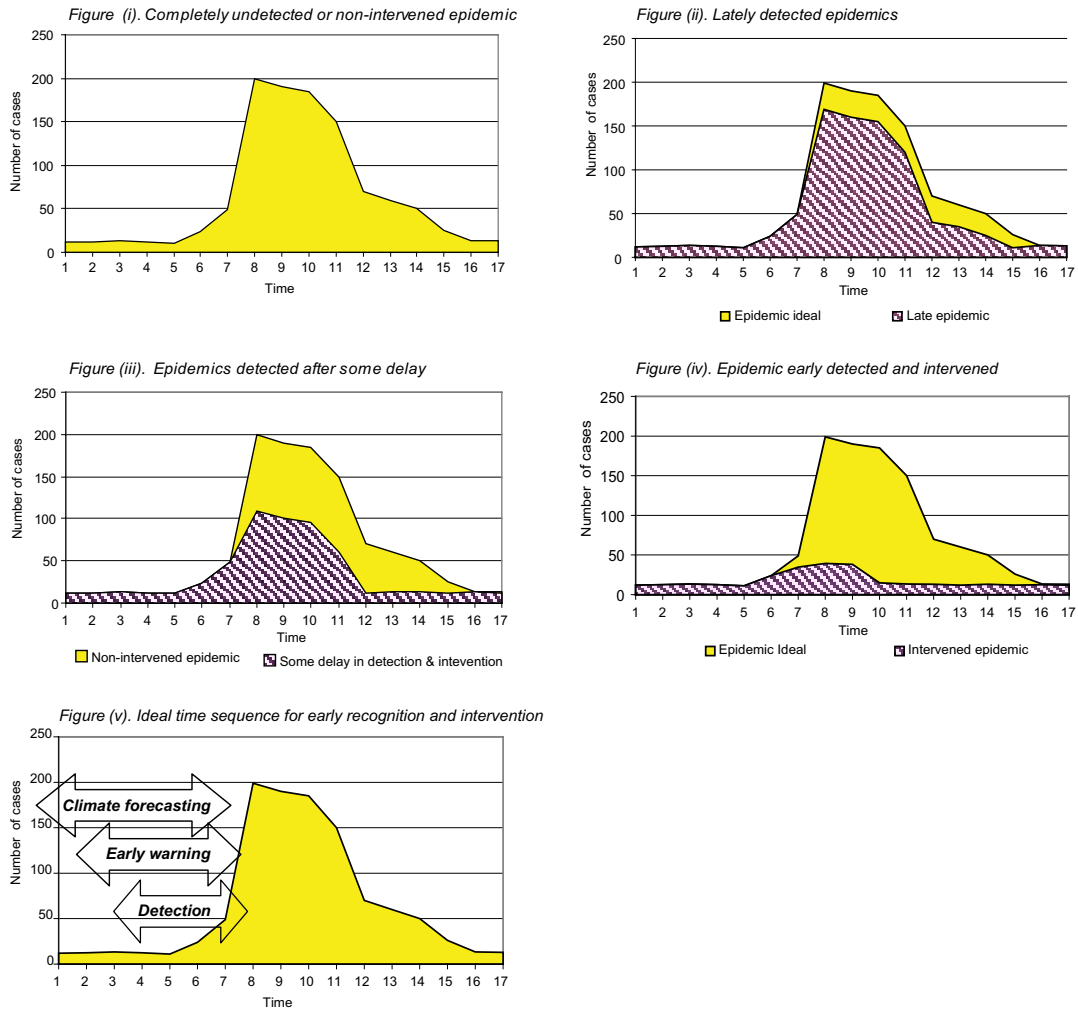
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Figure 20.1 Malaria epidemics and different scenarios of intervention timings and their outcomes

c. *Column 5 or Figure (iv) shows the existence of proper preparedness and response (better malaria control programme) as discussed in (b).*

d. *Figure (v) would be the ideal time sequence of climate forecasting, early warning and detection for complete prevention of epidemics with a cost-effective monitoring system. This would lead to either of the following:*

   ▸ *very early recognition of emergency and immediate control measures*

   ▸ *implementation of preventive measures before epidemic state occurs*

20.2 Case management and drug policy during epidemics

Exercise 20.4

a. *In the acute phase of the malaria epidemic, facilities for parasitological diagnosis are usually so overwhelmed with case load that parasite-based diagnosis prior to treatment in all fever cases is impossible. In such situations, treatment based solely on fever may be given to the majority of patients. Parasite-based diagnosis is required for severe malaria and suspected treatment failures Although RDTs offer the advantage of being rapid and simple to perform in epidemic situations, microscopy is also needed to confirm treatment failures.*

b. *Yes, during epidemics it could be possible to use medicines (for uncomplicated malaria) that are different from the medicines used in normal endemic settings in the same country. There may be a need to decide on emergency drugs which have a potential impact on malaria transmission.*

c. *Most malaria patients in epidemics and emergencies are non-immune or otherwise vulnerable to severe disease. An active search for febrile patients to ensure that as many patients as possible receive adequate treatment should be established to complement the passive treatment of cases through fixed or mobile clinics. This strategy is called Mass Fever Treatment which is the treatment of suspected malaria cases on clinical grounds without laboratory confirmation for each patient. This may be a temporary operational necessity in epidemic situations when medical staff are dealing with overwhelming malaria case-loads during a confirmed malaria epidemic. Whenever this strategy is adopted, a full treatment course should always be given. Mass Fever Treatment should not be confused with Mass Drug Administration (i.e. the administration of antimalarial medicine to every individual in a defined population including the people who are not sick and not infected with malaria parasites at the time).*

d. *Due to the acute workload, there is a need to develop more practical approaches to manage severe malaria during epidemics as compared to the "normal" routine situation. WHO recommends the use of parenteral artesunate (IV/IM) for the treatment of severe malaria. Artemether IM or quinine IV/IM is an acceptable alternative if parenteral artesunate is not available. Managing severe malaria cases with quinine IV is not easy even in "normal" contexts where referral hospitals are suitably equipped and have specialised health staff. The 7-day quinine regimes are not well tolerated and adherence is likely to be poor if treatment is not observed. Therefore, if artesunate is not available artemether IM can be recommended instead of quinine during epidemics. Artemether IM, administered once a day, is easier to implement in peripheral health clinics, have efficacy equivalent to quinine and limited side-effects.*

In pre-referral facilities where parenteral treatment is not available, WHO recommends artesunate suppositories as pre-referral treatment plus referral of the patient to a facility where complete parenteral treatment of severe malaria can be instituted. Availability, use and stock management of the antimalarial medicine to use as emergency stocks at country level should be decided by NMCP as part of the epidemic preparedness plan of action.

20.3 Vector control options for prevention and control of malaria epidemics

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Indoor residual spraying (IRS)

Exercise 20.5

Allow participants to discuss this in small working groups to estimate the time required for the development of infective vectors and transmission of sporozoites to non-immune individuals.

a. *Effectiveness of IRS for prevention of epidemics basically depends on the residual effect of the insecticides and the surfaces treated. It also depends on the accuracy of the epidemic prediction. In areas where the onset of malaria epidemic can be predicted, an IRS applied just before the onset of the epidemic and with an insecticide that has a residual efficacy extending beyond the period of the epidemic, can effectively prevent a malaria epidemic.*

b. *In a situation where an epidemic is detected rather late, for IRS to be effective (see graph 20.1 on the scenarios depicted in Figures i, ii, iii, iv), it needs to be carried out within 2 weeks of epidemic onset and coverage needs to be >100%.*

c. *Coverage is critical for the effectiveness of IRS. A sprayed house does not protect its occupants from transmission if most of the houses in the neighbourhood are not sprayed, because the vectors survive. If coverage is low people can still be bitten and infected in the unsprayed houses.*

d. *Vector control interventions such as IRS should be carried out when the vectorial capacity is low. Effectiveness of IRS also depends on the indoor resting behaviour of the vector involved.*

e. *The following important criteria need to be considered when indoor residual spraying operations are planned especially in the context of managing insecticide resistance:*

- *Use of an insecticide with adequate residual effect that covers the entire transmission period (DDT has a residual effect of at least 6 months, pyrethroids last 3–6 months, carbamates last 2–6 months, organophosphates last 2–6 months)*

- *Good susceptibility of vectors to the selected insecticide*

- *Good insecticide stability for storage, easy formulation and application*

- *Acceptable cost (DDT is the cheapest)*

- *Safety to the general population, and for spray-men, and for domestic animals and honey bees*

- *Good acceptance by the population (odour, staining of walls etc.)*

- *Good effectiveness against other household pests (bed bugs, fleas, etc.)*

- *Minimum environmental effect*

DDT is an example that initially met most of the criteria above. But because of it is persistent pollutant and increasing resistance of the vector to the insecticide, it is not suitable in all settings.

Insecticide-treated mosquito nets (ITNs) and other materials

In epidemic-prone areas, malaria control programmes are encouraged to maintain stocks of vector control products, including LLINs, so that they are rapidly deployed for maximum impact.

Exercise 20.6

a. *For ITNS/LLINs to be fully effective, the coverage must be high. High coverage is important because of the need for a mass effect on vector survival; if ITNs/LLINs are used only by a small proportion of the community where transmission is occurring, the vector population will continue to transmit malaria.*

b. *Coverage and acceptance of ITNs/LLINs in epidemic-prone areas is low because the insect nuisance is generally low in these areas.*

c. *Emergency vector control measures, such as the use of pre-impregnated shelters or space spraying operations, can be applied in emergency settings such as refugee camps.*

Space spraying

There is little evidence of any impact of this intervention on malaria. Thus, this measure is generally not recommended, but can be considered in exceptional circumstances (e.g. outdoor biting and resting mosquitoes). Such activity would need to be maintained over time to have any impact, and entomological expertise is required if this intervention is deployed.

Exercise 20.7

a. *Aerial sprays mainly target adult mosquitoes actively flying or resting outdoors.*

b. *These operations are obviously expensive and can only be considered during special occasions like emergency situations in refugee camps.*

Larval source management

Larval source management (LSM) is the targeted management of mosquito breeding sites, with the objective to reduce the number of mosquito larvae and pupae. It includes habitat modification and manipulation; larviciding and the use of biological control agents. As a supplementary malaria vector control measure, it should not be used to replace core vector control interventions, such as long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS).

Larviciding using WHO recommended products, is probably the only LSM approach that may be feasible and practical in responding to malaria epidemics in conjunction with IRS or LLINs. This is based on the assumption that larviciding is applied at the early stages of the malaria epidemic to potential breeding sites that are easy to find, treat at least weekly and are not shifting.[1,2]

Exercise 20.8

a. *Given the above limitations, larviciding can be applied in:*

- ▶ Urban centres

- ▶ Near irrigation projects

- ▶ Rural villages in arid areas with limited and well-known breeding habitats.

b. *While considering larviciding the following biological and operational factors need to be considered:*

- ▶ Knowledge of the breeding preference of local vectors

- ▶ Breeding sites are few, fixed and findable, and high coverage can be attained

- ▶ The necessary logistics and resources, including the necessary entomological skills, are available to apply the larvicide once weekly

- ▶ A high level of community participation must be assured

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[1.] WHO (2012). Interim position statement: the role of larviciding for malaria control in sub-Saharan Africa, Geneva, Switzerland. http://www.who.int/malaria/publications/atoz/larviciding_position_statement/en/index.html

[2.] WHO (2013). *Larval source management: a supplementary measure for malaria vector control.* Geneva, Switzerland. http://www.who.int/malaria/publications/atoz/9789241505604/en/index.html

Larviciding is more effective when undertaken prior to the occurrence of epidemics, or at the very early indications of increased transmission, than when employed at a later stage to mitigate ongoing epidemics. Such measure should be based on sound knowledge of the vector abundance and types of mosquito breeding habitats.

Entomological information such as density of larvae could often be misleading because larval abundance climaxes after the peak in the adult population and monitoring this parameter could be too late to have an impact in epidemic control.

20.4   Malaria in relation to epidemic diseases

Exercise 20.9

a. WHO now recommends universal diagnostic testing for all suspected malaria case. The WHO Global Malaria Programme's initiative T3 calls for all suspected malaria case, that all confirmed cases are treated with effective medication and that all cases are tracked through efficient surveillance systems.[1] However, in areas without laboratory facilities, the definition of a malaria case is empirical and often clinically based. All patients who have received an antimalarial drug treatment can be considered as presumed malaria cases. What is more important from an epidemiological point of view is the consistency of recording presumed malaria cases over time is closely monitored, especially in relation to the scale-up of diagnostic testing. Efforts should be made to provide laboratory-based diagnosis.

b and c. Prevention and control of malaria epidemics should not be handled in isolation. Disease surveillance and outbreak alert systems cover multiple epidemic-prone diseases. WHO recommends that epidemic-prone diseases such as yellow fever, meningitis, cholera, dysentery, viral haemorrhagic fevers, measles, plague, etc.[2] should be investigated, notified, verified and reported.

If an unusual increase of febrile cases occurs and suspected to be due to malaria, RDT or blood smear examination should be carried out on a sample to confirm a malaria outbreak.

Preventive interventions for malaria epidemics:

d. Monitoring relevant precipitating factors as predictors of increased risk of transmission, so that preventive measures can be established in advance, is more cost effective than intervening during or after epidemics. Cost-effectiveness is closely correlated with the level of accuracy of the predictors of increases in malaria transmission.

20.5   Measuring the impact of preventive/control measures

Exercise 20.10

In many settings, the number of malaria cases and deaths averted in a targeted population cannot be accurately measured. Estimates can be obtained through the analysis of the epidemic curve, its precipitating factors and the type, timing and coverage of control interventions. In most cases, only estimates can be made: the assumptions in making such estimates need to be made explicit. For example the following assumptions can be offered:

[1.]   WHO (2012). *T3 Scaling up diagnostic testing, treatment and surveillance.* Geneva, Switzerland.

[2.]   AFRO technical guideline for integrated disease surveillance and response.

▶ Estimated prevalence of malaria during epidemics: 0.5 malaria episode per person is expected during epidemic periods

▶ Proportion or prevalence of severe cases depending on the localities and species of parasite involved: < 5% of malaria episodes are severe malaria

▶ Case Fatality Rate: CFR of severe malaria (according to WHO criteria) maybe as high as ~10% even in reasonably well-equipped referral hospitals, and >20% during epidemics depending on availability of staff and drugs. Treatment of severe malaria with parenteral artesunate decreases the case fatality rate of severe malaria although these treatments have only recently became widely available.

▶ Socioeconomic impact

20.6 Other managerial issues for preparedness and response during epidemics

Exercise 20.11

a. *In acute emergencies, if there is limited knowledge of the malaria situation and background immunity of the people concerned (including in the setting up of refugee camps), the following interventions can be recommended:*

  ▶ Case management of uncomplicated malaria with ACT. Since capacity is weak, use RDT to confirm malaria diagnosis and provide antimalarial drugs only to confirmed malaria cases.

  ▶ Case management of severe malaria preferably with artesunate IV or IM. If artesunate is not available, artemether or quinine is acceptable alternative. (See module on *Malaria Case Management* for details).

  ▶ Consider insecticide treated plastic sheets or/and impregnated materials like blankets to be used in refugee camps. Evidence for these interventions is lacking, and there is not currently a WHO recommendation for their use. plastic sheets or/and other impregnated materials like blankets to be used in refugee camps.

  ▶ IRS operations if implemented early and if local staff are familiar with this intervention.

  ▶ Re-treatment of ITNs if there is a documented high coverage rate and people are already familiar with ITNs and use them. Re-treatment is not needed for the LLINs , which are now the standard in most places.

b. *Assign small working groups to discuss the different stages of malaria epidemics illustrated in Figure 20.1 in the Guide for Participants and to fill in the check list (Table 20.1) as right (✓) or wrong (X). Encourage participants to fill in with full understanding of the logic and reason behind the answers.*

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Table 20.1   Operational responses to different stages of malaria epidemics

No.	Interventions or operational measures	Starting epidemic	Accelerated epidemic	Epidemic peak
1	Ensure all clinics and health facilities are operational and have sufficient drugs, equipment and trained staff	✓	✓	✓
2	Establish treatment centres (temporary clinics or mobile clinics) where access is difficult or health facility coverage is low	✓	✓	✓
3	Ensure that the correct diagnosis and treatment is provided at all health facilities and at community level	✓	✓	✓
4	Promote pro-active clinical case detection and management/referral	✓	✓	✓
5	In areas where facility for IV is not available, reinforce the referral system and consider the introduction of artesunate suppositories, artesunate IM, artemether IM or quinine IM, according to availability, as a pre-referral treatment.	✓	✓	✓
6	Intensify/maintain effective preventive measures for pregnant women	✓	✓	✓
7	Reinforce health information systems for reporting and epidemic monitoring, preferably on a weekly basis	✓	✓	✓
8	Conduct specific epidemic health education campaigns	✓	✓	✓
9	Organize regular press releases/conferences/articles for public information	✓	✓	✓
10	IRS in area previously sprayed	✓ Monitor coverage and susceptibility using bio-assays	✓ Same as for starting epidemics: change chemicals for IRS if bio-assay shows susceptibility is low	✓ Less public health impact at this stage
11	IRS in areas previously not sprayed	✓ If Malaria epidemiology, type of housing, rapid deployment and logistics show that effective IRS in target areas is possible	✓ Same as for starting epidemics	X

No.	Interventions or operational measures	Starting epidemic	Accelerated epidemic	Epidemic peak
12	ULV space spraying only	✓ If properly-timed, in highly populated areas such as refugee/IDP camps especially if shelters are small, and if IRS is not an option	✓ Same as for starting epidemics	X
13	Distribution of ITNs/LLINs and other materials	✓ If ITNs/LLINs use and coverage in the area is high	X	X

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LEARNING UNIT **21**

Post-epidemic assessment and preparedness plan of action

Learning Objectives:
by the end, participants should be able to...

■ Undertake a quick assessment of the epidemic detection and control response

■ Develop a preparedness plan of action

Answers

21.1   The post-epidemic assessment exercise

Exercise 21.1

a. Assign small working groups to discuss a logical flow and steps of an epidemic cycle and request them to produce a diagram and present it for class discussion. The diagram should resemble Figure 21.1. Groups may prepare different patterns but they should have a logical flow.
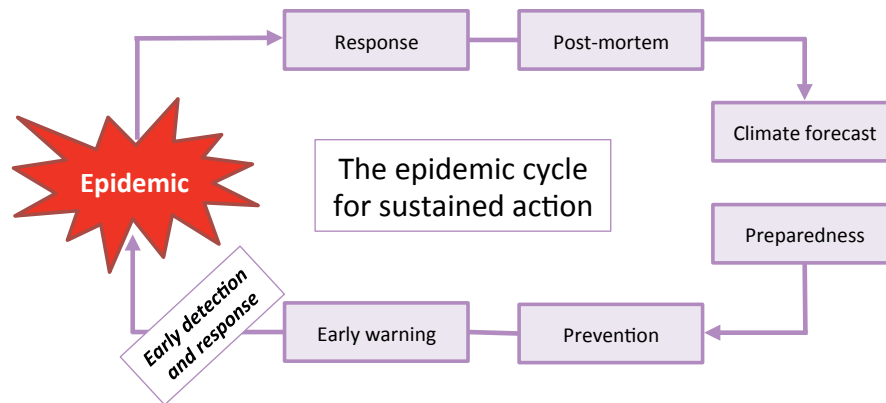

Figure 21.1 The steps in the epidemic cycle

Pre-season preparedness and early identification provide the malaria manager with an increasing number of tools to deal with an epidemic. Maintain surveillance, keep database up-to-date, think ahead, be prepared.

b. During the post-epidemic assessment exercise, the factors that could be assessed include:

▶ Whether early warning and detection systems were useful

▶ The cost-effectiveness of the response components including operational and financial aspects

▶ Role and usefulness of partnerships before and during epidemic

Discuss with the participants coming from countries with areas prone to malaria epidemics if they are aware of post-epidemic assessment exercises undertaken in their country. Discuss why it is beneficial, and why, often, it is not undertaken.

21.2   Strategic elements of a preparedness plan of action

Exercise 21.2

Assign small working groups to discuss a logical flow and steps for strategic elements that need to be included in a preparedness plan of action for the prevention and control of malaria epidemics. Participants should produce a simple diagram that summarizes these steps and present it for class discussion. The tutor should lead the discussion and provide hints on the indicators for epidemics, investigation, reporting and response. The diagram should resemble Figure 21.2. Groups may come with different patterns but these should have a logical flow.
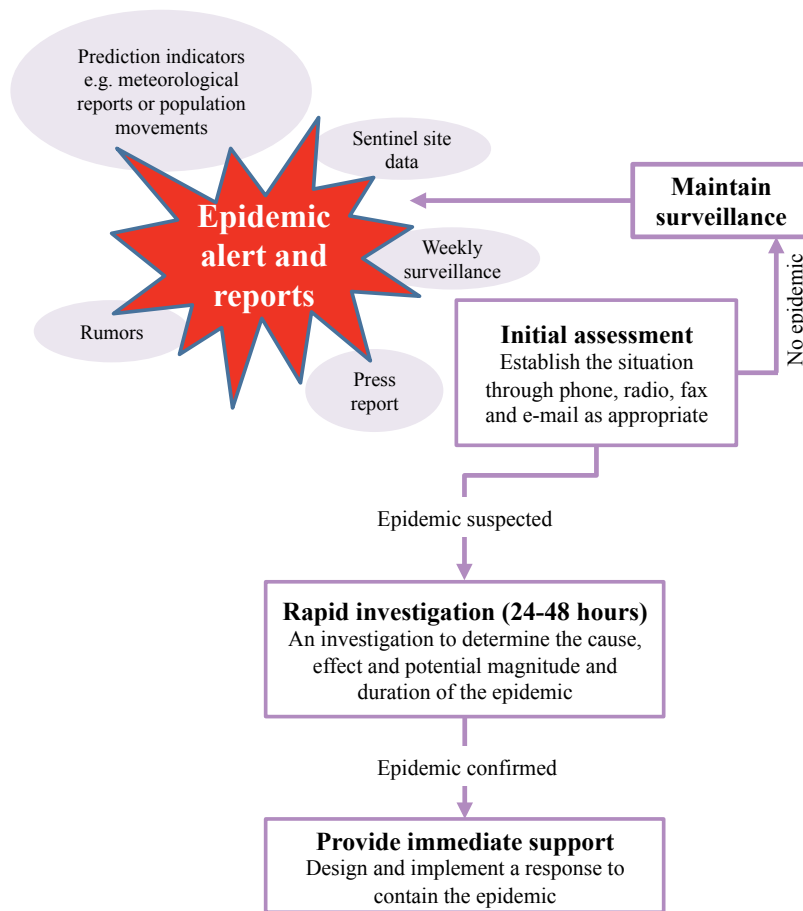
Figure 21.2 Strategic elements of a preparedness plan of action

Exercise 21.3

a. *No. The preparedness plan of action should not be planned in isolation and has to be co-ordinated and integrated with other diseases with epidemic potential. It should be developed at national level targeting populations living in epidemic-prone areas. Epidemic-prone districts when developing their annual plan of action, should include and budget the interventions which are directly linked to prevent and control epidemic-prone diseases including malaria. The national Preparedness Plan of Action (PPOA) should include the set up and maintain sub-regional emergency stocks of agreed antimalarial drugs, insecticides and other emergency facilities*

b. *Since epidemics can affect several countries at the same time, it is vital to ensure/ facilitate exchange of information especially between countries and with neighbouring epidemic-prone districts. Exchange of information with neighbouring countries, e.g. through sub-regional meetings organized by WHO or other partners, should provide an opportunity to coordinate strategies and interventions which can speed up the national and inter-country response.*

c. *There is no single right or wrong answer for this question as the reasons may vary from place to place depending on local situations, socioeconomic status and culture. Participants may give varied responses which could have field relevance; the tutor may encourage individual responses and then move towards consensus in class, ranking the reasons according to their views and experience. Some examples:*

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▸ No system in place for rapid epidemic detection: Monitoring malaria on a weekly basis is not generally practised in most epidemic-prone areas; most record monthly data which are usually late and/or not useful.

▸ Lack of capacity and resources at the district or peripheral levels to take action for epidemic response: Inadequate or poor laboratory facilities and capacity to verify suspected malaria epidemics. Even in situations where malaria epidemics are detected relatively early, these health facility levels usually do not have the necessary preparedness, guidance and capacity, and have to wait for interventions from higher levels.

▸ Poor communication and poor reporting mechanisms among local authorities and health office at district and peripheral levels.

▸ Poor communication and coordination in connection with epidemics of other diseases.