INDICATORS TO MEASURE THE IMPACT OF MALARIA CONTROL

Catherine Watt and Chris Dye
Communicable Disease Prevention, Control and Eradication, WHO, Geneva

All correspondence to: Dr C. Dye (email dyec@who.ch)

Geneva, July 2000
Summary

Aim

To select indicators that can be used to monitor progress towards RBM’s goal of reducing malaria mortality rates by at least 50% by 2010.

Methods

The review is in three parts: choice and definition of indicators, methods of measurement, methods of attributing changes in indicators to interventions. From October 1999 – January 2000 we reviewed published and unpublished reports, consulted malariologists worldwide, and carried out further analyses of selected data.

Conclusions and recommendations (see pp 25-27, and Appendix 1)

The “core indicators” in areas of high transmission (>10% approx. prevalence of infection, 2-9 year-olds) are all-cause and malaria-attributed Under-Five Mortality. The recommended method of measurement is through demographic surveillance systems (DSS, longitudinal) or national demographic and health surveys (DHS, cross-sectional). DSS (the INDEPTH network) and DHS are now established at numerous sites in developing countries They can measure changes in all-cause mortality and, potentially, malaria-specific mortality, though further field tests are needed to see how accurately they can do so. Some health facilities may be able to record changes in the incidence rate of severe malaria.

In low-transmission areas (<10% prevalence in 2-9 year-olds), the core indicator is the incidence rate of symptomatic cases with parasitaemia, expressed as the Annual Parasite Incidence (API/1000), by age, sex and parasite species. The recommended method of measurement is by routine surveillance, with checks for quality and coverage of reporting.

Because the impact of RBM programmes will be monitored using data collected outside formal experiments, it will not always be easy to attribute observed reductions in mortality to any given intervention. We suggest, as a partial remedy, carrying out fuller quantitative assessments of all available data, using meta-analysis, multivariate statistical techniques and mathematical modelling.

Next steps

In the context of this review, three are self-evident: seek wider agreement on the choice of core indicators; identify, and analyse in detail, historical data from (especially) national control programmes; explore the full potential of DSS and DHS through the collection and analysis of further data.

Going beyond the present study, it will be crucial for RBM to assess the epidemiological evidence that malaria mortality can, in principle, be cut by half by the year 2010.
Aims

The principal target of Roll Back Malaria is to “reduce malaria mortality rates by at least 50% by the year 2010” (World Health Organization, 1998a). The main aim of the present exercise is to select impact indicators that can be used to assess whether this target has been reached. The question of whether the target can be reached is quite different, and must be the subject of a separate study. The analysis has three steps, of which the last is most demanding:

- choose and define indicators to measure malaria incidence and death rates,
- define methods to measure and calculate these indicators, and changes in space and time,
- show, with examples, whether and how short and long-term changes can be attributed to given interventions, especially non-experimental interventions.

Methods used to compile this report

The analysis was carried out between 1 October 1999 and 14 January 2000 through:

- review of published and unpublished reports (listed in reference section)
- expert consultation (those contacted are listed in Appendix 2)
- further analysis of selected historical data (methods given where appropriate)

Our approach was to search for data showing which indicators have been used, and how successfully they have been used, to monitor the impact of malaria control.

Results

We begin with an overview of case definitions, the indicators derived from these, and field sampling methods. We then illustrate, by means of examples, how the indicators have been used to evaluate changes in malaria burden, and to attribute changes to malaria control. Finally, we make some recommendations about appropriate indicators for measuring the impact of malaria control in different epidemiological settings.

Case definitions

The standard definitions of confirmed malaria cases and deaths are as follows (World Health Organization, 1998b):

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malaria case (uncomplicated)</td>
<td>Person with symptoms, plus parasitological confirmation (microscopy, immunodiagnostic test)</td>
</tr>
<tr>
<td>Malaria case (severe)</td>
<td>Confirmed case requiring hospitalisation</td>
</tr>
<tr>
<td>Malaria death</td>
<td>Death of a confirmed case</td>
</tr>
</tbody>
</table>

Taken at face value, these definitions are too restrictive. For example, where *P. falciparum* and *P. vivax* (or one of the other two species) co-exist, they should be distinguished.
In places where the incidence of infection is high, frequent challenge leads to protective immunity, which lowers the risk of illness following infection. Diagnosis of illness due to *Plasmodium* infection is therefore more demanding in areas of high transmission (>10% approx. prevalence of parasitaemia in children 2-9 years, i.e. mainly in parts of Africa south of the Sahara), and these are usually the areas with less sophisticated diagnostic facilities. In these areas a malaria case can be defined with greater specificity as symptoms (acute febrile illness) together with parasitaemia above a threshold, for example 100 parasites per 200 white blood cells (Lyimo *et al.*, 1991; Smith *et al.*, 1994). However, it is not usually possible to measure the intensity of parasitism in addition to identifying parasites to species as part of routine surveillance.

**A brief survey of indicators**

Indicators to measure the impact of control are derived from the above case definitions. A vast array of indicators has already been defined (e.g. World Health Organization, 1994); with limited resources, the problem is to select “core indicators” that give indispensable information and can be used widely. The following are intended to measure incidence (new cases or deaths/unit time) rather than prevalence (cases existing at one time).

**Malaria cases.** We concentrate here on parasitologically confirmed, symptomatic cases on the grounds that, wherever malaria is an important disease, microscopic diagnosis (to parasite species) should be considered a minimum requirement. The fundamental measure is the proportion of blood smears from symptomatic persons positive for malaria parasites, the slide positivity rate (SPR). Note that positive blood smears taken from asymptomatic persons (for example, as part of active case detection (ACD) activities), should be presented separately, as these represent malaria infection, but not malaria cases. Where most persons with symptoms plus parasitaemia in a given population, or a representative sample of them, provide blood smears through passive or active case detection, SPR can be used to calculate the widely-used indicator, Annual Parasite Incidence (API):

\[
\text{Annual Parasite Incidence} = \frac{\text{No. parasitologically confirmed malaria cases/year}}{\text{Population at risk}} \times 1000
\]

which may be calculated by age and sex. The total number of cases is the product of API and population size, and the measured API may be representative of a larger population than has been sampled. Where *P. falciparum* exists alongside other species, it is important to record separately the Annual Falciparum Incidence (AFI). With good surveillance in low-transmission areas, API and AFI may come close to measuring the true incidence of disease. When coverage is consistent, if not exhaustive, API and AFI may measure a constant proportion of cases, in which case the data can accurately describe trends. Calculations of relative change (e.g. % cases averted) are always more reliable than calculations of absolute change (e.g. number of cases averted).
We already noted that, when the incidence of infection is high, greater specificity is achieved by use of a case definition based on symptoms, plus parasite density above a threshold. In such situations, API is less valuable as an indicator of malarial illness, and a more useful indicator, in principle, may be defined as (AMI):

\[
\text{Annual Malaria Incidence} = \frac{\text{No. febrile cases with parasites > threshold}}{\text{Population at risk}} \times 1000
\]

However, the highest incidences of infection tend to be in areas (especially of sub-Saharan Africa) where health information systems (HIS) are weak, and many acute febrile cases are never seen by health services. The failure of routine surveillance in high-incidence areas seriously limits the use of AMI as an indicator of morbidity.

Hospital and clinic records are the only source of information is some areas, and the above indicators could be adapted for severe cases defined in various ways, including cases which have been hospitalized. It will be difficult (or impossible) to make geographical comparisons of the incidence of severe malaria based on hospital records because the chance of a patient being hospitalized will vary greatly from one setting to another. However, if reporting is consistent, trends in hospitalized cases may reflect real changes in the incidence of severe disease.

**Malaria deaths.** By analogy with API and AMI, the Malaria Death Rate (MDR) is:

\[
\text{Malaria Death Rate} = \frac{\text{No. parasitologically confirmed malaria deaths/year}}{\text{Population at risk}} \times 1000
\]

which can also be calculated by age, sex and parasite species. The Case Fatality Rate is the dimensionless MDR/AMI. If malaria deaths cannot be separated from others, then we use indicators of all-cause mortality. The Crude Death Rate (CDR) per year:

\[
\text{Crude Death Rate} = \frac{\text{Total deaths/year}}{\text{Population at risk}} \times 1000
\]

CDR can be calculated for whole populations and by age and sex.

By convention, indicators of mortality in children are not rates per year, as above, but the proportions of live births (expressed per 1000) surviving to a given age (they are, nonetheless, often called “mortality rates”). Under-Five Mortality (σ5) is the probability of dying before the age of 5:

\[
\text{Under - Five Mortality} = \frac{\text{number of deaths of children under 5/year}}{\text{number of live births/year}} \times 1000
\]

Neonatal Mortality refers to the first 28 days of life, Postnatal Mortality to deaths between 28 days and one year of age, Infant Mortality to children up to one year of age and Child Mortality to children of age 1 up to 5 years.
In areas of high transmission, it may be neither possible nor desirable to distinguish malaria deaths from deaths from other causes. There are three main reasons for this. First, it is difficult to attribute deaths to malaria, partly because many patients are never seen by medical services. Often one can do no better than to record death with febrile illness, presumed to be malaria. Even when cases are seen before death, malaria is commonly diagnosed by exclusion. Second, malaria interacts strongly with other causes of illness and death. Where the crude death rate (CDR) is low, interventions against malaria can have indirect as well as direct benefits, reducing deaths partly attributable to other conditions (Cohen, 1988; Molineaux, 1985, 1997). Conversely, where CDR is high, malaria is sometimes a “competing risk”, in which case fewer malaria deaths are offset by more deaths from other causes. Finally, a number of RBM interventions will not be specific to malaria, e.g. management of anaemia in pregnancy (de Savigny, 1999).

**Evaluating the quality of routine surveillance systems.** If we intend to use routinely reported case numbers to monitor the impact of malaria control it is important that the data are of good, or at least known, quality. The proportion of units reporting gives a crude indication of the quality of a surveillance system, measured as:

\[
\frac{\text{Number of districts reporting in a year}}{\text{Total number of districts}} \times 100
\]

But we would like to know how well these reports reflect the actual number of cases. This depends on how reliably health facilities (including village health workers or equivalent where appropriate) diagnose and report malaria cases, and also of what proportion of malaria cases are seen by health facilities. The latter will depend on the accessibility of health facilities (in terms of distance to travel and cost), and on the treatment seeking behaviour of the population.

**Sampling methods for measuring mortality**

Epidemiological surveys, whatever they are measuring, are essentially cross-sectional or longitudinal. Cross-sectional studies can, in principle, measure prevalence (directly) at one point in time, or incidence (indirectly) by collecting information (retrospectively) about events that have happened over a period of time in the past. Estimates of incidence from retrospective data often use age as a proxy for time. Here, we are most interested in cross-sectional methods that have been used to estimate malaria- and all-cause mortality rates.

Longitudinal studies may collect data passively (many surveillance systems) or actively (population surveys). They may follow the same subjects through time (a cohort), or take samples of different subjects repeatedly from a population (repeated cross-sectional surveys). In this study, we are most interested in passive and active malaria case finding, and in cohort studies that measure malaria- and all-cause mortality rates.

Case-control studies can identify risk factors for a condition by comparing exposure rates among passively-identified “cases” (here malaria cases or deaths) and a set of controls carefully chosen to avoid bias (Hayes, 1992; Lengeler & Snow, 1996; Snow
et al., 1998; Bennett et al., 1999). Subjects with a relatively rare condition can be found (often passively) without taking large samples from a population. The outcome is an approximate calculation of the relative risk (obtained via the odds ratio) associated with exposure to selected factors, some of which might be manipulated in a control programme. Despite the potential of this method, it has not yet been widely used to measure the impact of malaria control (but see Carne et al., 1994; Koram et al., 1995; D’Alessandro et al., 1997; Luckner et al., 1998).

Malaria mortality. The best estimates of malaria death rates are obtained where surveillance finds and confirms most cases, and where all severe cases are hospitalized. The worst estimates come from high-transmission areas with poor health information systems, where many deaths occur at home, often without any contact with medical services. Most vital registration systems outside industrialised countries are poor. In principle, cause of death can be assigned retrospectively by verbal autopsy (VA), but the sensitivity is low for malaria in Africa (about 50% on average; Snow et al., 1992; Anker et al., 1999). The effects of the sensitivity and specificity of VA on estimates of cause-specific mortality depend on the true proportion of deaths due to the cause (Anker, 1997). Misclassification under-estimates the number of malaria deaths, but also weakens the power of studies designed to detect spatial or temporal differences in malaria death rates (Maude & Ross, 1997).

All-cause mortality. Where malaria is a prominent cause of death, effective malaria control could affect overall mortality rates in children. Measuring and monitoring all-cause mortality rather than malaria-specific mortality avoids the difficulty of attributing deaths to malaria (see above). Furthermore, as discussed earlier, malaria control may reduce indirect malaria deaths, where malaria contributes to but is not the sole cause of death, or malaria deaths prevented may be replaced by non-malaria deaths. Thus the effect of malaria control on all-cause mortality may be greater or less than the effect on direct malaria mortality. Accurate vital registration is rare in countries where malaria is endemic, so mortality must be estimated either retrospectively from surveys of birth histories, or prospectively in populations under demographic surveillance. An overview is given in Table 1.

Retrospective methods of mortality estimation. The classic, indirect (Brass) method of estimating childhood mortality obtains numbers of children ever born and of children surviving from women of reproductive age. The proportions of dead children are tabulated by age of mother, and standard life tables are used to produce mortality estimates for the last 5 to 20 years. Reports of older women are used to estimate mortality further back in time. This method is of limited use for estimates in the recent past, as younger mothers are atypical, having begun their child bearing early, and having a high proportion of first births. It is also difficult to apply in populations of low literacy, where many women do not know their age.

More recent estimates of mortality can be obtained by the collection of detailed (generally truncated) birth histories. The dates of birth and death of all children born in (for example) the last five years are collected, in what is, in effect, retrospective vital registration. Life tables can then be constructed and mortality rates calculated directly. This method requires skilled interviewers in order to obtain all the information required, and is difficult to apply where knowledge of dates is poor. It is
difficult to collect data of sufficiently high quality to make estimations of mortality using this method (David et al., 1991; Chen et al., 1993).

A third approach is the Preceding Birth Technique (PBT) (Hill & Macrae, 1985; Hill & David, 1988). Women are asked, around the time of the birth of a child (at ante natal clinic, delivery, or first immunisation of child), about the survival of the preceding birth. In most populations, where the birth interval is around 30 months, the proportion of preceding births surviving is a good approximation of survival to age 2. This method can be extended to the second-to-last child, to give an estimate of survival to age 5. This information is relatively simple to collect, and does not rely on the recall of distant events. Using immunisation clinics generally gives good coverage, but it is sometimes difficult for those asking and responding to questions to understand their relevance. Bairagi et al. (1997) compared estimates of mortality using the PBT applied at ante natal or immunization clinics with estimates calculated using data from a demographic surveillance system of the same population. In this setting (with rather long birth intervals) PBT estimated survival to age 3 rather than 2, and reflected trends in mortality over time and differences between areas.

All these methods could be used in national demographic and health surveys (DHS), which are carried out biannually in 29 African countries (de Savigny, 1999).

Prospective methods (demographic surveillance). There are now over 40 sites throughout the world (28 in Africa) employing demographic surveillance systems (DSS), where births, deaths and migrations in a population are monitored. Each of these sites provides detailed demographic information for a defined population, by following an initial census with continuous collection of vital events. There is increasing interest in using demographic surveillance of sentinel sites to monitor changes in all-cause and, if possible, malaria mortality (the latter being more difficult), together with the impact of health programs (Binka et al., 1996; Binka et al., 1999; the INDEPTH network at http://www.indepth-network.org/).

A note on causation

The evaluation dilemma for RBM is that impact cannot be evaluated by formal experiments (e.g. randomized controlled trials). And yet, weaker designs necessarily yield weaker inferences about the cause of observed changes in incidence and mortality. Methods range from simple, cheap and approximate (e.g. passive surveillance) to complex, expensive and accurate (e.g. randomized controlled trials). The methodological task is to identify the compromise.

Outside controlled experiments, the most persuasive demonstrations of impact will be when a long-term, steady trend in the incidence or death rate changes abruptly (downwards) following an intervention. However, clear and dramatic changes in trend are likely to be rare, and confounding explanations common. For example, mortality
Table 1: Comparison of methods for estimating all-cause mortality

<table>
<thead>
<tr>
<th>Method</th>
<th>Source of information</th>
<th>Information collected</th>
<th>Assumptions made</th>
<th>Strengths of technique</th>
<th>Limitations</th>
<th>References (technique)</th>
<th>References (application)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brass indirect</td>
<td>Household survey</td>
<td>Number of live births, number still alive, age of mother</td>
<td>Standard life tables used to calculate mortality rates</td>
<td>Can get estimates of mortality for 5 to 20 years preceding survey.</td>
<td>Estimates for years immediately preceding survey are poor</td>
<td>United Nations, 1983</td>
<td>David et al., 1991</td>
</tr>
<tr>
<td>Detailed birth histories – direct lifetable calculations</td>
<td>Household survey</td>
<td>Dates of births and deaths of all children, or of children born in last 5 years</td>
<td></td>
<td>Can get good estimates of recent mortality, in theory.</td>
<td>Relies on good recall of dates and events, and skilled interviewers.</td>
<td>Hill &amp; Macrae, 1985</td>
<td>Hill &amp; David, 1988</td>
</tr>
<tr>
<td>Preceding Birth Technique</td>
<td>Ante natal clinics, delivery services, immunisation clinics</td>
<td>Has woman had previous live birth? Is previous child still alive? (can be extended to second-to-last child). Dates may of births also be collected.</td>
<td>If no dates collected, birth interval of about 30 months assumed. Proportion of previous births surviving is approximately the likelihood of surviving to age 2, the proportion of second-to-last births surviving is approximately the likelihood of surviving to age 5.</td>
<td>Data is simple and easy to gather.</td>
<td>Need to ensure good coverage, and to minimise bias in selection. Repeated or continuous data collection needed to study changes in mortality over time.</td>
<td>Hill &amp; Aguirre, 1990</td>
<td>David et al., 1991</td>
</tr>
<tr>
<td>Demographic Surveillance (prospective monitoring)</td>
<td>Census followed by regular monitoring</td>
<td>Dates of birth and death, in- and out-migration (in some cases pregnancies monitored too)</td>
<td>Very detailed information, recall problems avoided</td>
<td></td>
<td>Requires intensive, sustained data collection. Changes with time can only be observed once the surveillance system has been operating for some time.</td>
<td>Binka et al., 1999</td>
<td>Pickering et al., 1989</td>
</tr>
</tbody>
</table>


rates are already in decline in some African countries for various reasons, and have been for several decades (Ewbank & Gribble, 1993; Hill et al., 1998). Also, most malarious countries have had control programmes for many years, to which small adjustments are made from year to year (see below). For these reasons, attributing impact to a given intervention will often require more subtle, multivariate statistical analysis or mathematical modelling, making use of all available data (Kirkwood et al., 1997). In the end, the evidence for attribution may not be persuasive at all.

**Impact of malaria control by country**

This section summarizes our rapid analysis of indicators that have been used to evaluate the impact of malaria control. Table 2 contains background data on malaria epidemiology (WHO’s seven categories, WHO, 1993a), the type of surveillance system, reported cases and deaths (especially due to *P. falciparum*) and control methods. For a selection of the countries listed in Table 2, we (i) review indicators and methods of data collection that have been used to demonstrate a change in mortality (mainly) or morbidity following various interventions, and (ii) examine the strength of inferences about causation. One striking finding of this survey is that there are few readily-available data with which to carry out such analyses.

Our review suggests that data can be classified into five groups, according to the strength of inference about the impact of malaria control. In what follows we have associated certain countries with each of the five categories; this refers to specific sets of data for each country, and is not intended to be a general appraisal for that country. We suspect that many more data are available for some countries and, with further analysis, these data could yield stronger conclusions.

**Type I - No observed change in morbidity or mortality (Kenya)**

**Kenya**

Failing to observe any change could mean either that an important change occurred but it could not be measured (a biometrical problem), or that there really was no important change following an intervention (an epidemiological result). An investigation by Spencer et al. (1987) on community-based treatment for malaria in Saradidi, Kenya, may have suffered from both problems. They investigated whether the death rate from all causes could be reduced by providing chloroquine via village health helpers (VHH). Deaths of people of all ages were counted before and during the intervention by longitudinal registration, and the authors concluded that community-based malaria control had no impact on overall death rates.

The design and outcome of this study highlight four recurrent themes of investigations of malaria impact. First, it is hard to draw inferences from studies that fall short of being full experiments. In this instance, death rates from two intervention areas (A and B) were compared with just a single control area (C). No baseline data were available for the control area. Second, malaria may compete with other diseases, like measles, for the lives of children in areas where the crude death rate is high (McGregor, 1964; Molineaux, 1985; Cohen, 1988). Measles caused many deaths in
<table>
<thead>
<tr>
<th>Region</th>
<th>Country</th>
<th>Year</th>
<th>Population (0000)</th>
<th>Yearly deaths (1,000)</th>
<th>Mortality rate (%)</th>
<th>Cases (100,000)</th>
<th>Decline of cases (%)</th>
<th>Decline of deaths (%)</th>
<th>Decline of mortality (%)</th>
<th>Decline of morbidity (%)</th>
<th>Decline of CDR (%)</th>
<th>Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFR</td>
<td>Ethiopia (Tigray)</td>
<td>1990</td>
<td>3.5</td>
<td>2.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3-5</td>
</tr>
<tr>
<td></td>
<td>Eritrea</td>
<td>1997</td>
<td>1.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Eritrea</td>
<td>1997</td>
<td>1.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1-2</td>
</tr>
<tr>
<td></td>
<td>Kenya</td>
<td>1997</td>
<td>27.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.12</td>
</tr>
<tr>
<td></td>
<td>Malawi</td>
<td>1997</td>
<td>9.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.12</td>
</tr>
<tr>
<td></td>
<td>Tanzania</td>
<td>1997</td>
<td>32.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.12</td>
</tr>
<tr>
<td></td>
<td>Brazil</td>
<td>1997</td>
<td>105.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>El Salvador</td>
<td>1996</td>
<td>8.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>Peru</td>
<td>1996</td>
<td>24.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td>Oman</td>
<td>1996</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.717</td>
</tr>
<tr>
<td></td>
<td>Amman</td>
<td>1996</td>
<td>2.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.1011</td>
</tr>
<tr>
<td></td>
<td>Azadshen</td>
<td>1996</td>
<td>7.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.9</td>
</tr>
<tr>
<td></td>
<td>Tabuk</td>
<td>1996</td>
<td>6.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>Turkey</td>
<td>1996</td>
<td>62.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.95</td>
</tr>
<tr>
<td></td>
<td>India (Maharashtra)</td>
<td>1996</td>
<td>87.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nepal</td>
<td>1997</td>
<td>21.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sri Lanka</td>
<td>1997</td>
<td>18.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Thailand (E)</td>
<td>1997</td>
<td>58.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Cambodia (K)</td>
<td>1997</td>
<td>10.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.2</td>
</tr>
<tr>
<td></td>
<td>China, HK, BAR (B, K, O)</td>
<td>1997</td>
<td>1244.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Laos (D)</td>
<td>1997</td>
<td>4.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>Malaysia</td>
<td>1997</td>
<td>21.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Papua New Guinea (11)</td>
<td>1997</td>
<td>4.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Philippines (12)</td>
<td>1997</td>
<td>71.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>Solomon Islands</td>
<td>1997</td>
<td>6.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.8</td>
</tr>
<tr>
<td></td>
<td>Viet Nam (13)</td>
<td>1996</td>
<td>76.7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.5</td>
</tr>
</tbody>
</table>

Notes on impact of control:
- Reduced CDR in children <5 years for 1 yr following interventions.
- Hospital admissions for severe malaria fell after change in first-line drug policy in 1993.
- Estimated reduction in cases and deaths, are 100% (0-0%) for 1996 after 7 years of control, 9
  Ammoni, south, unknown case detection rate, result loss cases for deaths, targets would be
  state.
- Cases have fallen dramatically since the early 80s. Heavy migration and substitution of 15
  forest areas, together with disruption of health services by rainy season associated with 15
  floods have blunted.
- Indigenous cases may have been controlled, but imported cases are still rising.
- Sharp increase in cases 1993, falling in 1996.
- Reported cases have been declining since 1983 (3 million cases).
- Cases declining since 1994, no discernible trend in cases.
- Only year of post-improvement data.
Table Notes, Table 2
1. Listed in order of importance:
   S = Sub-Saharan, PNG;
P = plains, valleys, ex. Africa;
H = highland, desert fringe;
A = agricultural;
U = urban, peri-urban;
F = forests, forest fringes;
W = war zones;
L = lagoons and mangrove swamps
2. H = HIS, S = sentinel sites, INDEPTH, I = full member, A = associate member, P = potential member, E = existence known
3. Italics indicates not lab confirmed, bold indicates don't know if confirmed
4. D - early diagnosis and treatment
   I - improved management of severe and complicated cases
   M - insecticide treated materials
   E - environmental management (lavricide, fish, filling in ditches etc)
   S - indoor residual spraying
   C - chemoprophylaxis of special groups
5. Italics indicates assessment of trend is based on cases reports (of unknown reliability) alone
6. Strength of inference about impact of control:
   I no observed change in morbidity or mortality
   II observed change in morbidity or mortality, not clearly attributable to intervention
   III observed change in morbidity or mortality, probably attributable to intervention, magnitude unquantifiable
   IV observed change in morbidity or mortality, probably attributable to intervention, magnitude quantifiable
   V observed change in morbidity or mortality, almost certainly attributable to intervention, magnitude quantifiable
7. Uncertain (?) or clear (Y) impact of control, but magnitude cannot be evaluated
8. Mekong initiative
9. "partial information only",
10. Excludes 7,829 unconfirmed cases.
11. 1,283,127 unconfirmed cases
12. 315,174 unconfirmed cases
13. Total reported cases: 445,200
14. Recommended indicators
   A: Crude death rate children <5 yr (surveys/sentinel sites)
   B: Cases and deaths (PD) by species (routine surveillance)
   C: Cases by species (routine surveillance)

Sources
1. World Health Organization, 1999a
2. Sauerbrey, in prep.
3. Pan American Health Organization, 1999
4. Department of Malaria Control, Tigray, 1999
5. Trigg, 1993
7. Ministry of Health, Oman, 1995
9. Sabatinelli, 1999
10. Romu, 1999
13. Regional Malaria Control Programme for Cambodia, Laos and Vietnam, 1999
14. Khalifa, 1999
15. Ortega, 1999; Hugo & Ortega, 1999
16. World Health Organization, 1993b
areas A and B in the year before the malaria intervention. The non-measles death rate, including the malaria death rate, rose during the intervention year. Did this increase happen despite the effective provision of chloroquine by the VHH? Third, exhaustive, longitudinal registration can measure the death rate very accurately, but we usually have to wait years for the results. The benefits of accuracy need to be weighed against the advantages of quicker, cross-sectional surveys to gather retrospective data. Fourth, the reason why there was no impact on the prime indicator – here the age-specific death rate – needs to be investigated with the help of supporting operational indicators, in this case to see whether the VHH really were supplying chloroquine to suspected malaria patients.

Type II - Observed change in morbidity or mortality, not clearly attributable to intervention (Malawi, India, Tanzania)

Malawi

Health service records suggest that malaria is a leading cause of mortality and morbidity in Malawi. In 1990, 41% of outpatients were diagnosed with malaria, and malaria caused 19% of paediatric hospital deaths (Wirima, 1994). In principal, access to health services is good: 80% of the population lives within 10km of a health facility, and services are free. However, the quality of the services is poor (Hill, 1998). The national malaria control program (NMCP) focuses on the prompt and appropriate treatment of fevers in children, and on the treatment of pregnant women (2 dose sulphadoxine-pyrimethamine, SP). A KAP study in 1992 (Schultz et al., 1994) found that the majority of pregnant women seek antenatal care (93% once, 85% twice), making a high coverage of treatment of pregnant women a realistic goal, and providing the opportunity for education about malaria in pregnancy and in childhood. However, in 1996 only 55% of women in a similar study reported having attended an antenatal clinic (Macro International Inc, 1996).

Private retail outlets are an important source of antimalarials: in 1996 the number of carers of children under 5 with fever who sought help from a shop selling medicine was about equal to the number going to a hospital or health centre (33% and 35%, respectively, of under 5s with fever fell into each category) (Macro International Inc, 1996).

From 1993 to 1995 admissions for cerebral malaria and anaemia fell by 5% and 39%, respectively, and deaths (recorded in hospital) due to malaria and anaemia fell by 8% and 26%, respectively (Nwanyanwu et al., undated). This may be the result of the change to SP as first line drug. In 1994 SP was not available in the villages where 90% of the population reside. Furthermore, the price was high. This prompted the government to allow retail stores to purchase drugs directly from Central Medical Stores, thus reducing the retail price. In 1996 an agreement was signed to allow the duty- and tax-free importation of Fansidar (Hill, 1998). USAID report that the availability of first line antimalarial drugs in rural private outlets increased from 20% in 1995 to 70% in 1997 (USAID, 1998).

The health information system (HIS) is hampered by a shortage of forms (due to insufficient budget allocation), poor quality data collection, slow and inaccurate data
entry and lack of computer hardware. The NMCP has established 12 sentinel surveillance sites for continuous monitoring of under 5 morbidity and mortality, and 6 sites for continuous drug efficacy studies (Macro International Inc, 1996).

Thus, while there are hints that malaria control is having a positive effect in Malawi, the poor quality of the HIS suggests it is unlikely to be useful for monitoring the impact of malaria control. It may be better to monitor Under-Five Mortality, by surveys or in sentinel sites. Given the emphasis on treatment of pregnant women, Maternal and Neonatal or Infant Mortality might also be useful indicators of the success of the programme.

India (Maharashtra State)

From 1986 to 1995 the number of reported malaria cases in Maharashtra State increased exponentially (Kondrachine, 1997; Figure 1). The proportion of cases caused by *P. falciparum* varied over this period between 27% and 37%, but showed no consistent trend. The increase in malaria cases was attributed to an acute staff shortage, the influx of migratory workers from malarious areas, inadequate supplies of insecticides, larvicides and antimalarials, breakdown of surveillance, difficulty accessing tribal villages, and insecticide and drug resistance.

![Graph showing reported malaria cases](image)

Figure 1. Number of malaria cases (symbols) reported in Maharashtra State from 1986 to 1996. The straight line represents logarithmic growth from 1986-95, and indicates the number of cases that would have been expected in the absence of improved control in 1996.

In 1995, in an attempt to reverse this trend, a “High Power Board” was established. Many vacant posts were filled, a large number of posts were created, and staff were relocated. Weekly surveillance activities were introduced in high risk areas (it is not specified what these activities were). Early detection and treatment were improved by ensuring that there was a laboratory technician in each Primary Health Centre. The drug policy was revised, and chemophylaxis for pregnant women provided. Drug supply was improved. Treated mosquito nets were distributed among high-risk groups. Pyrethroids were used for spraying (replacing DDT and malathion). Larvivorous fish were introduced. There was a large-scale community awareness campaign, and teams were established to respond to malaria outbreaks.
Comparing the number of cases in 1996 with the number that would have occurred had the exponential increase in cases continued gives an estimated case reduction of 32%. However, we do not have any information about the reliability of the case data. It is likely that case detection improved in 1996, making this a conservative estimate of the proportional reduction in cases. We only have data for one year after the introduction of improved malaria control. If data from subsequent years show a continued decline in case numbers our confidence in the effect of control will be increased.

Since no data were provided for severe cases or deaths, we cannot estimate the effect of control on these. It is likely, however, that deaths will have been reduced by at least as much as cases. Early detection and improved case management could result in mortality falling faster than morbidity.

**Tanzania**

Malaria is the leading cause of morbidity and mortality in Tanzania, being responsible for an estimated 17% of deaths (Ministry of Health, Tanzania, 1994). The impact is highest in children under 5 years old, among whom an estimated 30% of deaths are a result of malaria. About 30% of outpatient diagnoses are malaria (Hill, 1998). Malaria in pregnant women leads to anaemia and low birth weight (LBW) babies. The geographic distribution of both anaemia and LBW in Tanzania mirror that of malaria. Resistance to chloroquine, quinine and SP have been reported.

![Graph showing reported malaria cases in Tanzania, 1986 to 1997](image)

Figure 2. Reported malaria cases in Tanzania, 1986 to 1997 (World Health Organization, 1999a).

The numbers of malaria cases reported annually have fallen since 1989 (Figure 2). These are probably health facility data, and without information about the reliability of the reporting system or about treatment seeking behaviour, we cannot know if this reflects a genuine reduction in malaria morbidity in the country. A survey of carers in 1992 found that 57% of children under 5 with fever were taken to a health facility or provider (Ngallava *et al*., 1993).
The main thrust of malaria control in Tanzania is early diagnosis and treatment (Menendez et al., 1997; Schellenburg et al., 1999). Specifically, the NMCP (established in 1990) includes plans to (i) improve availability of diagnosis at Health Centre (divisional) level and up; (ii) improve management of severe and complicated malaria (by training clinical staff); the case fatality for under 5s admitted to hospital is estimated at 12-15%; (iii) improve availability of drugs for treatment of uncomplicated malaria. Insufficient drugs are available at the periphery - antimalarials in the monthly EDP are generally exhausted after 2 weeks (Hill, 1998). There is a national policy of chemoprophylaxis for pregnant women (weekly chloroquine), but coverage is probably low.

There is a Health Information System (HIS), but it is not clear how well it is functioning. There is potential for good routine data collection, since there is a defined administrative structure, down to village level, and 10-household units in Dar es Salaam. Furthermore, there are several demographic surveillance sites in Tanzania which are members of the INDEPTH network (Tanzanian Essential Health Intervention Project; Adult Morbidity and Mortality Project; Ifakara), and a strong interest in using these to monitor the impact of malaria control. These are likely to be an extremely useful source of data in the absence of, or in combination with, HIS data.

Appropriate indicators, as in other high transmission areas, are likely to be Under-Five Mortality, and perhaps Infant or Neonatal Mortality, measured in special surveys or by surveillance in sentinel sites. Malaria-specific mortality is more difficult to measure, but can at least be attempted by verbal autopsy in DSS sites. Hospital admissions data will only provide an accurate indication of trends in severe malaria cases if treatment-seeking behaviour is consistent. Note that changes in the proportion of hospital admissions and deaths due to malaria can provide an indication of changes in the malaria situation, but can be confounded by changes in other causes of admissions and deaths. Furthermore, the case fatality rate of hospitalized cases provides an indication of the quality of case management.

Type III - Observed change in morbidity or mortality, probably attributable to intervention, magnitude unquantifiable (Armenia, Nepal)

Armenia

After 30 malaria-free years, 196 imported cases of malaria were recorded in Armenia in 1994, principally among soldiers stationed along the border with Azerbaijan. Over the next four years the number of imported cases increased, and local transmission began to occur in areas bordering Turkey. During 1998, 15 laboratories were equipped to diagnose malaria, and technicians were trained. Posters and leaflets were used to draw the attention of general practitioners to the disease. Drugs were supplied, an indoor spraying campaign was planned and implemented, and environmental management was begun. Active case detection was initiated in areas surrounding malaria foci, the surveillance system was improved, and a mass media campaign used to inform people about malaria.
Figure 3. Number of indigenous and imported malaria cases recorded in Armenia, 1992-98 (World Health Organization, 1999b).

The establishment of diagnostic laboratories, and improved surveillance mean that case detection probably improved in 1998. Even so, reported indigenous cases, which had been rising dramatically, fell slightly (Figure 3). It is likely, therefore, that the various malaria control activities reduced the number of indigenous cases. However, it is not possible reliably to predict how many cases would have been expected in 1998 in the absence of control.

The number of imported cases has continued to grow, perhaps the result of improved case detection. The number of cases reported in neighbouring countries was lower in 1998 than in 1997, but without knowing the number of people returning from (or coming from) those countries, it is impossible to estimate the expected number of imported cases. No cases of falciparum malaria have been reported in Armenia, and no deaths.

Malaria control activities and surveillance have continued, and the number of indigenous cases will probably continue to fall. Diagnosis and treatment of imported cases will help reduce the likelihood of re-introduction, but numbers of imported cases will continue to be influenced by the conditions in neighbouring countries, and the number of people exposed to malaria in those countries. Continued separate reporting of imported and indigenous cases is essential to monitor the situation.
Nepal

Routine surveillance data gathered between 1963 and 1997 show 4-5 malaria epidemics, with peaks and troughs more pronounced for *P. falciparum* than for *P. vivax*, as expected (Figure 4, top). The number of reported cases peaked at over 40,000 in 1985, 18% caused by *P. falciparum*. 17 deaths among *P. falciparum* cases were reported in 1996 and 1997. Malaria surveillance effort peaked at 1.6 million blood slides examined in 1978, and fell to 160,293 in 1997. AVI and AFI are clearly correlated, which suggests that the driving force behind the epidemics is not the epidemiology of the two parasites (their generation times are different), but the changing abundance of the mosquito vectors (both parasites are transmitted by *A. fluviatilis* and *A. maculatus*).

![Graph showing AVI and AFI over time](image)

**Figure 4.** Dynamics of *P. falciparum* (open circles) and *P. vivax* (closed circles) in Nepal (top) in relation to insecticide use (bottom). AVI = annual vivax incidence, i.e. number of *P. vivax* cases/1000 population; AFI = annual falciparum incidence (Vector Borne Disease Research and Training Centre, Nepal, 1997; Epidemiology and Disease Control Division, Nepal, 1999).

Insecticide usage could be the principal determinant of changes in mosquito abundance. The decline in AVI after the 1974/5 epidemic was associated with a sharp rise in the number of people protected by insecticide (Figure 4, bottom); conversely, AVI rose between 1980 and 1985 as insecticide coverage waned. Most cases in the 1985 epidemic were in the Far-Western Region. That epidemic was apparently
checked by focal spraying; the 600,000 or so people protected in 1987 do not stand out in national statistics (Figure 4, bottom). The fall in AVI and API after an epidemic in the Central region in 1991 might also be explained by local spraying. The data available to us do not clearly show this, but a fuller compilation of Nepal data might do so. There is no sign that epidemics have become less frequent since the 1960’s, and *P. falciparum* cases increased between 1995 and 1997.

Assuming that insecticide did curtail past epidemics, we would ideally evaluate impact against some expectation of what would have happened without spraying. This would require some speculative and perhaps unconvincing modelling of malaria epidemics. The approach taken by the MCP is more pragmatic: to set targets for the Annual Parasite Incidence (API, or AVI and AFI separately) based on the above data; to ensure that surveillance can detect the early signs of outbreaks (especially of *P. falciparum*), and to respond rapidly to these outbreaks with prompt treatment and focal spraying. Data available to us do not include a measure of surveillance coverage: to be confident that cases are not missed, we need to know that surveillance reaches everyone at risk of malaria, e.g. that there are microscopes and trained staff in every health post, and that all units report at regular intervals.

In sum, although the quality of surveillance reports has varied over the past 30 years, the malaria surveillance system apparently has the potential to monitor numbers of cases and deaths with sufficient accuracy. Whilst it is not easy to quantify the impact of insecticide and case management, it is reasonable to suppose that both have diminished the size of malaria epidemics. By strengthening surveillance, and by maintaining supplies of drugs and insecticides, Nepal is in a position to set, and to reach, a realistic target for case numbers (e.g. maintain API < 0.5). Key indicators of malaria control are: coverage of surveillance system (e.g. % units reporting quarterly); numbers of routinely reported *P. falciparum* and *P. vivax* cases (expressed e.g. as AFI and AVI) and deaths; trends in numbers of *P. falciparum* and *P. vivax* cases and deaths (to rapidly detect outbreaks).

**Type IV - Observed change in morbidity or mortality, probably attributable to intervention, magnitude quantifiable (Brazil, Thailand, Viet Nam)**

**Brazil**

Nine Amazon states account for the majority (>90%) of all reported malaria cases in Brazil, and in 1989 the government implemented the Amazon Basin Malaria Control Project (PCMAM). The number of cases notified increased exponentially between 1974 and 1989 (Figure 5). Although PCMAM is not a controlled experiment, and it is unclear what fraction of malaria cases were detected each year, it is likely that the 1989 downturn in reported incidence was due to the new programme of improved diagnosis and treatment, and vector control. The gap between reported and expected cases in Figure 5 provides an estimate of the number of cases saved by the control programme. API was observed to be 23.9 in 1996, as compared with 56.1 expected without intervention, a reduction of 57%. Akhavan *et al.* (1999) estimate that nearly 2 million cases were saved between 1989 and 1996.
The proportion of cases due to *P. falciparum* began to fall before 1989 (and had also declined during the 1970's), so the contribution of the programme in reducing malaria severity, and hence deaths, is less clear (Figure 5). Attributing the relatively rapid fall in *P. falciparum* cases to the programme, and making further inferences about the decline in case fatality due to treatment, Akhavan et al. (1999) estimated the number of deaths prevented at 231,000. Their calculations give 191 deaths in 1996, instead of 1872 expected, a reduction of 90% for that year.

![Graph showing number of malaria cases and P. falciparum cases reported from 9 Amazon states, 1970-97. The straight line indicates the number of cases that would have been expected in the absence of control beginning in 1988. The light, unmarked line shows the percentage of cases due to P. falciparum (Akhavan, 1997; Akhavan et al., 1999).](image)

In the special circumstances of this programme, it was possible to estimate, with some confidence, the proportional reduction in morbidity and mortality (especially morbidity) among those cases that were detected (observed), or that would have been detected (expected). The exercise succeeded in this respect because logarithmic growth in case numbers was steady for 15 years prior to the intervention (a clear epidemic trajectory), after which there was a sudden impact of control, the effects of which persisted for 7 years. Such strong deductions will not always (or even usually) be possible from routine surveillance data.

It is not possible to assess the proportional reduction of all malaria cases and deaths due to this programme because we do not know the proportion of cases detected. The fact that case reports were received from 98% of municipalities in 1993 does not solve the problem, because we know nothing about case detection within municipalities. Self-medication might be commonplace, especially for mild cases. Thus, we cannot be sure, with the data at hand, that this programme reduced all malaria deaths by more than 50%, the target set by Roll Back Malaria.

From the perspective of measuring impact, these observations call for a measure of the quality of the surveillance system (from the perspective of minimizing health
service costs, we may be willing to do without data on mild malaria cases). We would like to be sure that passive surveillance (PCD), and hence treatment services, are at least finding all severe malaria cases (e.g. *all P. falciparum* cases in Brazil). This implies carrying out checks, probably on a random sample of districts.

In sum, Brazil is in a position to maintain and strengthen its malaria surveillance system, and set State targets for cases and deaths. The targets could be (a) threshold numbers of cases and deaths, (b) % reductions by year X compared with an earlier year, or (c) % reductions by year X, compared with expectations for year X in the absence of control. The first 2 of these are relatively easy; the last is hard. Again, the general problem is in attributing reductions in malaria cases and deaths specifically to malaria control activities.

**Thailand**

National case reports show a steady decline in the malaria incidence rate between 1989 and 1995, part of a long-term decline dating back to at least 1949 (Ministry of Public Health, Thailand, 1995). From these data alone, it is not possible to attribute the fall in incidence to control activities.

**Figure 6.** Changes in the number of malaria cases at Shoklo, Thailand, in response to the introduction of mefloquine (M25) and a mefloquine + artesunate (M+A) combination (MAS3), and insecticide impregnated bednets (IBN). Data from Nosten et al. (in press).

Certain local data are, however, more persuasive. Figure 6 shows changes in the incidence rate of *P. falciparum* (PF) coincident with the introduction of mefloquine (M25), and a mefloquine plus artesunate combination (MAS3), in Shoklo refugee camp (Nosten *et al.*, in press). The study probably found all, or nearly all, malaria by a mixture of passive and active case finding. As in other examples described above,
these data show the results of an uncontrolled experiment. However, there was a fall in the *P. falciparum* incidence rate between 1991 and 1995. The reduction in incidence is attributable to the intervention because it was large (about 50%), and because it happened while *P. vivax* (PV) incidence continued to rise in the study area, and while *P. falciparum* incidence did not fall outside the study area.

**Viet Nam**

Numbers of reported cases of malaria in Viet Nam over the last 20 years have varied considerably (Figure 7). The patterns in the numbers of cases appear to correspond to the history of malaria control over that period, although a number of interacting factors make it difficult to demonstrate a definite causal link between events and case numbers (World Health Organization, 1998c). Large scale DDT spraying in the late 1950s and early 1960s had a dramatic effect. In the late 1960s and early 1970s insecticide coverage fell and cases rose. From 1976 coverage with DDT began to increase, and cases fell, but during the early 1980s problems were encountered: drug resistance, insecticide resistance, decay of the general health services. In 1984 government subsidies stopped, and in 1985 the USSR stopped supplying DDT. Between 1986 and 1992 numbers of reported cases fluctuated, but it is difficult to know if this reflects genuine fluctuations in the number of malaria cases, or the quality of reporting over that period.

Since 1991, the government has increased funding for the NMCP, and malaria control has been a high priority, with high political commitment and action. This has involved improved diagnosis and treatment by village and commune health services and mobile health teams, epidemic surveillance and preparedness, residual spraying and the use of impregnated bednets.

![Diagram](image_url)

Figure 7. Trends in numbers of cases and deaths reported from Viet Nam, 1976-98 (Cong, 1998; Phan et al. 1998; Regional Malaria Control Programme for Cambodia, Laos and Vietnam, 1999).
There is a routine reporting system, and all 61 provinces report monthly. Reported are population at risk, numbers of cases, complicated cases and deaths. The number of slides examined is reported, the percentage of positive slides (SPR), and the number positive for *falciparum*. Case finding is a mixture of active and passive. Only a small proportion of cases (about 6%) is confirmed parasitologically.

In estimating the effect of control, 2 approaches were used. For the first approach, the number of cases in the most recently reported year was compared directly with the number of cases in the year in which major changes to the malaria control program were introduced. This is, in effect, equivalent to assuming that in the absence of intervention the numbers of cases and deaths would have been constant. This approach gives an estimated reduction in confirmed cases 65%, and in deaths of 97% (expressed as a percentage of the 1991 numbers).

For the second approach, it was assumed that, in the absence of intervention, the SPR would have continued to increase exponentially, and that the epidemic would not have peaked or levelled off naturally. Changes in SPR will reflect changes in the incidence of malaria only if the relative amounts of active and passive detection stay the same, and if the SPR is low. We do not know if the first of these criteria is met, although it may be possible to find out. The SPR ranges from 3 to 7%, and increases over the period 1980 to 1992.

![Graph showing changes in log(SPR) from 1975 to 2000](image)

**Figure 8.** Changes in the slide positivity rate (SPR, expressed as a logarithm) in Viet Nam over 21 years, 1976-97.

By fitting an exponential model to the SPR for years preceding the introduction of the current MCP (1980 to 1991), the expected SPR for 1997 was calculated (Figure 8). Comparing the observed (2.7%) and expected (18.5%) SPR suggests a reduction in cases of 85%. The case fatality rate (CFR) has fallen over the period 1991 to 1997. It was assumed that this fall would not have occurred in the absence of intervention. To estimate the proportional reduction in deaths, the 1997 CFR was applied to the
observed SPR, and the 1991 CFR to the predicted SPR, giving an estimated reduction in deaths of 98%.

The fact that the change in the trend of SPR coincides with the change in malaria control program provides support for the suggestion that it is the result of malaria control. However, we can not know how long the increasing trend seen from 1980 to 1991 would have continued in the absence of intervention. It seems reasonable to assume that the SPR would have increased in the absence of intervention, but difficult to know how much. The predicted SPR for 1997 (18.5%) is higher than the highest values previously reported in North Vietnam (8% in 1958) and South Vietnam (12% in 1976). By calculating the reduction in cases and deaths by assuming no increase, as in the first approach and by assuming an exponential increase, as in the second approach, we obtain estimates at either end of the likely range of values.

Type V - Observed change in morbidity or mortality, almost certainly attributable to intervention, magnitude quantifiable (insecticide impregnated nets)

The most convincing data come from experiments conducted under the most demanding conditions - randomized controlled trials (RCTs). RCTs are unlikely to be used to evaluate RBM interventions, which will be carried out under operational rather than experimental conditions. Nonetheless, RCTs set the standard for drawing inferences about the impact of malaria control.

![Graph showing protective efficacy of bednets](image)

Figure 9. Protective efficacy of bednets (% reduction in mortality) plotted against the annual (pre-intervention) death rate of children aged 1-59 months. Data from four studies in Africa compiled by Lengeler (1998).

Insecticide impregnated bednets are probably the most important intervention against malaria that has been subjected to comprehensive investigation in the last decade. Lengeler (1998) has already provided an excellent overview of the numerous trials carried out in many countries. Those that measured an impact on mortality are listed in Table 3. Lengeler noted that protective efficacy (PE) tended to be lower where
transmission intensity was higher. More striking, perhaps, is the inverse relation between PE and the initial crude death rate (Figure 9), which is consistent with the view that malaria is more likely to be a competing (rather than additive) cause of death when the overall death rate is high (Cohen, 1988).

The set of trials reviewed by Lengeler is the current benchmark by which the efficacy of impregnated bednets is judged. Lengeler & Snow (1996) have pointed out how effectiveness can be calculated by combining measures of efficacy and coverage. The main inferential problem from such calculations comes from judging whether the potential effectiveness achieved in tightly-controlled experiments (phase III trials) can be replicated under operational conditions. A “phase IV” assessment in The Gambia showed a relatively small reduction in mortality with impregnated bednets (D’Alessandro et al., 1995), as compared with a phase III trial (Alonso et al., 1991).


<table>
<thead>
<tr>
<th>Country</th>
<th>Transmission intensity (EIR)</th>
<th>Intervention rate</th>
<th>Control rate</th>
<th>Un-adjusted protective efficacy (95% CI-corrected)</th>
<th>Rate difference (95% CI-uncorrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gambia</td>
<td>1-10</td>
<td>18.7</td>
<td>24.3</td>
<td>23% (1-41%) (9-35%)</td>
<td>5.6 (0.4 - 10.7) (2.0 - 9.2)</td>
</tr>
</tbody>
</table>

Comparison 2: control group = untreated nets

Comparison 1: control group = no nets

<table>
<thead>
<tr>
<th>Country</th>
<th>Transmission intensity (EIR)</th>
<th>Intervention rate</th>
<th>Control rate</th>
<th>Un-adjusted protective efficacy (95% CI-corrected)</th>
<th>Rate difference (95% CI-uncorrected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kenya</td>
<td>10-30</td>
<td>9.4</td>
<td>13.2</td>
<td>29% (3-47%) (9-34%)</td>
<td>3.8 (not avail.) (1.1-6.6)</td>
</tr>
<tr>
<td>Ghana</td>
<td>100-300</td>
<td>28.2</td>
<td>34.2</td>
<td>18% (1-30%) (8-26%)</td>
<td>6.0 (1.4-10.6) (2.3-9.5)</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>300-500</td>
<td>41.8</td>
<td>48.7</td>
<td>14% (8-30%) (5-23%)</td>
<td>6.9 (-2.5-16.2) (2.0-11.8)</td>
</tr>
</tbody>
</table>

Lengeler’s Cochrane review focused on the inferences that could be made from RCTs, and was rightly fastidious about inclusion criteria. But this meant rejecting, partially or wholly, the results of 47 trials of types III and IV in our classification. In principle, it is possible for inclusion criteria to be too strict, leading to the rejection of meaningful data. The analytical challenge here is to show what degree of confidence can be placed in the results of studies that are not formal experiments. The Cochrane
reviews serve an important function in promoting good investigative practice, but control programme managers have to make decisions using the best available evidence. Most of the time, they will have at their disposal data that are less persuasive than the results of RCTs, but better than nothing at all. The question is: how much better?

Conclusions and recommendations

Our conclusions are, in part, endorsements of the views now held by many of the malaria experts we have consulted around the world. They are listed below according to our three main themes: choice of indicators, methods of measurement, and attributing changes to specific interventions.

Choice of indicators (see also Appendix 1)

1. A comprehensive view of the impact of malaria control is highly desirable, but limited funds and personnel demand the selection of a set of “core indicators”. Attempts to develop “integrated surveillance” systems for communicable diseases are encouraging more frequent comparison, selection and rejection of indicators.

2. In high-transmission areas (mainly, but neither exclusively nor in its entirety, Sub-Saharan Africa, “savannah malaria”) the core indicators are all-cause and malaria-attributed Under-Five Mortality, measured through repeated household surveys or demographic surveillance. Both all-cause and malaria-attributed mortality are recommended because:

   (a) there are circumstances where changes in all-cause mortality can be reliably measured, but where deaths counted in surveys cannot accurately be attributed to malaria.

   (b) where all-cause Under-Five Mortality is lower, interventions against malaria can have indirect as well as direct benefits, reducing deaths partly attributable to other conditions; it is highly desirable to quantify these additional, indirect benefits.

   (c) where all-cause Under-Five Mortality is higher, malaria is sometimes a “competing risk”, in which case fewer malaria deaths are offset by more deaths from other causes (McGregor, 1964; Molineaux, 1985; Cohen, 1988); when there is no measurable change in all-cause Under-Five Mortality, we need to distinguish between two possible explanations - the failure of malaria control (including health system failure) and compensating mortality.

   (d) a number of RBM interventions will not be specific to malaria, e.g. management of anaemia in pregnancy.

Further impact indicators (e.g. mortality and malaria mortality of other age groups) will be appropriate in many settings.

Although RBM’s global target for malaria control has been expressed in terms of mortality (50% reduction in deaths by 2010), many countries will want to set additional impact targets. In high-transmission areas, changes in the incidence rate of severe malaria can be measured at health facilities that keep consistent records, which
are representative of the population at risk (to be defined). It will not, in general, be possible to measure the overall incidence rate of malaria because cases are not easily diagnosed, and because routine health information systems (HIS) are often poor.

3. Outside high-transmission areas, the core indicator is the incidence of symptomatic cases with parasitaemia, measured as Annual Parasite Incidence (API), by age, sex and parasite species, and derived from the slide positivity rate (SPR). The recommended method of measurement is by routine surveillance. Many countries in Europe, Asia, Oceania, North Africa and Latin America have shown that they can measure API by routine surveillance (patients with symptoms contacting health services), and identify *Plasmodium* spp by microscopy. While parasitological confirmation is not currently possible in all parts of these countries, it is obviously highly desirable. A morbidity indicator will suit many low-transmission areas because:

(a) diagnosis of malaria is relatively easy,
(b) reducing incidence is the principal goal, and reduced incidence is likely to mean fewer deaths,
(c) many countries have high case loads, but few malaria deaths, e.g. where *P. vivax* predominates, and where most *P. falciparum* cases are treated.

The measurement of malaria deaths is also recommended even for those countries where there are few malaria deaths. Increases in death rates can serve as a warning of increased drug resistance, or of the introduction of *P. falciparum* into areas where it was not previously found. For some countries it will be realistic to set a target of no malaria deaths.

4. We can distinguish between the use of indicators (i) to set targets, and (ii) to measure impact. Some countries state their targets in annual reports; many others apparently do not. Targets for control can and should be set even with imprecise information about the efficacy of an intervention, because the strategy for controlling malaria next year should be based on the best information available this year. Any strategy will have an expected outcome, or a range of expected outcomes, and targets can be set according to these expectations.

**Methods of measuring indicators**

5. Where API is the core indicator, countries should be able to confirm that suspected malaria cases carry *Plasmodium* infections. They should also be able to identify the species of parasite, or at least to separate *P. falciparum* from the other three. This can be done by microscopy, or in future with an immunodiagnostic test.

6. There is an immediate need to evaluate the quality of routine surveillance systems, and the data they produce. To ensure high coverage, an indicator should be used to monitor the performance of the malaria surveillance system. One quantitative measure is:

\[
\text{Number of districts reporting in a year} \times 100 \over \text{Total number of districts}
\]
Ideally, checks will also be carried out on the quality and coverage of reporting within districts, or other relevant administrative units.

7. The Demographic Surveillance Systems (DSS) – the INDEPTH network - that have now been set up at 40 sites in developing countries (28 in Africa) have considerable potential for collecting (longitudinal) data on all-cause, and perhaps malaria attributed (e.g. from verbal autopsies), Under-Five Mortality. Further field testing of DSS and other survey methods is needed to show whether changes in these indicators can be measured accurately in a variety of settings, and to investigate the trade-off between information and cost. DSS has the potential to measure malaria deaths outside Africa, supporting morbidity data, but field tests must show that deaths can be attributed correctly to malaria in areas where malaria causes a small fraction of all deaths.

8. National Demographic and Health Surveys (DHS) are less suitable for measuring CDR and Under-Five Mortality, particularly because mortality is estimated from cross-sectional data with a 2-5 year time lag. However, DHS can provide useful information about the availability of health services and treatment-seeking behaviour. The inclusion of a malaria module in future surveys will provide more detailed information of relevance to malaria control, e.g. bed net usage.

9. It will be vital to provide training for surveillance staff in countries on the selection and measurement of indicators, and on the subsequent analysis of data.

Attributing changes to specific interventions

10. The impact of RBM programmes will be monitored using data collected outside formal experiments (such as randomized controlled trials). As a result, it will be more difficult to attribute observed reductions in incidence and death rates to any given intervention. The exception will be where an abrupt change in mortality or incidence rate follows a single intervention, and where the effects of any potentially confounding activities (e.g. vaccinating children) can be excluded. It will undoubtedly be difficult, in some circumstances, to credit results directly to RBM interventions. If the reasons for success are unclear, it will be difficult to repeat or improve on the success elsewhere. Where the intervention is a mix of activities, such as vector control with case management, or even a set of interventions against a range of diseases, it might be hard to identify the best mix in future interventions.

11. RBM should be clear and consistent about targets. We refer in this paper to the goal of reducing “malaria mortality rates by at least 50% by the year 2010”. But other sources refer simply to “deaths”, or “burden”. There is also the question of how to interpret a 50% reduction. Does this mean that the death rate in 2010 will be half that in 1998 (or some other year), or half what it would have been in the absence of RBM? The first would be easier to calculate, but the second might be easier to achieve, if deaths would have increased in the absence of RBM.

12. Better and fuller analysis of the available data would provide a partial remedy to the problem of attribution. One striking finding of this study is that there are very few, recent analyses of the impact of malaria control, outside experimental trials, i.e., there
are few studies of the kind carried out by Akhavan (1997, 1999) for Brazil and M. Over (forthcoming) for the Solomon Islands. Presumably, similar data exist in many countries. Presumably, many are latently rich in information, but have not been analysed. Malaysia may be a case in point (K. Palmer, pers. comm.). Further effort should be made to identify these data, and they should be subjected to a wide range of analytical techniques, including meta-analysis, and multivariate statistical analysis and mathematical modelling. Illuminating analyses of this kind have been carried out for at least 50 years (Molineaux, 1985). More are needed now.

Next steps

In the context of this review, three are self-evident:

1. Seek wider agreement on the choice of “core indicators”. RBM has already begun a process of broad consultation.

2. Identify, and analyse in detail, historical data from (especially) national control programmes. Epidemiological analyses could be carried out under the same headings as used in this report: choice of indicators, methods of measurement, attribution of impact to specific interventions. A study of “malaria success stories” by RBM is underway, with data reconnaissance visits to countries planned for the first half of 2000.

3. The full potential of DSS and DHS needs to be examined through the collection and analysis of more data. Numerous such projects are underway, or proposed.

Going beyond the present study, it will be crucial for RBM to assess the epidemiological evidence that malaria mortality can, in principle, be cut by half by the year 2010.

Acknowledgements

We are most grateful to all those listed in Appendix 2 who responded to our numerous questions, especially Charles Delacollette, Renato Gusmao, Louis Molineaux, Mead Over, Kevin Palmer, Guido Sabatinelli, Don de Savigny, Allan Schapira, Philip Setel, Bob Snow and Nick White.
References


de Savigny, D. *Information for malaria control in Africa: are we ready?* Presentation at the MIM Malaria Congress, Durban, South Africa (March 1999).


Khalifa, M. A. *The malaria eradication programme in the Sultanate of Oman: situation analysis*, (Department of Environmental Health and Malaria Eradication, Muscat, 1999).


33


Trigg, P.I. *Report on mission to Turkey*, unpublished document (Malaria Unit, Department of Control of Tropical Diseases, World Health Organization, Geneva, 1993).

USAID. *Population, health and nutrition briefing sheet, Malawi.*


<table>
<thead>
<tr>
<th>Impact</th>
<th>Source of information</th>
<th>Operational Definition</th>
<th>Field-tested / being used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>Estimated % reduction in under-five mortality (all-cause)</td>
<td>% reduction in malaria mortality (under-fives only, other age groups).</td>
<td>(i) Longitudinal Demographic Surveillance System (DSS), (ii) Cross-sectional Household Surveys, including Demographic and Health Surveys (DHS)</td>
</tr>
<tr>
<td>Mortality</td>
<td>Estimated % reduction in under-five mortality (all-cause)</td>
<td>% change in Malaria Death Rate for all age groups (MDR = number of deaths per year / population at risk). By convention, (a) is a proportion.</td>
<td>As part of routine monitoring of many Malaria Control Programmes (MCPs), (i) via special surveys and reports (ii) via routine surveillance systems (iii) via operational research.</td>
</tr>
<tr>
<td>Morbidity</td>
<td>% reduction in malaria incidence rate</td>
<td>Estimated % reduction in malaria incidence rate (a proportion of patients with malaria symptoms and confirmed parasitaemia per year population at risk). Based on clinical malaria diagnosis.</td>
<td>Reliant on high coverage or representative samples and consistent reporting.</td>
</tr>
<tr>
<td>Morbidity</td>
<td>% reduction in malaria incidence rate</td>
<td>% change in Malaria Incidence Rate for all age groups (MDR = number of cases per year / population at risk).</td>
<td>Routine surveillance data (passive or active case finding).</td>
</tr>
<tr>
<td>Morbidity</td>
<td>% reduction in malaria incidence rate</td>
<td>% change in Malaria Incidence Rate for all age groups (MDR = number of cases per year / population at risk).</td>
<td>Routine surveillance data (passive or active case finding).</td>
</tr>
<tr>
<td>Morbidity</td>
<td>% reduction in malaria incidence rate</td>
<td>% change in Malaria Incidence Rate for all age groups (MDR = number of cases per year / population at risk).</td>
<td>Routine surveillance data (passive or active case finding).</td>
</tr>
</tbody>
</table>
Appendix 2: List of persons consulted during the preparation of this report

Dr P. Arbani  WHO-SEARO RMA*
Dr A. Beljaev  WHO-EMRO RMA
Dr F.N. Binka  WHO-HQ
Dr A. Bosman  WHO-HQ
Dr J.W. Bryce  WHO-HQ FCH/CAH
Ms S. Chungong  WHO-HQ CSR/ISR
Dr C. Delacollette  WHO-HQ
Dr S. Foster  Boston University of Public Health, Boston, USA.
Dr R. Gusmao  WHO-AMRO RMA
Dr D. Heymann  WHO-HQ CDS
Dr Y. Kassankogno  WHO-AFRO RMA
Dr A. Kondrachine  WHO-HQ CPE/CCS
Dr A. Lopez  WHO-HQ GPE/EBD
Dr P. Lozano  WHO-HQ GPE/EBD
Dr A. Marx  WHO-HQ FCH/CAH
Dr S. Meek  Malaria Consortium, London, UK.
Dr J-P Meert  WHO-HQ CSR/ISR
Dr K. Mendis  WHO-HQ CDS/RBM
Dr L. Molineaux  Geneva, Switzerland
Dr D. Nabarro  WHO-HQ CDS/RBM
Dr I.I. Ortega  WHO-HQ CDS/RBM
Dr M. Over  World Bank, Washington D.C., USA.
Dr K. Palmer  WHO-WPRO
Dr J. Remme  WHO-HQ CDS/RBM
Dr A. Rietveld  WHO-HQ CDS/RBM
Dr G. Rodier  WHO-HQ CSR/ISR
Dr M Ryan  WHO-HQ EIP
Dr G. Sabatinelli  WHO-EURO RMA
Dr D. de Savigny  International Development Research Centre, Dar es Salaam, Tanzania.
Dr Alan Schapira  WHO-WPRO RMA
Dr P. Setel  Adult Morbidity and Mortality Project (AMMP), Tanzania / University of Newcastle upon Tyne, UK
Dr R. Snow  Ministry of Health, Kenya / Wellcome Trust
Dr A. Teklehaimanot  WHO-HQ CDS/RBM
Dr P. Trigg  WHO-HQ CDS/RBM
Prof. N. White  Mahidol University, Thailand.

* RMA = Regional Malaria Advisor