Chapter 2

Goals, targets, policies and strategies for malaria control and elimination

This chapter summarizes the internationally agreed goals for malaria control and the policies and strategies recommended by WHO to achieve them. It has four sections: (i) goals and targets; (ii) policies and strategies; (iii) malaria elimination; and (iv) indicators to track progress.

2.1 Goals and targets for malaria control and elimination

The year 2010 was an important milestone on the way to achievement of internationally agreed goals and targets for malaria control. It was the date set by the World Health Assembly in 2005 to ensure that at least 80% of those at risk of, or suffering from, malaria would benefit from major preventive and curative interventions, in order to reduce the malaria burden by at least 50% compared to the levels in 2000 (1). In 2008, the UN Secretary General set a more ambitious objective: to halt malaria deaths by ensuring universal coverage of malaria interventions by 2010. The aim was to make indoor residual spraying (IRS) and long-lasting insecticidal nets (LLINs) available to all people at risk of malaria, especially children and pregnant women in Africa, and for all public health facilities to be able to provide reliable diagnosis and effective treatment for malaria (2). Also in 2008, and aligned with these targets, the Global Malaria Action Plan (GMAP) was launched by the Roll Back Malaria Partnership (RBM) as a blueprint for the control, elimination and eventual eradication of malaria, setting as its objective the reduction of the number of preventable malaria deaths worldwide to near zero by 2015 (3).

In the light of progress made by 2010, RBM updated the GMAP targets in June 2011. Maintaining an overall vision of a “malaria-free world” (4), the targets are now to: (i) reduce global malaria deaths to near zero by end-2015, (ii) reduce global malaria cases by 75% from 2000 levels by end-2015, and (iii) eliminate malaria by end-2015 in 10 new countries since 2008, including in the WHO European Region (5) (Table 2.1). These targets will be met by: achieving and sustaining universal access to and utilization of preventive measures; achieving universal access to case management in the public and private sectors and in the community (including appropriate referral); and accelerating the development of surveillance systems.

Achievement of these objectives and targets are based on a number of critical assumptions:

- Sufficient and timely domestic and international funding is available to accomplish and sustain scale-up of the interventions needed to meet the objectives, targets and milestones.

- Scale-up of preventive measures and greater access to diagnostic testing and treatment through the public and private sectors and community case management, along with referral when needed, are sufficient to allow effective treatment of all cases of confirmed malaria.

- Political commitment to sustain malaria control interventions and high-quality surveillance – including the elimination of malaria where that is technically, operationally, and financially feasible – continues even as malaria cases and deaths decline significantly.

- Access to vulnerable populations and the safety and security of health workers are maintained to ensure surveillance, outbreak response, and delivery of diagnostic, treatment, and preventive interventions to populations in fragile and conflict-affected states.

Acknowledging that ‘business as usual’ will not be enough for achieving the agreed goals, the World Health Assembly in May 2011 urged Member States, WHO, and international partners to undertake a series of actions to sustain the gains that have been made in decreasing the burden of malaria and reducing transmission – among others, to take immediate action to combat resistance to artemisinin-based medicines and resistance to insecticides (6).

The deadline for achieving the RBM objective coincides with that of the Millennium Development Goals (MDGs). Malaria control forms part of MDG 6 – to have halted and begun to reverse the incidence of malaria and other major diseases by 2015. Given that malaria accounted for 8% of deaths in children under 5 years of age globally in 2008 and 16% of deaths in children under 5 in Africa (7), it is also central to MDG 4 – achieving a two-thirds reduction in the mortality rate among children under 5 years of age between 1990 and 2015. Malaria control is additionally expected to contribute to achievement of MDG 1 (eradicate extreme poverty and hunger), MDG 2 (achieve universal primary education) MDG 3 (promote gender equality and empower women), MDG 5 (improve maternal health) and MDG 8 (develop a global partnership for development) (8).

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1 In areas where public health facilities are able to provide a parasitological test for all suspected malaria cases, near zero malaria deaths is defined as no more than 1 confirmed malaria death per 100,000 population at risk.
TABLE 2.1
Goals and targets for malaria control

<table>
<thead>
<tr>
<th>Targets for 2005</th>
<th>Targets for 2010</th>
<th>Targets for 2015</th>
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<tbody>
<tr>
<td>Reduce global malaria deaths from 2000 levels by 50% (3)</td>
<td>Reduce global malaria deaths to near zero (5)</td>
<td>Achieve universal access to and utilization of prevention measures: By end 2013, in countries where universal access and utilization have not yet been achieved, achieve 100% access to and utilization of prevention measures for all populations at risk with locally appropriate interventions (5)</td>
</tr>
<tr>
<td>Reduce global malaria cases from 2000 levels by 50% (3)</td>
<td>Reduce global malaria deaths from 2000 levels by 75% (1)</td>
<td>Sustain universal access to and utilization of prevention measures. By 2015 and beyond, all countries sustain universal access to and utilization of an appropriate package of preventive interventions (5)</td>
</tr>
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<td>At least 60% of those at risk of malaria particularly pregnant women and children under five years of age, benefit from the most suitable combination of personal and community protective measures (5)</td>
<td>Achieve universal coverage for all populations at risk of malaria using locally appropriate interventions for prevention and case management (3)</td>
<td>At least 80% of pregnant women receive intermittent preventive treatment in areas where malaria transmission is stable (1, 10)</td>
</tr>
<tr>
<td>At least 60% of all pregnant women who are at risk of malaria, especially those in their first pregnancies, have access to chemoprophylaxis or presumptive intermittent treatment (9)</td>
<td>80% of people at risk from malaria are protected, thanks to locally appropriate vector control methods such as insecticide-treated nets (ITNs), and, where appropriate, indoor residual spraying (IRS) and, in some settings, other environmental and biological measures (1, 10)</td>
<td>At least 80% of pregnant women receive intermittent preventive treatment within 24 hours of the onset of symptoms (9)</td>
</tr>
<tr>
<td>At least 60% of those suffering from malaria have prompt access to and are able to use correct, affordable and appropriate treatment within 24 hours of the onset of symptoms (9)</td>
<td>80% of malaria patients are diagnosed and treated with effective antimalarial medicines, e.g. artemisinin-based combination therapy (ACT) within one day of the onset of illness (1, 10)</td>
<td>Achieve universal access to case management in the public sector: By end 2013, 100% of suspected cases receive a malaria diagnostic test and 100% of confirmed cases receive treatment with appropriate and effective antimalarial drugs (2)</td>
</tr>
<tr>
<td>Achieve universal coverage with effective vector control (5)</td>
<td>Achieve universal access to case management, or appropriate referral, in the private sector. By end 2015, 100% of suspected cases receive a malaria diagnostic test and 100% of confirmed cases receive treatment with appropriate and effective antimalarial drugs (5)</td>
<td>Achieve universal access to community case management (CCM) of malaria. By end 2015, in countries where CCM of malaria is an appropriate strategy, 100% of fever (suspected) cases receive a malaria diagnostic test and 100% of confirmed uncomplicated cases receive treatment with appropriate and effective antimalarial drugs, and 100% of suspected and confirmed severe cases receive appropriate referral (5)</td>
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<tr>
<td>Accelerate development of surveillance systems: By end 2015, all districts are capable of reporting monthly numbers of suspected malaria cases, number of cases from all public health facilities, or a consistent sample of them (5)</td>
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2.2 Malaria control policies and strategies

The strategic approaches to malaria control come within two major domains: (i) prevention and (ii) case management. Together, these strategies work against the transmission of the parasite from mosquito vector to humans, and the development of illness and severe disease.

2.2.1 Malaria prevention through malaria vector control

The goals of malaria vector control are two-fold:

• to protect individual people against infective malaria mosquito bites, and

• to reduce the intensity of local malaria transmission at community level by reducing the longevity, density and human-vector contact of the local vector mosquito population.

The two most powerful and most broadly applied interventions are long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). These interventions work by reducing human-vector contact and by reducing the lifespan of female mosquitoes (so that they do not survive long enough to transmit the parasite).

Insecticide-treated nets (ITNs), which include both LLINs and conventional nets that are later treated with an insecticide, work both by protecting the person sleeping under the net (individual level) and by extending the effect to an entire area (community level). Personal protection operates by preventing contact between the mosquito and the person under the net. The wider effect occurs when the insecticide in the net actually kills the mosquitoes that touch it, therefore affecting the vector population and lowering the overall intensity of transmission in the targeted area. However, the protective effect of ITNs for people sleeping outside the net within the same household is less than for those sleeping under the net (11). Therefore, since 2007, WHO has recommended universal coverage with ITNs (preferably LLINs), rather than a pre-determined number per household.

IRS involves the application of residual insecticides to the inner surfaces of dwellings, where many vector species of anopheline mosquito tend to rest after taking a blood meal (12). IRS is effective in rapidly controlling malaria transmission, hence in reducing the local burden of malaria morbidity and mortality, provided that most houses and animal shelters (e.g. > 80%) in targeted communities are treated (13).

Achieving universal coverage with effective vector control requires a sustained programme of vector control delivery operations which are carried out correctly and on time. This in turn requires specialized personnel at national, provincial and district levels. As well as practical experience in the delivery of vector...
control interventions, these teams must also have the capacity to monitor and investigate vector-related and operational factors that may compromise intervention effectiveness, for which specialized entomological knowledge and skills are essential.

WHO recommendations for vector control are the following:

**Insecticide-treated nets**

1. As high coverage rates are needed to realize the full potential of vector control, WHO recommends that in areas targeted for malaria prevention, ITNs should be made available to all people at risk, i.e. “universal access” (14). Because of the operational advantages of LLINs over ITNs, and the fact that the vast majority of nets being procured and distributed today are indeed LLINs, the remainder of this section will refer to LLINs rather than ITNs. In order to meet the target of universal access, it is currently proposed that one LLIN should be distributed for every two people. At the household level, the distribution of one LLIN for every two members of the household will entail rounding up in households with an odd number of members (e.g. 3 LLINs for a household with 5 members, etc). Because of this rounding up, the achievement of “one LLIN for every two people” at household level requires an overall ratio, for procurement purposes, of 1 LLIN for every 1.8 people in the target population (13).

2. LLINs should be provided either free of charge or be highly subsidized. Cost should not be a barrier to making them available to all people at risk of malaria, especially those at greatest risk such as young children and pregnant women (14).

3. Universal access to LLINs is best achieved and maintained by a combination of delivery systems. The basic concept is a combination of ‘catch up’ and ‘keep up’. Catch up means mass distribution campaigns, which can rapidly achieve universal coverage of LLINs. However it is essential to complement such campaigns with continuous ‘keep up’ delivery systems, particularly routine delivery to pregnant women through antenatal services and to infants at immunization clinics. In malaria-risk areas, ensuring that these routine systems have the sustained LLINs stocks needed to provide an LLIN to all pregnant women receiving antenatal care, and to all infants receiving routine immunization, should be given as much priority as repeated campaigns (14).

**WHO recommended long-lasting insecticidal mosquito nets.**


**Report of the fourteenth WHOPES working group meeting.**


**Global Fund proposal development: WHO Policy brief.**


**WHO recommended long-lasting insecticidal mosquito nets.**


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4. In order to be protected, households must not only own LLINs but also use them. Behaviour change interventions including information, education, communication (IEC) campaigns and post-distribution “hang-up campaigns” are strongly recommended (14).

5. Only LLINs recommended by the WHO Pesticide Evaluation Scheme (WHOPES) should be procured by national malaria control programmes and partners for malaria control. At present there are 12 recommended products (15, 16, 17). Detailed guidance on good practice in the handling and use of pesticides, and on quality control in procurement, can be found on the WHOPES website (18). Independent quality control of products (including insecticides) should be undertaken before shipment, to ensure that sub-standard products are not delivered to countries. The supplier of pesticide should bear the cost of analysis, including for samples to be sent to an accredited or recognized laboratory for analysis for countries that do not have national quality control laboratories (19).

6. It is now recognized that the lifespan of LLINs is variable, among settings and among products. Therefore, all large-scale LLIN programmes (including those implemented by non-governmental organizations) should make efforts to monitor LLIN durability in the local setting, using standard methods published in 2011 (20). The collection of local data on the comparative durability of alternative LLIN products, using rigorous and auditable methods, is expected to enable procurement decisions to be made on the basis of “price per year of protection” rather than unit price per net; this in turn is expected to bring rapid and potentially substantial cost savings. This is important because LLINs represent a large proportion of the global malaria control budget (21).

**Indoor residual spraying**

7. IRS is applicable in many epidemiological settings, provided the operational and resource feasibility are considered in policy and programming decisions. IRS requires specialized spray equipment and techniques, and both the equipment and the quality of application must be scrupulously maintained.

8. Currently 12 insecticides belonging to 4 chemical classes are recommended by WHOPES for IRS (22). An insecticide for IRS is selected in a given area on the basis of data on resistance, the residual efficacy of the insecticide, costs, safety and the type of surface to be sprayed.

9. DDT has a comparatively long residual efficacy (≥ 6 months) as an insecticide for IRS. The use of DDT in agriculture is banned under the Stockholm Convention, but countries can use DDT for IRS for as long as necessary and in the quantities needed, provided that the WHO guidelines and recommendations are followed and until locally appropriate, cost-effective alternatives are available for a sustainable transition from DDT (23).

**Larval control**

10. In a few specific settings and circumstances, the core interventions of IRS and LLINs may be complemented by other methods, such as larval source control including environmental management. However, larval control is appropriate and advisable only in a minority of settings, where mosquito breeding sites are few, fixed, and easy to identify, map and treat. In other circumstances, it is very difficult to find a sufficiently high proportion of the breeding sites within the flight range of the vector (13). Currently 8 compounds and formulations for mosquito larval control are recommended by WHOPES for Larval Source Management (LSM). In Africa, larviciding interventions are most likely to be appropriate in urban settings, and are unlikely to be cost-effective in most rural settings (24).

**2.2.2 Insecticide resistance**

11. The spread of insecticide resistance, especially pyrethroid resistance in Africa, is a major threat for vector control programmes. Insecticide resistance management has to be considered as important as epidemiological cost-effectiveness in all programmatic decisions about vector control, including the selection of insecticides for IRS (25). In particular:

- Resistance management measures should be part of every vector control programme, and deployed pre-emptively, without waiting for signs of the presence of resistance or of control failure.

- A substantial intensification of resistance monitoring is needed, using both bioassay (susceptibility) tests and genetic methods. Resistance monitoring should be seen as a necessary element of any medium- or large-scale deployment of an insecticidal intervention (including LLIN distribution by NGOs); it is the responsibility of the implementing agency to make sure that this testing is done properly. All data on vector resistance should be submitted (in confidence if necessary) to the national malaria control programme within three months of the test performance, even if the study is not yet complete. Donors financing insecticide procurement should ensure that the decision regarding the choice of insecticide is supported by adequate and up-to-date information on resistance among local anopheline vectors.

- Using the same insecticide for multiple successive IRS cycles is not recommended; it is preferable to use a system of rotation with a different insecticide class being used each year. In areas where IRS is the main vector control intervention, this rotation system may include the use of a pyrethroid.

- In areas with high LLIN coverage, pyrethroids should not be used for IRS.

12. Currently, there is heavy reliance on pyrethroids for malaria vector control especially in the form of LLINs. The preservation of pyrethroid susceptibility in target vector populations is therefore an overwhelming priority in the choice of vector control methods. The combination of non-pyrethroid IRS with LLINs involves significantly increased costs, but it has two expected advantages. First, there is evidence that the presence of a non-pyrethroid on the wall reduces the strength of selection for pyrethroid resistance that might occur as a result of an LLIN in the same room; this combination is therefore recommended as a means of insecticide resistance management (25). Second, there is observational evidence suggesting that the combination of IRS and LLINs is more effective than either intervention alone, especially if the combination helps to increase overall coverage with vector control (26). Such evidence, is limited and collection of data from a wide variety of settings is needed. It should be noted that in areas with high levels of LLIN coverage in which pyrethroid resistance is identified, focal IRS is recommended. Broad deployment of IRS and LLINs in combination, while potentially very effective, is currently financially unsustainable.
WHO is currently developing a Global Plan for Insecticide Resistance Management in malaria vectors (GPIRM) through extensive consultation with a wide variety of stakeholders; it will be released in early 2012.

2.2.3 Diagnosis and treatment of malaria

The main objectives of an antimalarial treatment policy are:

- to reduce morbidity and mortality by ensuring rapid, complete cure of Plasmodium infection, thus preventing the progression of uncomplicated malaria to severe and potentially fatal disease, as well as preventing chronic infection that leads to malaria-related anaemia;
- to reduce the frequency and duration of malaria infection during pregnancy and its negative impact on the fetus; and
- to curtail the transmission of malaria by reducing the human parasite reservoir.

The 2nd edition of the WHO Guidelines for the treatment of malaria was published in March 2010 (27). The current WHO recommendations for diagnosis and treatment are as follows:

1. Prompt parasitological confirmation by microscopy, or alternatively by rapid diagnostic tests (RDTs), is recommended in all patients with suspected malaria before treatment is started. Antimalarial treatment solely on the basis of clinical suspicion should only be considered when a parasitological diagnosis is not accessible.\(^1\) Treatment based on diagnostic testing is good clinical practice and has the following advantages over presumptive treatment of all fever episodes:
   - improved care of parasite-positive patients because of confirmation of infection;
   - identification of parasite-negative patients, in whom another diagnosis must be sought and treated accordingly;
   - avoidance of antimalarial medicine use in parasite-negative patients, thereby reducing side effects, drug interactions and selection pressure for drug resistance, and potentially resulting in financial savings;
   - better public trust in the efficacy of artemisinin-based combination therapy (ACT) when it is used only to treat confirmed malaria cases; and
   - better public trust in diagnosis and treatment of non-malaria causes of febrile illness.

2. Uncomplicated \textit{P. falciparum} malaria should be treated with an ACT. In addition to an ACT, a single dose of primaquine is recommended for treatment of \textit{P. falciparum} malaria as an anti-gametocyte medicine (particularly as a component of a pre-elimination or an elimination programme), subject to consideration of the risks of haemolysis in patients with glucose-6-dehydrogenase (G6PD) deficiency.

3. \textit{P. vivax} malaria should be treated with chloroquine in areas where this drug is effective; an appropriate ACT (not artesunate plus sulfadoxine-pyrimethamine) should be used in areas where \textit{P. vivax} resistance to chloroquine has been documented. Both chloroquine and ACTs should be combined with a 14-day course of primaquine for the treatment of \textit{P. vivax} malaria in order to prevent relapses, subject to consideration of the risk of haemolysis in patients with G6PD deficiency.

4. The 5 ACTs currently recommended for use are artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine, and dihydroartemisinin plus piperaquine. The choice of the ACT should be based on the efficacy of the combination in the country or area of intended use.

5. Artesinin and its derivatives should not be used as oral monotherapies for the treatment of uncomplicated malaria as poor adherence to the required 7 days of treatment results in partial clearance of malaria parasites which will promote resistance to this critically important class of antimalarials.

6. Severe malaria should be treated with a parenteral artemunate and followed by a complete course of an effective ACT as soon as the patient can take oral medications. Where complete parenteral treatment of severe malaria is not possible, e.g. in peripheral health posts, patients should be given pre-referral treatment and referred immediately to an appropriate facility for further treatment. Options available for pre-referral treatment are: artesunate (rectal), quinine (IM), artesunate (IM) or artemether (IM).

7. In settings with limited health facility access, diagnosis and treatment should be provided at community level through a programme of community case management (formerly known as home-based management) of malaria. The introduction of parasitological testing of malaria allows the identification of non-malaria febrile illnesses, which also need appropriate care, notably pneumonia and other causes of childhood mortality. The successful implementation of community case management therefore requires diagnosis and treatment for other frequent causes of febrile disease. This new strategy is termed integrated community case management (iCCM) of childhood illness.

2.2.4 Intermittent preventive treatment

Intermittent preventive treatment is the administration of a full course of an effective antimalarial treatment at specified time points to a defined population at risk of malaria, regardless of whether the recipients are parasitaemic, with the objective of reducing the malaria burden in the target population.

1. \textit{Intermittent preventive treatment in pregnancy (IPTp)}: All pregnant women at risk of \textit{P. falciparum} infection in countries in sub-Saharan Africa with stable malaria transmission, should receive at least 2 doses of sulfadoxine-pyrimethamine (SP), given at the first and second scheduled antenatal care visits (at least one month apart) after “quickening” (the first noted movement of the fetus). The doses of SP should be taken under direct observation during the antenatal visits (28).

2. \textit{Intermittent preventive treatment in infants (IPTi)}: All infants at risk of \textit{P. falciparum} infection in countries in sub-Saharan Africa with moderate to high malaria transmission should receive 3 doses of SP along with the DTP2, DTP3 and measles immunization through the routine immunization programme (29, 30).

\(^1\) Within a short time (less than 2 hours) of the patient’s presentation at the point of care.
2.2.5 Resistance to antimalarial drugs

Antimalarial drug resistance is a major public health problem which hinders the control of malaria. Continuous monitoring of the efficacy of and resistance to antimalarial drugs is important to inform treatment policy and ensure early detection of changing patterns of resistance.

Therapeutic drug efficacy studies allow measurement of the clinical and parasitological efficacy of medicines and the detection of subtle changes in treatment outcome when monitored consistently over time. Therapeutic drug efficacy studies are considered the gold standard for determining antimalarial drug efficacy, and their results are the primary data used by national malaria control programmes to revise the national malaria treatment policies for first- and second-line drugs and ensure appropriate management of clinical cases. Therapeutic drug efficacy studies are also used to detect suspected artemisinin resistance, defined as an increase in parasite clearance time, as evidenced by ≥ 10% of cases with parasites detectable on day 3 after treatment with an ACT.

BOX 2.2
The Global Plan for Artemisinin Resistance Containment (GPARC)

The Global Plan for Artemisinin Resistance Containment (GPARC) was released in January 2011, in response to the emergence of artemisinin resistance in the Greater Mekong subregion. The goal of the GPARC is to protect ACTs as an effective treatment for *P. falciparum* malaria by defining priorities for the containment and prevention of artemisinin resistance. Five activities are recommended by the GPARC as important for successful management of artemisinin resistance:

1. **Stop the spread of resistant parasites.** In areas for which there is evidence of artemisinin resistance, an immediate comprehensive response using a combination of malaria control and elimination measures is needed to stop the survival and spread of resistant parasites.

2. **Increase monitoring and surveillance to evaluate the threat of artemisinin resistance.** Regular monitoring and surveillance are essential to rapidly identify new foci of resistant parasites and to provide information for containment and prevention activities. Countries endemic for malaria should undertake routine monitoring of antimalarial drugs at sentinel sites every 24 months in order to detect changes in their therapeutic efficacy (31).

3. **Improve access to diagnostics and rational treatment with ACTs.** Programmes should ensure: consistent, accurate diagnostic testing of suspected malaria cases; better access to ACTs for confirmed cases; compliance with ACT treatment; and removal from the market of oral artemisinin-based monotherapies as well as substandard and counterfeit antimalarial medicines.

4. **Invest in artemisinin resistance-related research.** Research is important to improve understanding of resistance and the ability to manage it. Priority should be given to research in five disciplines should be a priority: laboratory research, research and development, applied and field research operational research, and mathematical modeling.

5. **Motivate action and mobilize resources.** Successful implementation of the GPARC will depend on motivating many stakeholders at global, regional and national levels to support or conduct the recommended activities.

The GPARC defines three tiers based on the evidence of artemisinin resistance. Each endemic country should evaluate its level of risk and apply the GPARC recommendations accordingly.

**Tier 1:** Areas with credible evidence of artemisinin resistance. The recommended response for tier 1 areas is a combination of intensified malaria control and tools for elimination including: parasitological diagnosis for all patients with suspected malaria; a full course of quality-assured ACTs plus primaquine for confirmed cases; vector control to lower transmission and minimize the spread of resistant parasites; and launch of specific activities to contain or eliminate resistant parasites such as intensified monitoring of therapeutic efficacy near current foci to track the spread of artemisinin resistance; enforcement to eliminate use of oral artemisinin-based monotherapies and substandard and counterfeit antimalarial medicines; programmes to reach mobile and migrant populations with adequate prevention, diagnosis and treatment; and epidemiological or transmission-reduction tools.

**Tier 2:** Areas with significant inflow of mobile and migrant populations from tier 1 areas or shared borders with tier 1 areas. As in tier 1 areas, the recommendations largely mirror those for malaria control. The specific recommendations for tier 2 areas are: intensify and accelerate malaria control activities; implement specific measures to manage the potential spread of resistant parasites from tier 1 areas, including programmes to reach mobile and migrant populations; launch of activities specific for the prevention of resistance, in particular intensified monitoring of therapeutic efficacy to track the spread of artemisinin resistance; and education and enforcement to eliminate the use of oral artemisinin-based monotherapies and substandard and counterfeit antimalarial medicines.

**Tier 3:** *P. falciparum* endemic areas which have no evidence of artemisinin resistance and have limited contact with tier 1 areas. In tier 3, the main objective is to prevent the emergence of artemisinin resistance in implementation and scale-up of effective control measures, including: increasing access to parasitological diagnosis; improving access to quality-assured ACTs for confirmed cases; increasing coverage with vector control to limit malaria transmission; monitoring the therapeutic efficacy of first- and second-line treatments every 24 months; introducing or enforcing actions to eliminate the use of oral artemisinin-based monotherapies or poor-quality drugs.

For more details see http://www.who.int/malaria/publications/atoz/artemisinin_resistance_containment_2011.pdf
To interpret and compare results within and between regions and to follow trends over time, therapeutic efficacy monitoring must be conducted with similar standardized procedures. WHO updated the protocol for assessing antimalarial drug efficacy in 2009 (31). WHO has also developed a guideline on genotyping malaria parasites to distinguish between reinfection and recrudescence, which is necessary as part of the therapeutic efficacy testing (32). The following recommendations are drawn from the 2009 edition of Methods for surveillance of antimalarial drug efficacy (31).

1. National malaria control programmes should establish sentinel sites (selected health facilities) for the surveillance of antimalarial drug efficacy. Experience suggests that 4–8 sites per country will achieve a balance between representativeness and practicality. The sentinel sites should represent all the epidemiological strata in the country but it is essential to select a ‘manageable’ number of sites to ensure proper monitoring and supervision.

2. Efficacy of first- and second-line medicines should be tested at least once every 24 months at all sites. For the purposes of comparability, assessments should always be conducted at the same time of year.

3. A follow-up of 28 days is recommended as the minimum duration for medicines with elimination half-lives of less than 7 days (amodiaquine, artemisinin derivatives, atovaquone–proguanil, chloroquine, lumefantrine, quinine, and sulfadoxine–pyrimethamine). For medicines with longer elimination half-lives (mefloquine, piperaquine), a longer follow-up period of 42 days is necessary.

4. The standard protocol to test the efficacy of medicines against P. falciparum needs adjustment for P. vivax. Since P. vivax infection has a dormant liver stage and therefore the potential to relapse, many countries recommend primaquine therapy for radical cure. Administration of primaquine concurrently or soon after administration of chloroquine may conceal resistance to chloroquine alone, resulting in underestimation of the risk of therapeutic failure or resistance to chloroquine. Therefore, in certain cases primaquine therapy should be postponed until after the 28-day follow-up. Nonetheless, if local health policy includes mandatory administration of primaquine with chloroquine, the failure rate should be considered to be that of the combination regimen.

5. Countries should consider changing the first-line treatment for malaria if the total failure (defined as the sum of the patients presenting with early treatment failure, late clinical failure or late parasitological failure) rate exceeds 10%; the selection of a new antimalarial treatment for use at public health level in the context of national treatment guidelines should be based on an average cure rate of ≥ 95% as assessed in clinical trials (27).

While therapeutic efficacy studies conducted according to a standard protocol provide an excellent indication of drug efficacy, additional studies are needed to confirm and characterize drug resistance. These additional studies include (i) in vitro studies to measure the intrinsic sensitivity of parasites to antimalarial drugs; (ii) molecular marker studies to identify genetic mutations and subsequently confirm the presence of mutations in blood parasites and (iii) pharmacokinetic studies to characterize drug absorption and drug action in the body. WHO has prepared a field manual on in vitro assays (33) and on methods for assessing exposure to antimalarial drugs (34).

Over the last decade, most countries endemic for P. falciparum have shifted their national treatment policies to ACTs, although therapeutic efficacy studies are still not routinely conducted in many of these countries (35). Resistance to artemisinins has been confirmed in the Greater Mekong subregion. Neither the mechanism of artemisinin resistance, nor a molecular marker to screen for it, has yet been identified. The current working definition of artemisinin resistance is:

- an increase in parasite clearance time, as evidenced by ≥ 10% of cases with parasites detectable on day 3 after treatment with an ACT (suspected resistance); or
- treatment failure after treatment with an oral artemisinin-based monotherapy with adequate antimalarial blood concentration, as evidenced by the persistence of parasites for 7 days, or the presence of parasites at day 3 and recrudescence within 28–42 days (confirmed resistance)1.

Following the confirmation of artemisinin resistance, the Global Plan for Artemisinin Resistance (GPARC) was developed (35), outlining the necessary actions to contain and prevent resistance to artemisinins (see Box 2.2).

### 2.3 Malaria elimination

From a country perspective, interruption of local mosquito-borne malaria transmission, i.e. elimination of malaria, is the ultimate goal of malaria control. The WHO recommendations regarding malaria elimination are summarized below: (36, 37)

1. In areas of high, stable transmission, where a marked reduction in malaria transmission has been achieved (as may be indicated by slide positivity rates of less than 5%4), a ‘consolidation period’ should be introduced, in which (i) control interventions are sustained, even in the face of limited disease; (ii) health services adapt to the new clinical and epidemiological situation with a lower case load and reduced levels of immunity; and (iii) surveillance systems are strengthened to allow rapid response to new cases. This transformation phase precedes a decision to re-orient programmes towards elimination.

2. Countries with low, unstable transmission (as may be indicated by less than 1 case per 1000 population per year should be encouraged to proceed to malaria elimination, with falciparum elimination preceding vivax elimination where these species co-exist. Before making this decision, however, countries should take account of the overall feasibility, including entomologic situation, programmatic capacity, fiscal commitment, political commitment, and potential threats to success, including the malaria situation in neighbouring countries. Malaria elimination may require regional initiatives and support and will require strong political commitment.

3. Countries with an absence of locally acquired malaria cases for 3 consecutive years, and with sufficiently robust surveillance and reporting systems in place to demonstrate this achievement, are eligible to request WHO to initiate procedures to certify that they are malaria-free.

1 This definition is prone to confounding factors (known and unknown) such as splenectomy, haemoglobin abnormalities and reduced immunity.

2 These milestones should be adjusted for each country and situation, keeping in mind the resources available for notification, investigation and follow-up of malaria cases.
4. Failure to sustain malaria control will result in a resurgence of malaria, as has happened in the past, and must be avoided. Therefore, public and government commitment to intensified malaria control and elimination needs to be sustained, even when the malaria burden has been greatly reduced.

5. Because malaria control today relies heavily on a limited number of tools, in particular artemisinin derivatives and pyrethroids, which could potentially become less effective because of resistance, the development of new tools is a necessary priority, particularly for vector control and other preventive measures, diagnostic testing, treatment and surveillance.

**BOX 2.3 Definitions (37)**

*Malaria control:* reducing the malaria disease burden to a level at which it is no longer a public health problem.

*Malaria elimination:* the interruption of local mosquito-borne malaria transmission; reduction to zero of the incidence of infection caused by human malaria parasites in a defined geographical area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required.

*Certification of malaria elimination:* the official recognition of malaria-free status granted by WHO after it has been proven beyond reasonable doubt that the chain of local human malaria transmission by Anopheles mosquitoes has been fully interrupted in an entire country for at least 3 consecutive years.

*Malaria eradication:* permanent reduction to zero of the worldwide incidence of infection caused by a particular malaria parasite species. Intervention measures are no longer needed once eradication has been achieved.

2.4 **Indicators**

The UN Inter-agency and Expert Group on MDG Indicators has established the following indicators for malaria (8):

- **6.6** Incidence and death rates associated with malaria
- **6.7** Proportion of children under 5 years sleeping under insecticide-treated bednets
- **6.8** Proportion of children under 5 years with fever who are treated with appropriate antimalarial medicines.

As policies and strategies for malaria control have evolved over the last decade, standard indicators have been adapted to reflect the latest recommendations. For example, indicator 6.7 has been expanded to consider also the proportion of the population of all age groups that sleep under ITNs (38). Similarly, indicator 6.8 does not reflect current policy recommendations to provide a parasitological test for all fever cases.

Table 2.2 summarizes 28 indicators recommended by WHO for use by national malaria programmes to measure coverage with malaria control interventions (ITNs, IRS, IPTp, diagnosis and treatment) and their epidemiological impact. The selection of indicators draws upon: the Abuja Declaration in 2000 (9), the resolution of the World Health Assembly in 2005 (1), the RBM Global Malaria Action Plan (3), the work of the RBM Monitoring and Evaluation Reference Group (MERG) (39), previous editions of the World Malaria Report (38, 40, 41) and guidelines on *Universal Access to Malaria Diagnostic Testing* (42). Of the 28 indicators, 17 are derived from routine information systems and would typically be available for monitoring on a monthly basis. Not all indicators are applicable to every epidemiological setting and individual programmes would use only a sub-set of the 17 routine indicators. The remaining 10 indicators are derived from household surveys and, while these would not normally be available every year for every country, they provide complementary information for programme assessment.

The major changes from the indicator list in the World Malaria Report 2010 are: (i) the addition of an indicator on the proportion of households with at least one ITN for every two people; (ii) the case management indicator of the proportion of malaria cases receiving appropriate treatment is modified to focus solely on cases with a positive test result, so that the indicator is now the proportion of confirmed malaria cases receiving first-line antimalarial treatment; (iii) the addition of an indicator, the proportion of all antimalarial medicines that are recommended as first-line therapies.

2.5 **Policy development**

In 2011 the WHO Global Malaria Programme embarked on a review and re-design of its policy-setting process so that it is more responsive to a rapidly evolving malaria landscape. The result is the establishment of the Malaria Policy Advisory Committee (MPAC), which will provide independent advice to WHO regarding policy recommendations to control and eliminate malaria (43).

The MPAC will advise WHO specifically on: appropriate malaria policies and standards based on data from malaria programme implementation by member states and malaria control partners as well as reviews of the best available evidence; engagement of WHO in malaria-related initiatives; major issues and challenges for achieving global malaria goals; and the identification of priority activities to address identified challenges. The MPAC is scheduled to become operative during the first quarter of 2012.

---

1. Updated guidelines on indicators from household surveys are being developed by RBM MERG and are due to be issued in 2012.
### TABLE 2.2
Malaria indicators, targets and sources of data

#### Trends in malaria cases and deaths

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Malaria cases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Confirmed malaria cases (microscopy or RDT) per 1000 persons per year</td>
<td>Confirmed malaria cases per year $\times 1000$</td>
<td>Population</td>
<td>All ages, &lt; 5, male, female, PCD, ACD</td>
<td>Routine surveillance system or HMIS</td>
<td>Reduction of cases per 1000 of $\geq 50%$ by 2010, and $\geq 75%$ by 2015 in comparison with 2000</td>
<td></td>
</tr>
<tr>
<td>1.2 Inpatient malaria cases per 1000 persons per year</td>
<td>No. of inpatient malaria cases per year $\times 1000$</td>
<td>Population</td>
<td>All ages, &lt; 5, male, female</td>
<td>Routine surveillance system or HMIS</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### In low transmission / elimination settings:

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.3 Number of active foci reported per year</td>
<td>Number of active foci reported per year</td>
<td>None</td>
<td>None</td>
<td>Routine surveillance system</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 Number of cases by classification</td>
<td>Number of cases by classification</td>
<td>None</td>
<td>Local (introduced, indigenous, relapsing), imported, induced</td>
<td>Routine surveillance system</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Malaria transmission

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 Malaria test positivity rate</td>
<td>No. of laboratory-confirmed malaria cases</td>
<td>No of suspected malaria cases with parasite-based test</td>
<td>Microscopy, RDT, P.f., P.v., PCD, ACD</td>
<td>Routine surveillance system or HMIS</td>
<td>No target set. Indicates level of control</td>
<td></td>
</tr>
</tbody>
</table>

#### In high-transmission areas:

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.6 Proportion of children aged 6-59 months with evidence of malaria infection</td>
<td>Number of children aged 6-59 months with malaria infection detected by microscopy or RDT</td>
<td>Total number of children aged 6-59 months tested for malaria parasites by microscopy or RDT</td>
<td>Household survey</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Malaria deaths

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.7 Inpatient malaria deaths per 1000 persons per year</td>
<td>No. of inpatient malaria deaths per year ($&lt; 5$ years or total) $\times 1000$</td>
<td>Population</td>
<td>All ages, &lt; 5, male, female, pregnant women</td>
<td>Routine surveillance system or HMIS</td>
<td>Reduction in deaths per 1000 of $\geq 50%$ by 2010, and $\geq 75%$ by 2015 in comparison with 2000</td>
<td></td>
</tr>
<tr>
<td>1.8 Malaria-specific deaths per 1000 persons per year</td>
<td>No. of malaria deaths per year $\times 1000$</td>
<td>Population</td>
<td>All ages, &lt; 5, male, female, pregnant women</td>
<td>Verbal autopsy (surveys), complete or sample vital registration systems</td>
<td>Reduction in deaths per 1000 of $\geq 50%$ by 2010, and $\geq 75%$ by 2015 in comparison with 2000</td>
<td></td>
</tr>
</tbody>
</table>

#### In high-transmission areas:

<table>
<thead>
<tr>
<th>Impact measure</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.9 All-cause under 5 mortality rate (5q0)</td>
<td>No. of deaths in children &lt; 5 years from all causes $\times 1000$</td>
<td>Number of live births</td>
<td>Household surveys, complete or sample vital registration systems</td>
<td>No specific malaria target set</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Coverage with interventions

<table>
<thead>
<tr>
<th>Control strategy</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vector control</strong></td>
<td>2.1</td>
<td>Proportion of population at risk potentially covered by ITNs distributed</td>
<td>No. of persons with ITNs distributed</td>
<td>No. of persons at risk of malaria</td>
<td>Household survey</td>
<td>≥ 80%</td>
</tr>
<tr>
<td></td>
<td>2.2</td>
<td>Proportion of targeted risk group receiving ITN</td>
<td>No. of ITNs distributed to risk groups</td>
<td>No. of persons in risk groups targeted for receiving ITN</td>
<td>Household survey</td>
<td>≥ 80%</td>
</tr>
<tr>
<td></td>
<td>2.3</td>
<td>Proportion of households with at least one ITN</td>
<td>Number of households surveyed with at least one ITN</td>
<td>Total number of households surveyed</td>
<td>Household survey</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.4</td>
<td>Proportion of households with at least one ITN for every two people</td>
<td>Number of households surveyed with at least one ITN for every two people</td>
<td>Total number of households surveyed</td>
<td>Household survey</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.5</td>
<td>Proportion of individuals with access to an ITN in a household</td>
<td>Number of individuals with access to an ITN in a household</td>
<td>Total number of individuals who slept in surveyed households the previous night</td>
<td>Household survey</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.6</td>
<td>Proportion of individuals who slept under an ITN the previous night</td>
<td>Number of individuals who slept under an ITN the previous night</td>
<td>Total number of individuals who slept in surveyed households the previous night</td>
<td>Household survey</td>
<td>≥ 80%</td>
</tr>
<tr>
<td></td>
<td>2.7</td>
<td>Percentage of population at risk protected by IRS</td>
<td>No. of persons protected by IRS</td>
<td>No. of persons at risk for malaria</td>
<td>Routine data from national malaria control programme</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.8</td>
<td>Households sprayed with insecticide among those targeted</td>
<td>No. of households sprayed in 1 year according to national guidelines</td>
<td>No. of households targeted according to national guidelines</td>
<td>Routine data from national malaria control programme</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>2.9</td>
<td>Proportion of households with at least one ITN and/or sprayed by IRS in the last 12 months.</td>
<td>Number of households that have at least one ITN and/or have been sprayed by IRS in the last 12 months.</td>
<td>Total number of households surveyed</td>
<td>Household survey</td>
<td></td>
</tr>
</tbody>
</table>

## Diagnosis and treatment

| | 2.10 | Percentage of all suspected malaria cases that receive parasitological test | No. of all suspected malaria cases that receive parasitological test | No. of all suspected malaria cases | Routine surveillance system or HMIS | ≥ 90% |
| | 2.11 | Proportion of children under 5 years old with fever in the last 2 weeks who had a finger or heel stick | Number of children under 5 years old who had a fever in the previous 2 weeks who had a finger/heel stick | Total number of children under 5 years old who had a fever in the previous 2 weeks | Household survey | |
| | 2.12 | Percentage of confirmed malaria cases receiving first-line antimalarial treatment according to national policy | No. of confirmed malaria cases receiving first-line antimalarial treatment at health facility | No. of confirmed malaria cases at health facility | Routine surveillance system, HMIS or special studies | 100% |
| | 2.13 | Proportion of first-line treatments among children under five years old with fever in the last two weeks who received any antimalarial medicines | Proportion of children under five years old with fever in the last two weeks receiving recommended first-line treatment | Proportion of children under five years old with fever in the last two weeks receiving antimalarial medicine | Household survey | 100% |

**In high-transmission areas:**

| | 2.14 | Pregnant women who received two doses of intermittent preventive therapy | No. of pregnant women who received two doses of intermittent preventive therapy | No. of pregnant women who made at least one antenatal care visit in 1 year | Routine data from HMIS | ≥ 80% |
| | 2.15 | Proportion of women who received intermittent preventive treatment for malaria during ANC visits during their last pregnancy | No. of women who received two or more doses of a recommended antimalarial drug treatment during ANC visits to prevent malaria during their last pregnancy that led to a live birth within the last 2 years | Total number of women surveyed who delivered a live baby within the last 2 years | Household survey | ≥ 80% |
### Management systems

<table>
<thead>
<tr>
<th>System</th>
<th>Indicator</th>
<th>Numerator</th>
<th>Denominator</th>
<th>Break-down</th>
<th>Data source</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Supplies</strong></td>
<td>3.1 Proportion of health facilities without stock-outs of key commodities by month</td>
<td>Number of health facilities without stock-outs of key commodities by month</td>
<td>No. of health facilities</td>
<td>ACTs, RDTs, ITNs</td>
<td>Routine reporting system or HMIS</td>
<td>100%</td>
</tr>
<tr>
<td><strong>Reporting</strong></td>
<td>3.2 Annual blood examination rate</td>
<td>No. of all suspected malaria cases that receive parasitological test</td>
<td>Population</td>
<td>ACD, PCD</td>
<td>Routine surveillance system or HMIS</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.3 Completeness of monthly health facility reports</td>
<td>No. of health facility reports received each month</td>
<td>No. of health facility reports expected each month</td>
<td>Commodities distributed, stock-outs, outpatient cases, inpatient cases</td>
<td>Routine surveillance system or HMIS</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td></td>
<td>3.4 Proportion of private facilities reporting to national malaria surveillance system</td>
<td>Number of private facilities in areas at risk for malaria reporting to national malaria surveillance system</td>
<td>Number of private facilities in areas at risk for malaria</td>
<td></td>
<td>Routine surveillance system</td>
<td></td>
</tr>
</tbody>
</table>

From references 36–42. Indicators derived from household surveys are in italics.

RDT, rapid diagnostic test; MDG, Millennium Development Goal; ITN, insecticide-treated net; IRS, indoor residual spraying; ACD active case detection; PCD passive case detection

a Use only if > 90% of suspected cases have examination for parasites (microscopy or RDT).

b Marker for severe malaria.

c Malaria test positivity rate < 5% during the malaria season is considered as an indicator of readiness for transition from control stage to pre-elimination stage.

d An updated RBM target was adopted in 2011: “near zero malaria deaths” by 2015. This target is more ambitious than the target of 75% reduction in malaria deaths by 2015.

e This indicator is estimated from the number of LLINs or ITNs distributed by ministries of health and partners. LLINs are assumed to protect for 3 years and conventional ITNs or retreated nets for 1 year. A single net is assumed to protect two persons. Hence the number of people potentially covered is the 2 * (number of LLINs delivered in last three years + number of conventional ITNs and retreatments delivered in last year). This indicator measures distribution and not hanging or use.

f This indicator is estimated from the number of ITNs available in each household. Each net is assumed to protect two persons. Thus a household with 5 residents will require 3 ITNs.

g Parasitological tests include microscopy and RDT.

h Per WHO recommendations all suspected cases should be given a diagnostic test and only treated with an antimalarial if they test positive for *Plasmodium*.

i Comments h apply to indicator 2.12 also. The intention is to treat all persons with an appropriate antimalarial medicine; however, children are at greatest risk, especially in areas of high transmission and many household surveys do not ask about antimalarial treatment over age 5 years. In areas of low transmission, it is recognized that this indicator may be less useful.

j This indicator can vary depending on data collection forms and reporting channels. For example, the inpatient data channel may be separate from the outpatient data channel, or the commodities and disease surveillance data channels may be combined.

k Facilities should report even if they have zero cases.

### References


