

WHO Malaria Technical Updates (Case Management and other uses of antimalarial medicines)

11th RBM CMWG Annual Meeting



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Global **Malaria** Programme



**World Health
Organization**

- **The Global Malaria Picture**

- 87 countries and territories
- Half world at risk (3.2 billion)

- **highly concentrated in sub-Saharan Africa**

- Globally, there were an estimated 241 million cases of malaria \approx 95% in Africa
- Globally, 627 000 deaths - 96% in Africa,
- malaria was the 4th highest cause of death among children in Africa (10% of child death in sub-Saharan Africa), - claiming the life of 1 child every 2 minutes.

GTS: Vision, goals, milestones and targets

Vision: A world free of malaria			
Goals	Milestones		Targets
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	≥40%	≥75%	≥90%
2. Reduce malaria case incidence globally compared with 2015	≥40%	≥75%	≥90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria-free	Re-establishment prevented	Re-establishment prevented	Re-establishment prevented

GTS: -Progress towards first milestone point (2020)

Goals	Milestones		Targets
	2020	2025	2030
1. Reduce malaria mortality rates globally compared with 2015	At least 40% ❌	At least 75%	At least 90%
2. Reduce malaria case incidence globally compared with 2015	At least 40% ❌	At least 75%	At least 90%
3. Eliminate malaria from countries in which malaria was transmitted in 2015	At least 10 countries ✓	At least 20 countries	At least 35 countries
4. Prevent re-establishment of malaria in all countries that are malaria free	Re-establishment prevented ✓	Re-establishment prevented	Re-establishment prevented

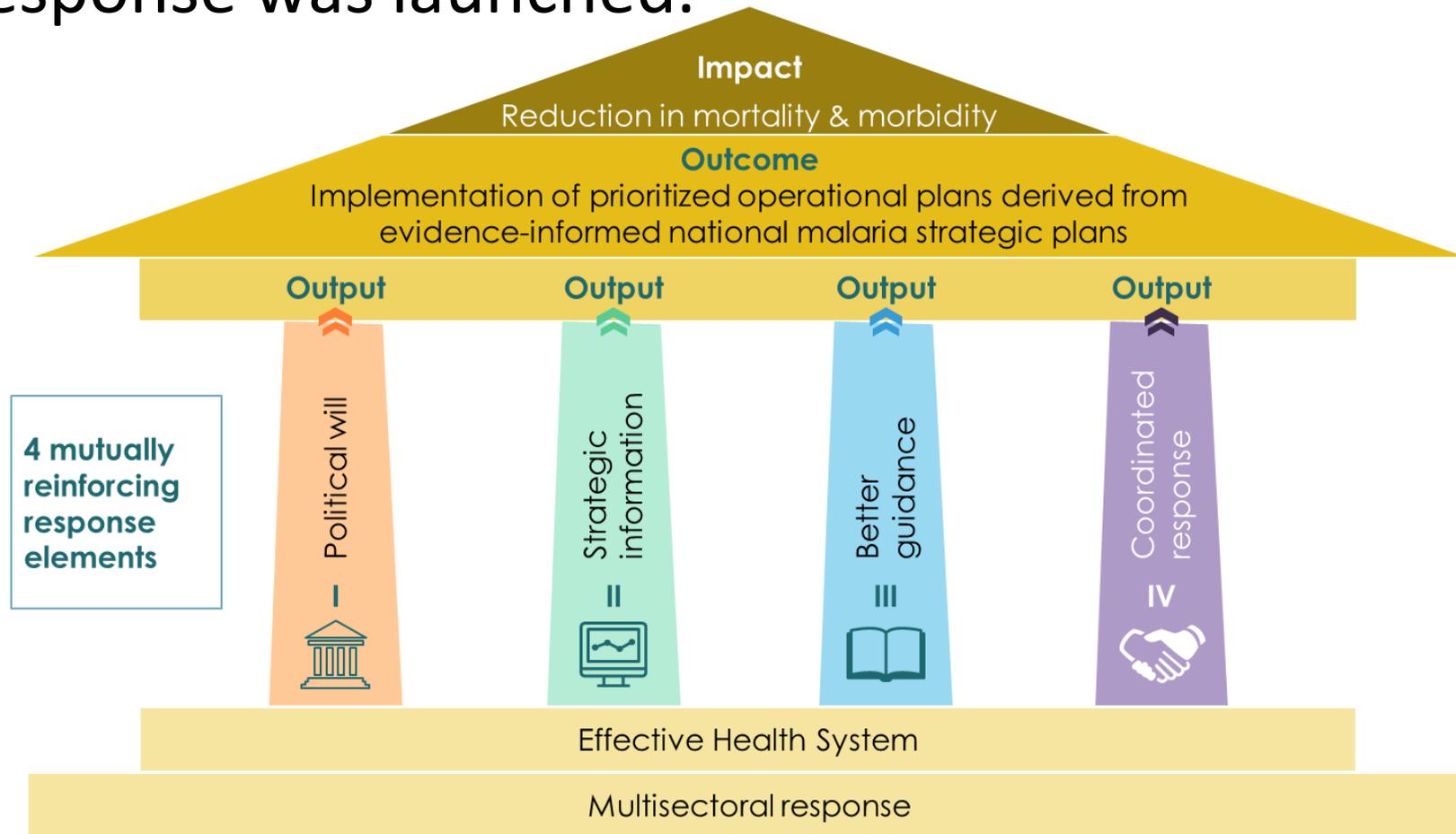
Global Technical Strategy for malaria 2016-2030

- Mortality reduction
 - 18% reduction achieved, but 22% off track
- Malaria cases
 - 3% reduction achieved, but 37% off track

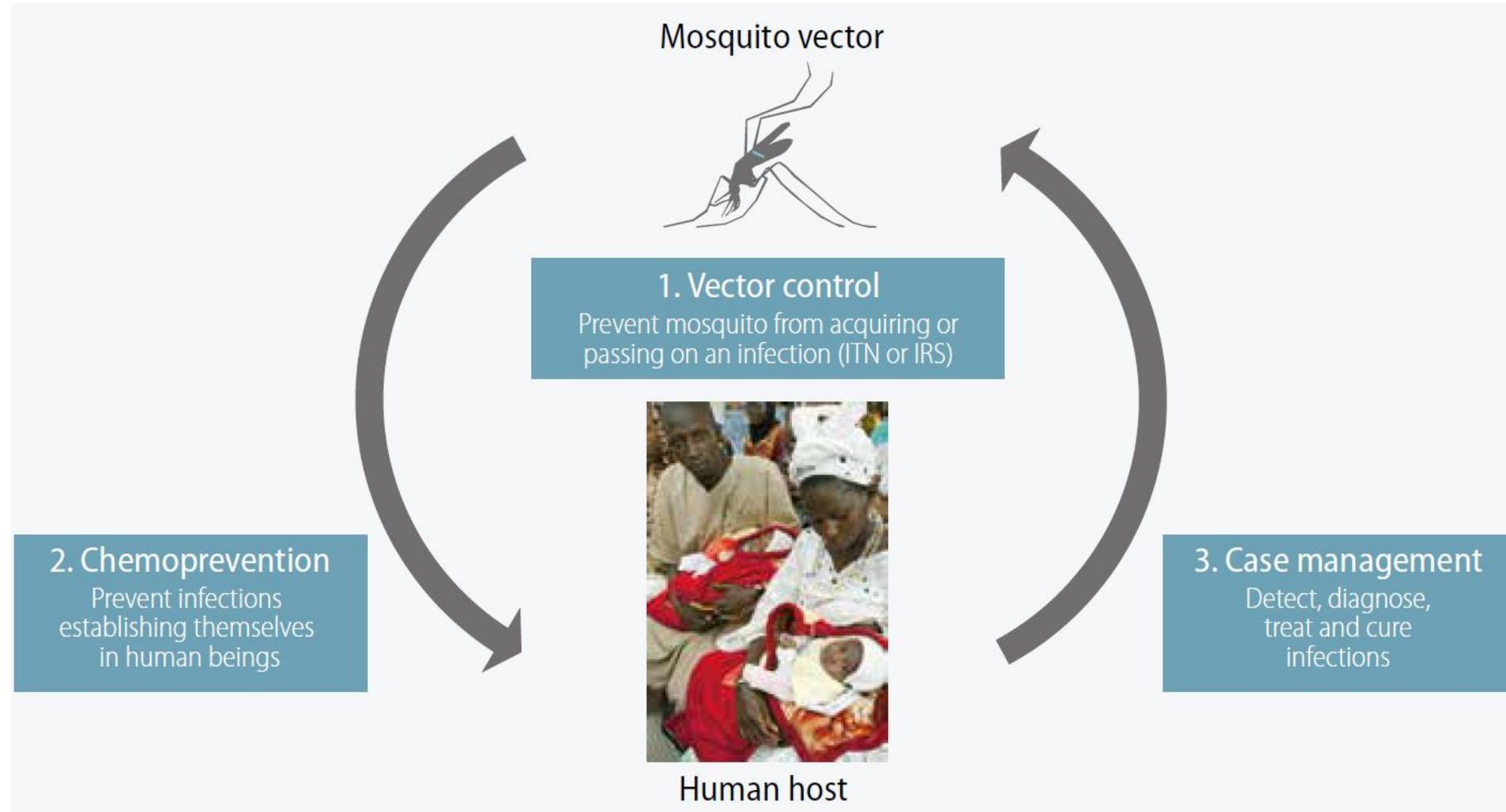
Off track to meet global targets

To get back on track, in 2018,

High Burden to High Impact: a targeted malaria response was launched.



Main malaria prevention and treatment strategies



Key antimalarial interventions & strategies

Prevention

- Insecticide-treated mosquito nets
- Indoor Residual Spraying

Preventive Chemotherapy

- IPT in pregnancy (IPTp)
- Perennial Malaria Chemoprevention (PMC /IPTi+)
- SMC
- IPT in School Children
- Post Discharge malaria chemoprevention
- MDA

Malaria vaccine

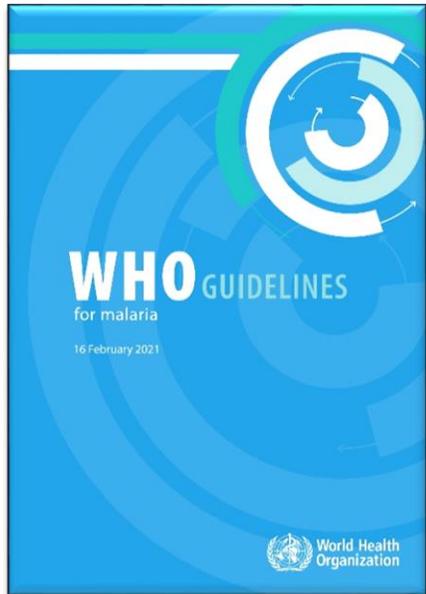
Diagnosis & Treatment

- Parasite based diagnosis
 - Microscopy
 - Rapid Diagnostic Tests
 - Artemisinin-based combination therapies (ACTs)
 - Severe Malaria
 - Artesunate
- Case management service delivery areas::
- Health facilities
 - Community Case Management
 - Private sector

Surveillance, M & E

- Routine HMIS
- Malaria surveillance and response systems
- Household surveys
- Health Facility Surveys

Strengthening health systems in endemic countries



- WHO Guidelines for Malaria (2021)
 - These consolidated guidelines replace 2 guideline documents on the WHO website: the Guidelines for the treatment of malaria, 3rd edition and the Guidelines for malaria vector control.
 - The sections in the WHO Guidelines for malaria includes
 - Prevention (Vector control, preventive chemotherapies and Vaccine)
 - Case Management
 - Elimination and prevention of re-introduction
 - Surveillance
 - As new evidence becomes available, the recommendations will be reviewed and updated, where appropriate, **using WHO's transparent and rigorous guideline development process.**
- Published in February 2021;
- Latest update – 3rd June 2022, and will be undated on a living basis
- Available online: <https://www.who.int/publications/i/item/guidelines-for-malaria>

Malaria Case Management



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- Malaria diagnosis (clinical & parasitological confirmation)
- Prompt and effective treatment :
- Support intervention for effective case management
 - Monitoring resistance of antimalarial medicines (therapeutic efficacy monitoring)
 - Pharmacovigilance



- All suspected malaria cases should have a parasitological test (microscopy or RDT) to confirm the diagnosis.
- Deployment of both microscopy and RDTs should be supported by a quality assurance programme
 - The results of parasitological diagnosis should be available within less than two hours of the patient presenting. In the absence or delay, patients with suspected severe malaria, and other high-risk groups, should be treated on clinical grounds.



- Treat children and adults with uncomplicated *P. falciparum* malaria (excluding pregnant women in their first trimester*) with an ACT.
 - artemether plus lumefantrine; artesunate plus amodiaquine; artesunate plus mefloquine; dihydroartemisinin plus piperazine; artesunate plus sulfadoxine-pyrimethamine; artesunate plus pyronaridine*
- Reducing transmissibility of treated *P. falciparum* infections
 - In low transmission areas, give a single dose of 0.25mg/kg primaquine along with ACT to patients with *P. falciparum* malaria (excluding pregnant and breastfeeding women and infants aged <6 months) to reduce transmission. G6PD testing is not required.

* Ongoing revision



- Treat pregnant women in the first trimester with seven days of quinine plus clindamycin (*use an ACT if quinine is not available or adherence to 7 days quinine not assured*). – **Currently under review***
- Treat infants weighing less than 5 kg with an ACT dosed at the same mg/kg target as for children weighing 5 kg
- In people who have HIV/AIDS avoid AS+SP if on treatment with co-trimoxazole and avoid AS+AQ if on treatment with efavirenz.
- Treat travelers returning to non-endemic settings with uncomplicated *P. falciparum* malaria with an ACT

*** Ongoing revision**



- In areas with chloroquine susceptible *P. vivax*, treat using either an ACT (*excluding pregnant women in their first trimester*) or chloroquine.
- In areas with chloroquine resistant *P. vivax*, treat with an ACT (*excluding pregnant women in their first trimester*).
- Treat pregnant women in their first trimester with **CQ resistant *P.vivax* malaria with quinine***

*** Ongoing revision**



- The G6PD status of patients should be used to guide the administration of primaquine for relapse prevention
- Where status is unknown and G6PD testing is unavailable, the decision to prescribe primaquine must be based on an assessment of the risks and benefits of treating versus not treating
- To prevent future relapse, treat people with vivax or ovale malaria (excluding pregnant or women breastfeeding, infants < 6 months of age, and people with G6PD deficiency) with a 14-day* course (0.25-0.5mg/kg daily) of primaquine in all transmission setting
- In people with moderate G6PD deficiency, consider relapse prevention with primaquine 0.75 mg base/kg once a week for 8 weeks under close medical supervision.
- In women who are pregnant or breastfeeding, consider weekly chemoprophylaxis with chloroquine until delivery and breastfeeding is complete, then treat with 14 days of primaquine to prevent future relapse.

* Ongoing revision



- **Therapeutic objectives**
 - Main objective is to prevent the patient from dying
 - Secondary objectives are to prevent disabilities and prevention of recrudescence infection
- **Death from severe malaria often occurs within hours of onset of symptoms or admission to hospital**
 - Essential that therapeutic concentrations of a highly effective antimalarial are achieved as soon as possible
- **Management of severe malaria comprises four main areas**
 - Clinical assessment of patient
 - Specific antimalarial treatment
 - Additional treatments (managements of other complications), and
 - Supportive care



- Treat all patients with severe malaria (including infants, pregnant women in all trimester, and lactating women) with intravenous or intramuscular artesunate for at least 24 hours and until able to tolerate oral medication.
- After at least 24 hours of parenteral therapy, AND able to tolerate oral therapy, complete treatment with three-days of an ACT
- Children weighing less than 20 kg should receive a higher dose of artesunate (3 mg/kg/dose) than others (2.4 mg/kg/dose) to ensure an equivalent drug exposure.
- If artesunate is not available, use artemether in preference to quinine for treating severe malaria



- **Pre-referral treatment**

- In settings where complete treatment of severe malaria is not possible, but injections are available, give children and adults a single dose of intramuscular artesunate and refer to an appropriate facility for further care. Use artemether or quinine if artesunate is not available
- In settings where intramuscular injections are unavailable, treat children below the age of six years with a single dose of rectal artesunate and refer immediately to an appropriate facility for further care.
- Where referral is not possible after the initial treatment,
 - pre-referral medication should be continued until the patient can tolerate oral medication, then,
 - administer a complete course of an effective ACT



- CCM of malaria delivered as part of integrated CCM (iCCM), which includes the treatment of pneumonia and diarrheal diseases.
- Trained community providers (CHWs, Medicine Sellers or Retailers) should be provided with:
 - Rapid Diagnostic Tests (RDTs)
 - ACTs for treatment of uncomplicated malaria.
 - Rectal artemisinin suppositories for pre-referral treatment of severe malaria.
 - Information, Education and Communication materials.
 - simple patient registers and reporting forms.



- **On-going policy reviews**
 - Treating in the 1st trimester of pregnancy – Use of ACTs
 - Use of artesunate+pyronaridine in the treatment of malaria
 - Shorter course (7day treatment) of standard and high dose anti-relapse primaquine treatment
- **Reviews in the pipeline**
 - Tafenoquine for anti-relapse treatment for vivax malaria
- **Malaria diagnosis**
 - G6PD quantitative point of care test

Malaria Prevention

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Chemoprevention recommendations – shift in approach

- The updated chemoprevention recommendations provide greater flexibility to NMPs to adapt control strategies to suit their settings.
- We no longer specify strict age groups, transmission intensity thresholds, numbers of doses or cycles, or specific drugs.
- NMPs are encouraged to consider local data to determine how best to tailor chemoprevention strategies to local needs and determine which age groups should be targeted where, for how long, how frequently, and with which drugs.

Intermittent preventive treatment of malaria in pregnancy (IPTp)

Strong recommendation for , Moderate certainty evidence

Updated

Intermittent preventive treatment of malaria in pregnancy (2022)

In malaria-endemic areas, pregnant women of all gravidities should be given antimalarial medicine at predetermined intervals to reduce disease burden in pregnancy and adverse pregnancy and birth outcomes.

- *SP has been widely used for malaria chemoprevention during pregnancy and remains effective in improving key pregnancy outcomes.*
- *IPTp-SP should start as early as possible in the second trimester and not before week 13 of pregnancy.*
- *Doses should be given at least one month apart, with the objective of ensuring that at least three doses are received.*
- *ANC contacts remain an important platform for delivering IPTp. Where inequities in ANC service and reach exist, other delivery methods (such as the use of community health workers) may be explored, ensuring that ANC attendance is maintained and underlying inequities in ANC delivery are addressed.*
- *IPTp is generally highly cost-effective, widely accepted, feasible for delivery and justified by a large body of evidence generated over several decades.*

Perennial Malaria Chemoprevention (former IPTi)

Conditional recommendation for,
moderate-certainty evidence

Updated

In areas of moderate to high perennial malaria transmission, children belonging to age groups at high risk of severe malaria can be given antimalarial medicines at predefined intervals to reduce disease burden.

- Perennial malaria chemoprevention (PMC) schedules should be informed by the age pattern of severe malaria admissions, the duration of protection of the selected drug, and the feasibility and affordability of delivering each additional PMC course (see “Practical info”).
- Sulfadoxine-pyrimethamine (SP) has been widely used for chemoprevention in Africa, including for PMC. Artemisinin-based combination therapies (ACTs) have been effective when used for PMC, but evidence is limited on their safety, efficacy, adherence to multi-day regimens, and cost-effectiveness in the context of PMC.
- Previously, PMC was recommended in infants (<12 months of age) as intermittent preventive treatment (IPTi). Since the initial recommendation, new data have documented the value of malaria chemoprevention in children aged 12 to 24 months.
- The Expanded Programme on Immunization (EPI) platform remains important for delivering PMC. Other methods of delivery can be explored to optimize access to PMC and integration with other health interventions.
- Moderate to high perennial malaria transmission settings are defined as areas with *P. falciparum* parasite prevalence greater than 10% or an annual parasite incidence greater than 250 per 1000 [29]. These thresholds are indicative and should not be regarded as absolutes for determining applicability of the PMC recommendation.

Seasonal Malaria Chemoprevention

Strong recommendation for, moderate-certainty evidence

Updated

In areas of seasonal malaria transmission, children belonging to age groups at high risk of severe malaria should be given antimalarial medicines during peak malaria transmission seasons to reduce disease burden.

- Eligibility for seasonal malaria chemoprevention (SMC) is defined by the seasonality of malaria transmission and age groups at risk of severe malaria. Thresholds for assessing these criteria change over time and location. Malaria programmes should assess the suitability of SMC based on the local malaria epidemiology and available funding. The added value of a seasonally targeted intervention is likely to be greatest where transmission is intensely seasonal.
- Monthly cycles of sulfadoxine-pyrimethamine plus amodiaquine (SP+AQ) have been widely used for SMC in African children under 5 years old and have been shown to be efficacious, safe, well tolerated, available and inexpensive [182].

Intermittent preventive treatment of malaria in school-aged children (IPTsc)

Conditional recommendation for , Low certainty evidence

New

Intermittent preventive treatment of malaria in school-aged children (2022)

School-aged children living in malaria-endemic settings with moderate to high perennial or seasonal transmission can be given a full therapeutic course of antimalarial medicine at predetermined times as chemoprevention to reduce disease burden.

- *IPTsc has been evaluated in children aged 5–15 years. The burden of malaria and benefits of IPTsc may vary across this age range, but evidence is limited.*
- *National malaria programmes can consider IPTsc if resources allow for its introduction among school-aged children without compromising chemoprevention interventions for those carrying the highest burden of severe disease, such as children < 5 years old.*
- *Schools may provide a low-cost means to deliver chemoprevention to school-aged children. However seasonal variation in malaria transmission and the timing of school terms, as well as equity concerns, may mean alternative delivery channels are needed to maximize impact.*
- *First- and second-line malaria treatments should not be used for IPTsc if safe and effective alternatives are available (see “Practical info”).*
- *The dosing schedule for IPTsc should be informed by the local malaria epidemiology and timed to give protection during the period of greatest malaria risk (see “Practical info”).*
- *Moderate to high malaria transmission settings are defined as areas with *P. falciparum* parasite prevalence greater than 10% or an annual parasite incidence greater than 250 per 1000 [31]. These thresholds are indicative and should not be regarded as absolutes for determining applicability of the IPTsc recommendation.*

Conditional recommendation for , Moderate certainty evidence

New

Post-discharge malaria chemoprevention (PDMC)

Children admitted to hospital with severe anaemia living in settings with moderate to high malaria transmission should be given a full therapeutic course of an antimalarial medicine at predetermined times following discharge from hospital to reduce re-admission and death.

- *PDMC should be given to children following admission with severe anaemia [138] that is not due to blood loss following trauma, surgery, malignancy or a bleeding disorder.*
- *PDMC implementation should be tailored to admissions of children with severe anaemia and consider the duration of protection of the selected antimalarial, and the feasibility and affordability of delivering each additional PDMC course (see “Practical info”).*
- *Moderate to high perennial malaria transmission settings are defined as areas with a *P. falciparum* parasite prevalence greater than 10% or an annual parasite incidence greater than 250 per 1000 [31]. These thresholds are indicative and should not be regarded as absolute for determining applicability of the PDMC recommendation.*

Support for National adoption and adaptation

- IPTp at community level
 - New field manual will be developed (2022)
- PMC (IPTi+)
 - Adoption and Implementation Guide available for IPTi
 - Pilots underway to inform expansion of IPTi beyond the current recommendation and transition to PMC.
 - Adoption Framework and Implementation Guide to be developed (2022)
- SMC
 - Adoption and Implementation Guide / Field Manual available
 - update in the pipeline before the end of the year (2022)
- IPTsc (school children)
 - Adaptation and implementation guidance to be developed
- PDMC (post discharge)
 - Adaptation and implementation guidance to be developed

Mass Drug Administration (MDA)

Technical area	Strength & evidence	For/against	Recommendation	New/update
MDA	Conditional, low-certainty	For	MDA in moderate-high transmission for short-term <i>P. falciparum</i> burden reduction	New
MDA	Conditional, low-certainty	For	MDA in emergency settings for short-term <i>P. falciparum</i> burden reduction	New
MDA	Conditional, low-certainty	For	MDA to reduce <i>P. falciparum</i> transmission in very low to low transmission	New
MDA	Conditional, very low-certainty	Against	MDA to reduce <i>P. falciparum</i> transmission in moderate to high transmission	New
MDA	Conditional, very low-certainty	For	MDA with antimalarial medicine to reduce <i>P. vivax</i> transmission	New
MDA	Conditional, very low-certainty	Against	MDA with 8-aminoquinoline alone to reduce <i>P. vivax</i> transmission	New

Conditional recommendation for

Conditional recommendation against

MALARIA ELIMINATION / PREVENTION OF RE-INTRODUCTION



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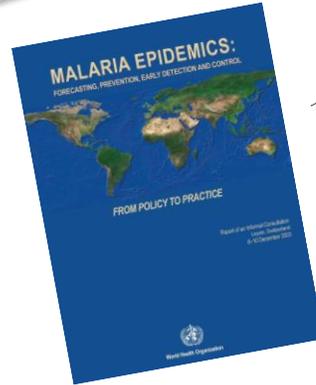
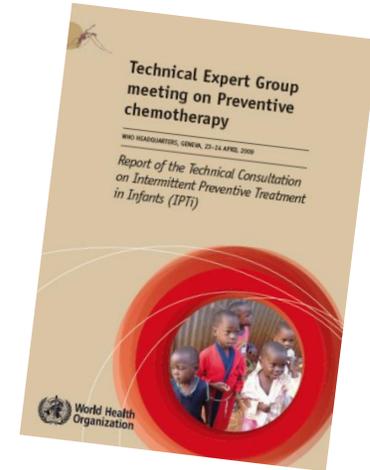
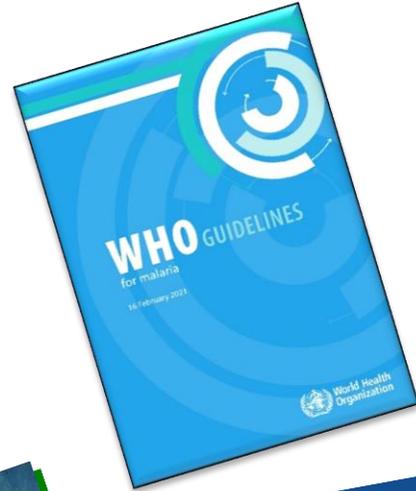
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Malaria Elimination Guidelines



Technical area	Strength & evidence	For/against	Recommendation	New/update
Elimination	Conditional, very low-certainty	For	Targeted drug administration to reduce transmission in low/very low transmission	New
Elimination	Conditional, moderate certainty	Against	Mass testing and treatment to reduce malaria transmission	New
Elimination	Conditional, very low-certainty	Against	Testing and treatment of people at increased risk to reduce transmission	New
Elimination	Conditional, low-certainty	For	Reactive drug administration to people near malaria cases to reduce transmission	New
Elimination	Conditional, very low-certainty	For	Testing and treatment of people near malaria cases to reduce transmission	New
Elimination	Conditional, very low-certainty	For	Reactive indoor residual spraying near malaria cases to reduce transmission	New
Elimination	Conditional, very low-certainty	Against	Routine test and treatment of people at points of entry to reduce importation	New
Elimination	Conditional, very low-certainty	For	Testing and treatment of groups from endemic areas to reduce importation	New





Keep our eye on the prize: a world free of malaria

Thank you