Malaria Policy Advisory Committee (MPAC) Draft Meeting Agenda

Dates: 16-18 September 2015. Location: Salle A, WHO HQ, Geneva

Thursday, 17 September 2015

Time	Session	Purpose	Type
9.00 am	Session 5; Malaria Terminology/Annex 1/Annex 2/Presentation *(R Steketee)*	For discussion	open

10.30 am	**coffee**		
11.00 am 11.45am	<u>Session 6:</u> Update on artemisinin and ACT resistance with special focus on the Greater Mekong Sub-region / Update September 2015 (*P Ringwald*) Update on the Greater Mekong Sub-region Elimination Strategy *(W Kazadi)*	For information For information	**open**
12.30 pm	**lunch**		
<u>Session 7:</u> 1.30 pm 2.00 pm 2:45 pm	Update on Malaria Elimination in the WHO European Region *(E Gasimov)* Update on ERG for Malaria Elimination Field Manual and Malaria Elimination Certification Panel I *(K Carter/H Atta)* WHO reform to support innovation, efficiency and quality in vector control tools/ Presentation *(R Vellayudhan)*	For information For discussion For information	**open**
3.30 pm	**Coffee**		
<u>Session 8:</u> 4.00 pm 4:30 pm	Final RTS,S results *(P Smith)* Cost-effectiveness of alternate malaria preventive interventions (*A Ghani*) Questions and clarifications	For discussion For discussion	**closed**
5.30 pm	**End of day**		

Malaria Policy Advisory Committee Meeting

16–18 September 2015, Geneva, Switzerland
Background document for Session 5

WHO update of malaria terminology

August 2015, Geneva, Switzerland

Introduction

The Malaria Policy Advisory Committee, at its last meeting in March 2015,[1] welcomed the initiative of the WHO Global Malaria Programme (GMP) Secretariat to update the WHO publication *Terminology of malaria and of malaria eradication*, which dates back to 1963 (1). Several WHO publications over the past 10 years have included a glossary of terms on multiple interventions related to malaria prevention, control, elimination and surveillance; however, the terminology of malaria has not been comprehensively reviewed over the past 50 years.

1 Process for updating malaria terminology

2.1 Desk review

The review focused on terms having programmatic relevance, related to malaria elimination and eradication, and having conflicting definitions and use. The process started with a desk review carried out between April and May 2015, covering the steps outlined below:

a. Compilation of all WHO terms and definitions used in WHO malaria publications since 1995, in addition to those contained in the glossary of Terminology of malaria and of malaria eradication (1) – 16 documents included.

b. Compilation of similar or identical terms and definitions used by other WHO departments; for example, "preventive chemotherapy for neglected tropical diseases (NTDs)" – 16 documents included.

c. Systematic research of scientific papers with definitions or glossary published over the past 10 years to identify recurrent terms that are the same or similar but are given different meanings, as well as new terms that are given similar meanings – 15 documents included.

Based on the findings of the desk review, a total of 292 terms were identified and draft definitions proposed. Terms were divided into four groups related to elimination (50), vector control (69), surveillance (85) and diagnosis and treatment (88), with many terms relevant to both surveillance and elimination.

2.2 Drafting committee review – Phase I

Based on the results of the desk review, a draft definition was proposed for each term. When relevant, an explanatory note was added to the definition. All 292 terms and their definitions were submitted to the members of the WHO Drafting Committee on Malaria Terminology.

1. http://www.who.int/malaria/mpac/mpac-march2015-meeting-summary.pdf

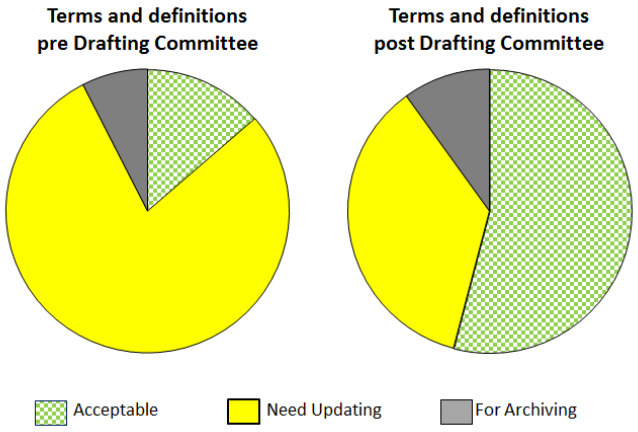
WHO/HTM/GMP/MPAC/2015.12

The committee members were Prof Andrei Beljaev, Prof Graham Brown, Dr Kamini Mendis, Dr José Najera, Dr Trenton Ruebush, Dr Rick Steketee (Chairperson) and Graham White. The committee received all draft terms by email and was asked to classify them into three groups:

1. Terms that were and are still relevant and properly described – definition to be reviewed for updating the language, but generally considered "good as they stand".
2. Terms that have been used in the past and have value for historical purposes, but are no longer in current use.
3. Terms that are relevant today but may have taken on a new meaning and different use – terms need to be reviewed and possibly redefined, or at least updated so that the language of the definition reflects their current use.

After the initial review, the committee was convened for a consultation in Geneva on 2–3 June 2015, to refine all definitions. Members worked in pairs on all terms, focusing on each of the four technical areas, and results were then presented in plenary for review by the whole committee. The work was further refined after the meeting, through multiple email exchanges among committee members. A concerted effort was made to simplify definitions as much as possible, and, as a result, the recommended definitions tended to be short and the explanatory note was used to provide qualifying information.

Before the June meeting, of the 292 terms, 40 were identified as being properly described (Group 1), 22 were proposed for archiving (Group 2) and 230 were identified as being in need of updating (Group 3). Following extensive work on the definitions, the drafting committee considered 153 terms as being properly described, 38 were proposed for archiving (Group 2), and 101 terms were identified as requiring additional inputs (see figure below).



2.3 External survey

A series of 101 terms with draft definitions was identified as requiring additional inputs and external review. To collect expert feedback in a systematic way, WHO developed an online survey and issued a weblink with 47 passcodes ("tokens") that were sent to 30 identified institutions or groups. These included the Asia Pacific Malaria Elimination Network (APMEN); the Foundation for Innovative New Diagnostics (FIND); Gates Foundation Malaria Program; Innovative Vector Control (IVCC); the Malaria Elimination Group University of California, San Francisco (UCSF); Medicines for Malaria Venture (MMV); PATH Malaria Control and Elimination Partnership in Africa (MACEPA); the Roll Back Malaria (RBM) Case Management Working Group; the RBM Monitoring Evaluation Reference Group; the RBM Vector Control Working Group; the US Centers for Disease Control and Prevention (CDC); US President's Malaria Initiative (PMI);

the Vector Control Advisory Group (VCAG); WHO/GMP; WHO/NTD; WHO Regional Malaria Advisers; WHO Technical Expert Group (TEG) on Antimalarial Drug Resistance and Containment; WHO TEG on Malaria Chemotherapy; WHO TEG on Surveillance, Monitoring and Evaluation; WHO TEG on Vector Control; WHO Collaborating Centre (CC) for Malaria; WHOCC for Surveillance of Antimalarial Drug Resistance; WHOCC pour l'Evaluation de nouveaux Insecticides destinés à la Lutte contre les Vecteurs; WHOCC for Ecology, Taxonomy and Control of Vectors of Malaria, Filariasis and Dengue; WHOCC for Malaria Diagnosis; WHOCC for Malaria Control, Elimination and Eradication; WHOCC for Clinical Management of Malaria; WHOCC in Geospatial Disease Modelling; WHOCC for Prevention and Control of Malaria; and the WHOCC on Early Warning Systems for Malaria and other Climate Sensitive Diseases.

Passcodes were dedicated to individual institutions or groups, and sent to the corresponding lead contacts (e.g. CEOs, chairs or co-chairs of working groups, directors and so on), who could designate additional technical resource persons from their institution or group to participate in the review by sharing the passcode. All inputs provided by the different reviewers of an institution or group were then recorded as a "single" response with a single token.

To facilitate review and inputs, the 101 terms were grouped into four categories:

- diagnosis and treatment (32 terms)
- elimination (28 terms)
- surveillance (21 terms)
- vector control (20 terms).

Each term had a draft definition and, where appropriate, an explanatory note. For each term, the reviewer was invited to recommend to: (1.) retain ("ok"), (2.) reject ("omit"), or (3.) amend ("modify") the suggested definition and/or the commentary, providing a written alternative text.

The survey was carried out between 6 and 26 July 2015, and responses were obtained from 25/47 tokens by 20/30 institutions/groups. Seven reviewers provided feedback on all four survey categories, the rest commented on one, two or three individual categories. A total of 19 reviewers provided feedback on terms in the diagnosis and treatment category, 11 on elimination, 10 on surveillance and 11 on vector control.

A total of 1260 entries was received: 884 entries for "ok", 75 entries for "omit" (=archiving), and 301 entries with recommendations to "modify". Only five terms were marked as "ok" by all reviewers: causal prophylaxis, passive case detection, stable transmission, unstable transmission and gonotrophic dissociation.

2.4 Drafting committee review – Phase II

All inputs were reviewed and compiled by the WHO/GMP Secretariat and the suggested modifications then submitted to the WHO drafting committee for review by email exchanges. The consolidated result of this work in the form of a glossary has now submitted to MPAC for final review, together with specific consideration on the term "malaria case", which generated significant debate among the members of the drafting committee and external reviewers.

3 Requested action by MPAC

MPAC is asked to provide the following to GMP:

4. Advice on malaria case definition (see Annex 1).
5. Feedback on the glossary with proposed terms and definitions (see Annex 2).
6. Advice on the process for reviewing and incorporating new terms.
7. Mechanisms for dissemination and promoting uptake following MPAC review.

4 Acknowledgements

The valuable support provided by Ms Mar Velarde, ISGlobal/ Malaria Eradication Scientific Alliance (MESA), for the phase of desk review and preparations for the drafting committee meeting is gratefully acknowledged. The external survey was ably developed and managed by Mr Ryan Williams, WHO/GMP, following the indications of the drafting committee, and the compilation of all inputs received and analysis of the survey results was efficiently completed by Ms Silvia Schwarte, WHO/GMP. The excellent contributions of all members of the drafting committee are well recognised, in particular Prof Andrei Beljaev, Prof Graham Brown, Dr Kamini Mendis, Dr José Najera, Dr Trenton Ruebush, Dr Rick Steketee and Dr Graham White. The precision and careful attention to the tasks, and the capacity to provide timely and precious feedback, have been instrumental in the work being complete. The excellent inputs received from over 20 institutions or groups is greatly appreciated. Dr Rick Steketee, Chairperson of the WHO Drafting Committee on Malaria Terminology has provided guidance in the different phases of planning and implementation of the review process, and Dr Andrea Bosman has served as Secretariat of the WHO work to update malaria terminology. The work has been funded as part of the contribution from the Bill & Melinda Gates Foundation to WHO/GMP.

Reference

1 WHO. Terminology of malaria and of malaria eradication. Geneva, World Health Organization (WHO). 1963 (https://extranet.who.int/iris/restricted/bitstream/10665/39007/1/9241540141_eng.pdf accessed 24 August 2015).

Malaria Policy Advisory Committee Meeting
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Background document for Session 5

Annex 1. Defining the term “malaria case”

WHO update of malaria terminology
August 2015, Geneva, Switzerland

The most challenging issue of the terminology of malaria and malaria elimination centered on the definition of a “malaria case”. Within the expert group, there was much discussion but no unanimous agreement.

A1.1 Background

A1.1.1 Definitions for “case”

General medical dictionaries

A general definition for “case” is as follows:

> **Case.** A particular instance of disease; sometimes used incorrectly to designate the patient with the disease (from Dorland's Illustrated Medical Dictionary (1) – general definition)

Malaria control programmes typically report “malaria cases” as the number of people presenting with illness who are diagnosed as having malaria infection – consistent with the above definition of an instance of illness or disease linked to infection. With the transition of a programme to elimination, an emphasis is placed on malaria infections that may remain asymptomatic for prolonged periods yet lead to ongoing transmission in the community. Based on this emphasis, in the elimination phase there is an evolution of the term “malaria case”, which is then applied to both symptomatic and asymptomatic infections.

WHO terminology

In 1963, the publication WHO terminology for malaria and malaria eradication (2) provided the following definitions for case and malaria case:

> **Case.** An occurrence or instance of infection or disease. The word is so vague that the type of case should always be specified, as, for instance, a malaria case or a fever case. (2)
>
> **Malaria case.** In malaria eradication terminology, occurrence of malaria infection in a person in whom, regardless of the presence or absence of clinical symptoms, the presence of malaria parasites in the blood has been confirmed by microscopic examination. During surveillance, every malaria case detected is classified, according to the origin of the infection, as indigenous or as imported, introduced, relapsing or induced. (2)

WHO/HTM/GMP/MPAC/2015.12b

This terminology was consistent with the idea that, as a country moves into a malaria elimination phase, the programme will reorient its strategies, including surveillance case definitions. In many countries where the national malaria control programme is investing to improve "control", the surveillance system is tracking malaria cases as those presenting with illness to health workers. In countries with very low transmission, by contrast, the surveillance system is tracking all infections, both symptomatic and asymptomatic.

A1.1.2 Definitions of case and infection are linked

The definitions of a case and an infection are linked, as shown by these definitions:

> **Infection.** Invasion and multiplication of microorganisms in body tissues, resulting in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. (Dorland's Medical Dictionary (1) – general definition)
>
> **Infection.** Entrance, establishment or maintenance in a host of a parasite, generally involving its multiplication; also the resulting condition in the host. (2)

Thus, according to WHO (2) "malaria case" was essentially equivalent to "malaria infection".

A1.1.3 Parasitological confirmation of all suspected malaria cases

With the recent progress regarding the emphasis on parasitological confirmation of malaria when an individual presents with illness that is suspected to be malaria, WHO recommends that all "cases" should be confirmed with available diagnostic tools.

A1.2 External survey

Given that there was no unanimous agreement on the definition and on the proposal to modify the case definition for the transition from control to elimination, the WHO Drafting Committee on Malaria Terminology decided to put two options to a wider audience to obtain input and comment. The text put to the external survey was as follows:

> Choose the best definition for "malaria case":
>
> **Definition #1:** Occurrence of malaria illness/disease in a person in whom the presence of malaria parasites in the blood has been confirmed by parasitological testing.
>
> Note: A malaria case can be classified as suspected, presumed, confirmed, and as autochthonous, indigenous, induced, introduced, imported (based on the origin of infection), and relapsing.
>
> **Definition #2:** Occurrence of malaria infection (symptomatic or asymptomatic) in a person in whom the presence of parasites in the blood has been confirmed by parasitological testing.
>
> Note: A malaria case can be classified as autochthonous, indigenous, induced, introduced, imported (based on the origin of infection), and relapsing.

The external feedback received by 11 groups of reviewers is summarized in the table below:

	Prefer definition #1	Prefer definition #2
Yes	7	3
Uncertain	2	4
No	2	3

The responses from the external reviewers suggest that there is not unanimity; however, 7 of 11 respondents (64%) preferred definition #1 while only 3 out of 10 (33%) preferred definition #2.

Among the reviewers preferring definition #1, the comments included:

- Either definition ought to specify "... the presence of asexual malaria parasites in the blood ..."
- The second definition is for the term "malaria infection".
- A malaria case can be classified as autochthonous, indigenous, induced, introduced, imported (based on the origin of infection), relapsing.
- I don't see any problem in a different definition at different programme phases (responded yes to both #1 and #2).
- The application of "case, malaria" referencing asymptomatic infection has been, and will always be confusing to national programmes, unless there is certified knowledge of non-infection state of the individual, prior to determination of the asymptomatic condition. Perhaps there is need to consider separate and clarified definition of "case, infection" and "case, illness".

Among the reviewers preferring definition #2, the comments included:

- Let's just simplify our lives and say that malaria infection is what we're interested in finding, curing, eliminating.
- This is the case definition in the surveillance guidelines. A country should report all cases of malaria found whether they are found by passive case detection or active.

Among the reviewers indicating that they were "uncertain", the comments included:

- Need to distinguish between parasitological and clinical cases. Need specific definitions. Please can we get rid of the word "autochthonous" and use "locally transmitted" instead.
- Both definitions have issues. I prefer definition #1 but based purely on confirmation. Suspected and presumed should be out.

A1.3 Review by drafting committee

After the completion of the survey and the compilation of the survey results, the drafting committee again reviewed the malaria case definitions, providing the following comments.

Five members of the committee expressed a preference for definition #2, based on the following points:

- Advantage of continuity, in using a case definition in line with the definition of the past.
- Definition needed for surveillance purposes.
- Not all infections are cases (e.g. hypnozoite carriers are infected, but are not cases).
- Best if exchangeable with the term infection.
- To reduce confusion, all malaria data sets should include malaria case definition.
- Terminology in line with action required for malaria elimination.

- Already adopted and in large use in malaria elimination programmes, including related terms (e.g. “case investigation”, “index case”, “case follow-up”).
- In line with requirement that countries should report as “malaria cases” only laboratory confirmed cases.

Two members of the committee expressed a preference for changing definitions #1 and #2, in the different phases of malaria control and elimination:

- While parasitological confirmation of is now recommended in all suspected malaria cases, for surveillance it only really becomes absolutely mandatory in elimination settings.
- It makes sense for surveillance to evolve as part of the reorientation of interventions from control to elimination.
- Case definitions for surveillance can change based on the operational setting.

A1.4 Requested advice from MPAC

Changing the definition of “malaria case” has important implications for malaria surveillance. In addition, numerous terms are linked to this definition – either using “case” or “infection”— including the following:

- suspected case,
- presumed case,
- case detection (passive, active),
- infection detection (active),
- case investigation,
- index case,
- secondary cases/infections,
- case follow-up,
- imported case/infection,
- induced case/infection,
- introduced case/infection

Given the challenges with this important set of terms (“case” and “infection”), we would like to ask the MPAC for inputs and recommendations to WHO on the most useful and appropriate definition.

A1.5 References

1 Dorland's Illustrated Medical Dictionary. Philadelphia, Elsevier Saunders. 2012.

2 WHO. Terminology of malaria and of malaria eradication. Geneva, World Health Organization (WHO). 1963 (https://extranet.who.int/iris/restricted/bitstream/10665/39007/1/9241540141_eng.pdf).

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World Health Organization

Annex 2. Glossary

WHO update of malaria terminology
August 2015, Geneva, Switzerland

Diagnosis and Treatment

Adherence	Compliance with a regimen (chemoprophylaxis or treatment), or with procedures and practices prescribed by a health care worker.
Adverse drug reaction	A response to a medicine that is noxious and unintended, and which occurs at doses normally used in man.
Adverse event	Any untoward medical occurrence in a person exposed to a biological or chemical product, and that does not necessarily have a causal relationship with this product. *Note:* As part of malaria interventions, adverse events can be reported following treatment with antimalarial medicines and/or exposure to insecticides. The standard definition under ICH GCP guidelines refers to pharmaceutical products only.
Adverse event, serious	Any untoward medical occurrence in a person exposed to a biological or chemical product, and which does not necessarily have a causal relationship with this product, and results in death, requires or prolongs inpatient hospitalisation, generates significant disability/incapacity or is life-threatening.
Antimalarial medicine	A pharmaceutical product, used in humans for the prevention or treatment or reduction of transmission of malaria.
Artemisinin-based combination therapy (ACT)	A combination of an artemisinin derivative with a longer-acting antimalarial that has a different mode of action.
Case management	Diagnosis, treatment, clinical care, counselling, and follow-up of symptomatic malaria infections.
Cerebral malaria	Severe *P. falciparum* malaria with coma (Glasgow coma scale < 11, Blantyre coma scale < 3) persisting for > 30 min after a seizure. *Note:* Initial neurologic symptoms of cerebral malaria are drowsiness, confusion, failure to eat or drink and convulsions (see current WHO definition of severe malaria - http://apps.who.int/iris/bitstream/10665/79317/1/9789241548526_eng.pdf)

Chemoprevention, Seasonal Malaria	The intermittent administration of full treatment courses of an antimalarial medicine during the malaria season with the objective to prevent malarial illness, by maintaining therapeutic antimalarial drug concentrations in the blood throughout the period of greatest malarial risk. *Note:* This intervention is only recommended for areas with highly seasonal malaria, where transmission occurs during a few months of the year.
Chemo-prophylaxis	Administration of a medicine, AT PREDEFINED INTERVALS typically in sub-therapeutic doses, to prevent either the development of an infection or the progression of an infection to a manifest disease. *Note:* The word chemoprevention as used in seasonal malaria chemoprevention refers to the administration of a full curative treatment course, as opposed to chemoprophylaxis which usually involves the administration of sub-therapeutic doses.
Combination therapy	A combination of two or more classes of antimalarial medicine with unrelated mechanisms of action.
Cure	Elimination from an infected person of all malaria parasites that caused an infection. *Note:* When applied to *P. vivax* and *P. ovale* the terms is equivalent to radical cure.
Cure, radical	Elimination of both blood-stage infection and latent liver infection in P. vivax and P. ovale infections, thereby preventing relapses. *Note:* Term used only for *P. vivax* and *P. ovale* infections to emphasise the need to use anti-hypnozoite medicines.
Cyto-adherence	Propensity of malaria infected erythrocytes to adhere to the endothelium of microvasculature of internal organs of the host.
Diagnosis	The process of establishing the cause of an illness (for example, a febrile episode), including both clinical assessment and diagnostic testing.
Diagnosis, molecular	Use of nucleic acid amplification-based tests to detect the presence of malaria parasites.
Diagnosis, parasite-logical	Diagnosis of malaria by detection of malaria parasites or plasmodium-specific antigens or genes in the blood of an infected individual.
Dosage regimen (or treatment regimen)	Information on formulation, route of administration, dose, dosing interval and treatment duration of a medicine.
Dose	Quantity of a medicine to be taken at one time or within a given period of time. The quantities of antimalarial medicines should be expressed as a base (when applicable) and fractions of a gram or milligrams.

Dose, loading	One or a series of doses that may be given at the onset of therapy with the aim of achieving the target concentration rapidly.
Drug efficacy	Capacity of an antimalarial medicine to clear parasites, when administered in recommended doses that are known to be well tolerated and have minimal risk of toxicity.
Drug resistance	The ability of a parasite strain to survive and/or multiply despite the administration and absorption of a medicine given in doses equal to or higher than those usually recommended. *Note:* Drug resistance arises as result of genetic changes (mutations or gene amplification) that confer reduced susceptibility to antimalarial medicines.
Drug safety	Characteristics of a medicine that describe the potential for causing harm, i.e. clinical adverse events (signs, symptoms or diseases), laboratory changes (biochemistry, hematology), or other physiological changes (e.g. ECG) when administered at the recommended dosage.
Drug, gametocytocide	A drug that kills gametocytes, thus preventing them from infecting a mosquito.
Drug, schizontocide	A drug that kills schizonts, either in the liver (tissue schizonticide) or blood (blood schizonticide).
Erythrocytic cycle	Portion of the life cycle of the malaria parasite from merozoite invasion of red blood cells to schizont rupture. The duration is approximately 24 h in *Plasmodium knowlesi*, 48 h in *P. falciparum*, *P. ovale* and *P. vivax* and 72 h in *P. malariae*.
Fixed-dose combination	A combination in which two antimalarial medicines are formulated together in the same tablet, capsule, powder, suspension or granule.
Gametocytes	Blood-borne sexual stages of malaria parasites that can have the potential to infect anopheline mosquitoes when ingested during a blood meal.
Hyper-parasitaemia	A high density of parasites in the blood, which increases the risk of deterioration of the patient's condition to severe malaria. *Note:* See current WHO current definition: http://apps.who.int/iris/bitstream/10665/162441/1/9789241549127_eng.pdf?ua=1
Hypnozoites	Persistent liver stages of *P. vivax* and *P. ovale* malaria that remain dormant in host hepatocytes for variable periods, usually from 3 weeks to a year (and exceptionally multiple years) before activation and development into a pre-erythrocytic schizont which then causes a blood stage infection (relapse).

Incubation period	Period between inoculation of malaria parasites and onset of clinical symptoms. *Note:* The shortest incubation period in mosquito-borne infections, ranges from 7 days in *P. falciparum* to 23 days in *P. malariae*. Long incubation in *P. vivax* and *P. ovale* is due to activation of hypnozoites and ranges from 3 weeks to a year (and exceptionally multiple years). In blood-induced infections, the incubation period may be shorter than in the sporozoite-induced infection, depending on the size of the inoculum.
Infection, mixed	Malaria infection with more than one species of *Plasmodium*.
Infectious	Capable of transmitting infection, a term commonly applied to the human host.
Infective	Capable of producing infection, a term commonly applied to the parasite (gametocytes, sporozoites, etc.) or to the vector (mosquito).
Intermittent preventive treatment in infants (IPTi)	A full therapeutic course of antimalarial medicine delivered to infants at the time of routine immunization visits, regardless of whether the child is infected with malaria.
Intermittent preventive treatment in pregnancy (IPTp)	A full therapeutic course of antimalarial medicine given to pregnant women at routine prenatal visits, regardless of whether the woman is infected with malaria.
Latent period	For *P.vivax* and *P.ovale* infections, the period between the primary infection and subsequent relapses. this stage is asymptomatic, parasites are absent from the bloodstream, but present in the hepatocytes.
Malaria pigment (haemozoin)	A brown to black granular material formed by malaria parasites as a by-product of haemoglobin digestion. Pigment is evident in mature trophozoites and schizonts. It may also be phagocytosed by monocytes, macrophages and polymorphonuclear neutrophils.
Merozoite	Extracellular stage of the parasite released into the host plasma when a hepatic or erythrocytic schizont ruptures. The merozoites can then invade red blood cells.
Monotherapy	Antimalarial treatment with a single medicine: either a single active compound or synergistic combination of two compounds with related mechanisms of action.
Parasitaemia	Presence of parasites in the blood. *Note:* If this condition is not accompanied by symptoms of malaria, it is known as asymptomatic parasitaemia.
Parasitaemia, asymptomatic	The presence of asexual parasites in the blood without symptoms of illness.

Parasite clearance time	Time elapsing from the first drug administration to the first occasion on which no parasites can be demonstrated in the blood. *Note:* Time depends on the sensitivity of the method used to detect the parasite.
Parasite density	Number of asexual parasites per unit volume of blood or per number of red blood cells. *Note:* Any level of parasite density can lead to clinical illness. However, generally the likelihood of clinical illness increases with increasing parasite density.
Patent period	Period during which malaria parasitaemia is detectable by microscopy.
Plasmodium	Genus of protozoan blood parasites of vertebrates that includes the causal agents of malaria. *P. falciparum*, *P. malariae*, *P. ovale* and *P. vivax* cause malaria in humans. Human infections with the monkey malaria parasite *P. knowlesi* and very occasionally with other simian malaria species may occur in tropical forest areas.
Pre-erythrocytic development	The development of the malaria parasite from the time when it first enters the host until the hepatic schizont ruptures. *Note:* After inoculation into a human by a female anopheline mosquito, sporozoites invade hepatocytes in the host liver and multiply there for a period ranging from 5.5 (*P. falciparum*) to 25 days (*P. malariae*), forming exoerythrocytic schizonts. These then rupture, liberating merozoites into the bloodstream, where they subsequently invade red blood cells. In vivax and ovale infections some sporozoites remain dormant in the liver in the form of hypnozoites for the duration of 3 weeks to 12 months and exceptionally several years.
Pre-patent period	Period of time from inoculation of parasites to the first appearance of parasitaemia.
Prequalification	Process that ensures that key health products are safe, appropriate and meet stringent quality standards for international procurement. *Note:* Prequalification is done by assessing product dossiers, inspecting manufacturing and testing sites, organizing quality control testing in the case of vaccines and medicines, validating the performance of diagnostics, and verifying that the products are suitable for use in the destination countries.
Prophylaxis	Any method of protection from or prevention of disease; when applied to chemotherapy it is commonly termed "chemoprophylaxis ".
Prophylaxis, causal	Complete prevention of erythrocytic infection by destruction of the pre-erythrocytic forms of the parasite.

Rapid diagnostic test	Immuno-chromatographic lateral flow devices for the rapid detection of malaria parasite antigens.
Rapid diagnostic test, combination	Malaria rapid diagnostic test that can detect multiple different malaria species.
Recrudescence	Recurrence of asexual parasitaemia following antimalarial treatment, due to incomplete clearance of asexual parasitaemia of the same genotype(s) that caused the original illness. Recrudescence must be distinguished from re-infection (usually determined by molecular genotyping in endemic areas), and relapse in *P. vivax* and *P. ovale* infections.
Recurrence	Reappearance of asexual parasitaemia after treatment, due to recrudescence, relapse (in *P. vivax* and *P. ovale* infections only) or a new infection.
Reinfection	Infection after initial infection. This is distinguished from recrudescence and relapses on the basis of the parasite genotype that will often (but not always) be different from that causing the initial infection.
Relapse	Recurrence of asexual parasitaemia in *P. vivax* or *P. ovale* infections arising from hypnozoites. *Note:* occurs when the blood-stage infection has been eliminated but hypnozoites persist in the liver and mature to form hepatic schizonts. After an interval, generally from three weeks to one year, the hepatic schizonts rupture and liberate merozoites into the bloodstream.
Ring form (Ring stage, ring stage trophozoite)	Young, usually ring-shaped malaria trophozoites, before malaria pigment is evident by microscopy.
Schizont	Stage of the malaria parasite in host liver cells (hepatic schizont) or red blood cells (erythrocytic schizont) that is undergoing nuclear division by a process called schizogony, and, consequently, having more than one nucleus.
Screening	Process of identifying risk groups that may need further intervention, such as diagnostic testing, treatment or preventive services.
Selection pressure	The force of an external agent that confers preferential survival (e.g. antimalarial medicines on malaria parasites, insecticides on anopheline mosquitoes). *Note:* The term is applicable to human populations as well. As a result of selection pressure induced by malaria certain genetic disorders (e.g. sickle cell anaemia and G6PD deficiency) that reduce the risk of severe malaria are more frequent in malaria endemic areas.
Sensitivity (of a test)	Proportion of people with malaria infection (true positives) who have a positive test result.
Serological assay	Procedure used to detect antimalarial antibodies in the serum.
Severe anaemia	Haemoglobin concentration of < 5 g/100 mL (haematocrit < 15%).

Severe falciparum malaria	Acute falciparum malaria with signs of severe illness and/or evidence of vital organ dysfunction. *Note:* See current WHO definition (http://apps.who.int/iris/bitstream/10665/79317/1/9789241548526_eng.pdf)
Single dose regimen	Administration of a medicine as a single dose to achieve a therapeutic objective.
Specificity (of a test)	Proportion of people without malaria infection (true negatives) who have a negative test result.
Sporozoite	Motile stage of the malaria parasite that is inoculated by a feeding female anopheline mosquito and may cause infection.
Testing, malaria	The use of a malaria diagnostic test to determine whether an individual has malaria infection.
Tolerance	A response in human or mosquito host that is less than expected to a given quantum of infection, toxicant or drug.
Treatment failure	Inability to clear malarial parasitaemia or prevent recrudescence following the administration of an antimalarial medicine, regardless of the resolution of clinical symptoms.
Treatment, anti-relapse	treatment aimed at killing hypnozoites and thereby preventing relapses or late primary infections of *P. vivax* or *P. ovale*.
Treatment, directly observed (DOT)	Treatment administered under the direct observation of a health care worker.
Treatment, first-line and second-line	First-line treatments are those recommended in the national treatment guidelines as the medicine of choice to treat uncomplicated malaria. Second-line treatments are those used for treatment failures that occur with the use of first-line treatment, or if the patient is allergic or unable tolerate the first-line treatment.
Treatment, presumptive	Administration of an antimalarial drug or drugs, to suspected malaria cases without testing or before the results of blood examinations are available. *Note:* This is not generally recommended by WHO as it may lead to wrong treatment of the underlying disease. All suspected malaria cases should be confirmed by a parasitological test.
Treatment, radical	Treatment to achieve complete cure. This only applies to vivax and ovale infections and consists of the use of medicines that destroy both blood and liver stages of the parasite.
Trophozoite	The stage of development of malaria parasites growing within host red blood cells from the ring stage to just before nuclear division. Trophozoites contain visible malaria pigment.

Uncomplicated malaria	Symptomatic malaria parasitaemia without signs of severity or evidence of vital organ dysfunction. *Note:* See current WHO definition (http://apps.who.int/iris/bitstream/10665/79317/1/9789241548526_eng.pdf Higher specificity for definition of malaria associated disease may be achieved with criteria related to degree of fever (e.g. Temp> 37.5°C), and level of parasitaemia (e.g. > 5000 parasites/µL).

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Elimination

Case, confirmed	Malaria case (or infection) in which the parasite has been detected by a diagnostic test, i.e. microscopy, rapid diagnostic test, or molecular diagnostic test. *Note:* On rare occasions, the presence of occult malaria infection in a blood or organ donor is confirmed in retrospect by the demonstration of malaria parasites in the blood or organ recipient.
Case detection	One of the activities of surveillance operations concerned with the search for malaria cases in a community. *Note:* Case detection is a screening process, using as indicator either the presence of fever or epidemiological attributes such as high risk situations or groups. Infection detection includes the use of a diagnostic test to identify asymptomatic persons with malaria infection.
Case detection, active	Detection by health workers of malaria cases at community and household level, sometimes in population groups that are considered at high risk. Active case detection can be conducted as fever screening followed by parasitological examination of all febrile patients or as parasitological examination of the target population without prior fever screening. *Note:* Active case detection may be undertaken in response to a confirmed case or cluster of cases, as screening and testing of a population potentially linked to such cases (referred to as "reactive case detection") or as screening of high risk groups, not prompted by detection of cases (referred to as "proactive case detection").
Case detection, passive	Detection of malaria cases among patients who, on their own initiative, visit health services for diagnosis and treatment, usually for a febrile illness.
Case follow-up	Periodic re-examination of patients with malaria (with or without treatment). *Note:* It may involve blood examination and giving treatment given if not responding to previous medicines. Case follow-up is a part of surveillance.

Case investigation	Collection of information to allow classification of a malaria case by origin of infection, i.e. imported, indigenous, induced, introduced or relapsing. *Note:* Case investigation may include administration of a standardized questionnaire to a person in whom a malaria infection is diagnosed, as well as screening and testing of people living in the same household or surrounding areas.
Case, fever	A persons with fever (current or recent). *Note:* Fever is often used as a screening criterion for performing a diagnostic test in malaria case detection.
Case, imported malaria	Malaria case or infection in which the infection was acquired outside the area in which it is diagnosed.
Case, index	A case whose epidemiological characteristics trigger additional active case or infection detection activities. The term index case is also used to designate the case identified as the origin of infection of one or a number of introduced cases.
Case, indigenous	A case contracted locally with no evidence of being imported or being directly linked to transmission from an imported case.
Case, induced	A case whose origin can be traced to a blood transfusion or other form of parenteral inoculation of the parasite but not to transmission by a natural mosquito-borne inoculation. *Note:* in controlled human malaria infections used in malaria research, the parasite infection (challenge) may originate from inoculated sporozoites, blood or infected mosquitoes.
Case, introduced	A case contracted locally, with strong epidemiological evidence linking it directly to a known imported case (a first generation local transmission).
Case, locally acquired (autochthonous)	A case acquired locally by mosquito-borne transmission *Note:* Note that locally acquired cases can be indigenous, introduced or relapsing. the term "autochthonous" is not commonly used.
Case, malaria -#1	Occurrence of malaria illness/disease in a person in whom the presence of malaria parasites in the blood has been confirmed by a diagnostic test. *Note:* A malaria case can be classified as suspected, presumed, confirmed (based on the level of confirmatory diagnosis) and as indigenous, induced, introduced, imported, relapsing (based on the origin of infection).

Case, malaria - #2	Occurrence of malaria infection with or without illness/disease in a person in whom the presence of malaria parasites in the blood has been confirmed by a diagnostic test. *Note:* A malaria case can be classified as indigenous, induced, introduced, imported, relapsing (based on the origin of infection).
Case, presumed	Suspected malaria case not confirmed by a diagnostic test but nevertheless diagnosed as malaria. Note: The designation of a presumed case is reserved for those uncommon situations where a diagnostic test cannot be performed in a timely manner.
Case, relapsing	Malaria case attributed to activation of hypnozoites of *P. vivax* or *P. ovale* that had been acquired previously (typically during an earlier transmission season) *Note:* The latency period for a relapsing case can be longer than 6-12 months. The presence of relapsing cases is not an indication of operational failure, but their existence should lead to evaluation of the possibility of ongoing transmission.
Case, suspected malaria	Illness suspected by a health worker to be due to malaria, generally based on presence of fever with or without other symptoms.
Certification of malaria-free status	Certification granted by WHO after it has been proved beyond a reasonable doubt that local human malaria transmission by Anopheles mosquitoes has been interrupted in an entire country for at least 3 consecutive years and a national surveillance system and a program for the prevention of reintroduction is in place.
Cluster	Aggregation of relatively uncommon events or diseases in space and/or time in numbers that are believed to be greater than could be expected by chance.
Epidemiological investigation	The study of the environmental, personal and other factors that determine the incidence/prevalence of infection or disease. *Note:* In malaria elimination epidemiological investigation is a part of surveillance operations and is concerned with ascertaining the origin and means of transmission for any malaria cases discovered. It involves epidemiological surveys, localized mass blood examinations and entomological surveys to ascertain the existence and nature of any malaria foci in the surrounding areas, to establish whether transmission is taking place and, if it is, its source and potential for spread.

Focus, malaria	A defined and circumscribed area situated in a currently or formerly malarious area that contains the epidemiologic and ecological factors necessary for malaria transmission. *Note:* Foci can be classified as endemic, residual active, residual non-active, cleared up, new potential, new active or pseudo focus.
Geographical reconnaissance	An activity including census and mapping to determine the distribution of the human population and other features relevant for malaria transmission in order to guide interventions. *Note:* It provides the basis for the selection of field centres and depots, for designing schedules and itineraries of operations, planning deployment of transport, and assessing completion of planned activities. Geographical reconnaissance can also be used to define as accurately as possible the geographical limits of malaria endemic areas and assess epidemic potential.
Infection chronic	Long-term presence of parasitaemia that is not causing acute or obvious illness, but can potentially be transmitted.
Infection, reservoir of	Any person or animal in which plasmodium lives and multiplies, such that it can be transmitted to a susceptible host.
Infection, submicroscopic	Low-density blood stage malaria infections that are not detected by conventional microscopy.
Malaria control	Reduction of disease incidence, prevalence, morbidity, or mortality to a locally acceptable level as a result of deliberate efforts. Continued intervention efforts are required to sustain control.
Malaria elimination	Interruption of local transmission (reduction to zero incidence) of a specified malaria parasite in a defined geographic area as a result of deliberate efforts. Continued measures to prevent re-establishment of transmission are required.
Malaria eradication	Permanent reduction to zero of the worldwide incidence of infection caused by human malaria parasites as a result of deliberate efforts. Intervention measures are no longer needed once eradication has been achieved.
Malaria Infection	Presence of *Plasmodium* parasites in blood or tissues, confirmed by diagnostic testing. *Note:* Diagnostic testing could include: microscopy, malaria rapid diagnostic testing or nucleic acid-based amplification methods (e.g. PCR assays for detecting parasite DNA or RNA).
Malaria risk stratification	Classification of geographical areas or localities according to factors determining the receptivity and vulnerability to malaria transmission.

Malaria stratification	Classification of geographical areas or localities according to the epidemiological, ecological, social and economic determinants for the purpose of guiding malaria interventions.
Malaria-free	An area in which there is no continuing local mosquito-borne malaria transmission and the risk for acquiring malaria is limited to introduced cases only.
Malaria-free	An area in which there is no continuing local mosquito-borne malaria transmission and where the risk for acquiring malaria is limited to introduced cases only.
Mass drug administration (MDA)	The administration of antimalarial treatment to every member of a defined population or geographical area (except in those in whom the medicine is contraindicated), at approximately the same time and often at repeated intervals. *Note:* MDA is usually performed for the purpose of greatly reducing the parasite reservoir of infection and thus transmission in a population.
Mass screen and drug administration	Screening an entire population for risk factors and treating individuals with risk factors, except in those in whom the medicine is contraindicated. *Note:* An example is seasonal malaria chemoprevention where age is the screening criterion to identify the target group that is then treated.
Mass screen, test, and treat	Screening an entire population for risk factors, testing individuals with risk factors and treating those with a positive test result.
Mass screening	Population-wide assessment of risk factors for malaria infection leading to the identification of subgroups for further intervention such as diagnostic testing, treatment, or preventive services.
Mass test and treat	Testing an entire population and treating individuals with a positive test result.
Mass test and focal drug administration	Testing a population and treating groups of individuals or entire households after detecting one or more infections in the group or household.
Population, target	The population in an implementation unit that is targeted for activities or services (e.g., prevention, treatment)
Preventive chemo-therapy	Use of medicines either alone or in combination to prevent the consequence of malaria infections. *Note:* It includes chemoprophylaxis, intermittent preventive treatment of infants, pregnant women, seasonal malaria chemoprevention and mass drug administration.

Reactive focal (screening, testing, treating, or drug administration)	In response to the detection of an infected person, applying screening, testing, treating, or drug administration, respectively to a subset of the population or a focus.
Transmission, interruption of	Cessation of mosquito-borne transmission of malaria in a geographical area as a result of the application of antimalarial measures.
Transmission, re-establishment of	Renewed presence of a measurable incidence of locally acquired malaria infection due to repeated cycles of mosquito-borne infections in an area in which the transmission had been interrupted. *Note:* A minimum indication of the possible re-establishment of transmission would be the occurrence of three or more introduced and/or indigenous malaria infections in the same focus, for two consecutive years for *P. falciparum* and for three consecutive years for *P. vivax*.

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Surveillance

Age groups	Subgroups of a population classified by age. The following age-grouping is usually recommended: • 0-11 months • 12-23 months • 2-4 years • 5-9 years • 10-14 years • 15-19 years • 20 years and over *Note:* reporting on age groups can be modified as appropriate to local transmission issues whereby certain age groups may be of specific interest (e.g., for passive immunity or assessment of ongoing transmission 0-5 months and 6-11 months; young migrant work force age 20-29 or older; elderly group >60years of age due to risk of complications).
Basic reproduction number	The number of secondary cases that single infection (index case) would generate in a completely susceptible population (referred to as R_0). *Note:* The term "Adjusted reproduction number" or R_c is reproduction number in the presence of a range of interventions in place, e.g. ITNs, IRS, access to treatment.
Case notification	Compulsory reporting of all malaria cases by medical units and medical practitioners, to either the health department or the malaria control programme, as prescribed by national laws or regulations.
Catchment area	A geographic area defined and served by a health programme or institution, such as a hospital or community health centre, which is delineated on the basis of population distribution, natural boundaries, and transport accessibility.
Coverage	A general term referring to the fraction of the population of a specific area which receives a particular intervention.
Endemic area	An area in which there is an ongoing, measurable incidence of malaria infection and mosquito-borne transmission over a succession of years.
Endemicity, levels of	Degree of malaria transmission in an area. *Note:* Various terms have been used to designate levels of endemicity, but none of them are fully satisfactory. Parasite rate or spleen rate in children (2-9 years) have been used to define different levels of endemicity, i.e. hypoendemic: 0-10%; mesoendemic: 10-50%, hyperendemic: constantly over 50%, and holoendemic: constantly over 75% with low adult spleen rate and parasite density declining rapidly between 2 and 5 years of age.

Epidemic	Occurrence of malaria cases highly in excess of the number expected in a given place and time. *Note:* Seasonal increases of malaria should not be confused with epidemics.
House	Any structure other than a tent or mobile shelter in which humans sleep
Household	The ecosystem embracing people and animals occupying the same house and the accompanying vectors.
Incidence, malaria	Number of newly diagnosed malaria cases during a defined period of time in a specified population.
Index, parasite-density	Mean parasite density of slides examined and found positive in a sample of the population; calculated as the geometric mean of the individual parasite density counts
Malaria prevalence (parasite prevalence)	Proportion of the population with malaria infection at one point in time in a specified population.
Malaria, cross-border	Malaria transmission associated with the movement of individuals or mosquitoes across borders.
Malariometric survey	Survey conducted in a representative sample of selected age-groups to estimate the prevalence of malaria and coverage of different interventions. *Note:* Current standard for such surveys is the Malaria Indicator Survey or related Demographic and Health Surveys or Multiple Indicator Cluster Surveys.
Malarious area	Area in which transmission of malaria is taking place, or in which transmission has been present during the preceding three years. *Note:* Initial malarious area in the area where malaria transmission was known to occur in historic time.
National focus register	Centralized database of all foci of malaria infection in a country that includes relevant data on physical geography, parasites, hosts and vectors for each focus.
National malaria case register	Centralized database with line listing of individual records of all malaria cases registered in a country.
Population at risk	Population living in a geographical area where locally acquired malaria cases occurred in the past three years.
Rate, annual blood examination	The number of people receiving a parasitological test for malaria per unit population per year.
Rate, cure	Percentage of treated individuals who no longer have asexual parasites detectable in their blood.

Rate, gametocyte	Percentage of individuals in a defined population in which sexual forms of malaria parasites have been detected. *Note:* This term generally refers to *P. falciparum*. The detection method should be mentioned when citing a gametocyte rate. percentage of cases of falciparum malaria with gametocytes is an indicator of the timeliness of diagnosis and treatment of malaria
Rate, importation	The number of malaria infections per unit time and per unit population that are brought into a particular area from another area
Rate, malaria mortality	Number of deaths from malaria per unit of population over a certain period.
Rate, rapid diagnostic test positivity	Proportion of positive results among all rapid diagnostic tests performed.
Rate, slide positivity	Proportion of blood smears -found to be positive for Plasmodium among all blood smears examined.
Receptivity	Ability of an ecosystem to allow transmission of malaria. *Note:* The ecosystem requires presence of competent vectors, suitable climate, susceptible population, etc.
Risk, importation	Probability of influx of infected individuals and/or infective anophelines. *Note:* Also referred to as vulnerability.
Risk, reintroduction	The risk that endemic malaria will be re-established in a specific area, following its elimination. *Note:* The risk is typically determined by a variety of factors including: climate, altitude, vector populations, human susceptibility, socio-economic status, urban/rural, and intervention coverage, and other factors.
Surveillance	Ongoing, systematic collection, analysis and interpretation of disease-specific data and use in planning, implementing and evaluating public health practice. *Note:* Surveillance can be carried out at different levels of the health care system (e.g. health facility-based, community-based), and using different detection systems (e.g. case-based, active, passive), and sampling strategies (e.g. sentinel sites, surveys).

Transmission intensity	The frequency with which people living in an area are bitten by anopheline mosquitoes carrying human malaria sporozoites. *Note:* Transmission intensity is often expressed as the annual entomological inoculation rate (EIR), which is the average number of inoculations with malaria parasites estimated to be received by one person by time period. Due to the difficulty in measuring IER, parasite rate in young children is often used as a proxy for transmission intensity.
Transmission season	Period of the year during which mosquito-borne transmission of malaria infection usually takes place.
Transmission, perennial	Transmission that occur throughout the year without great variation in intensity.
Transmission, seasonal	Transmission that occurs only during some months and is markedly reduced during other months.
Transmission, stable	Epidemiologic type of malaria transmission characterized by a steady prevalence pattern that does not show great variations from one year to another, except as the result of rapid scale-up of malaria interventions or exceptional environmental changes affecting transmission. *Note:* In areas with stable transmission, the affected population often shows high levels of immunity, and malaria vectors usually have high longevity and man-biting rates.
Transmission, unstable	Epidemiological type of malaria transmission characterized by high variation in prevalence patterns from one year to another. *Note:* In areas with unstable transmission epidemics are common and the population usually shows low levels of immunity.
Vigilance	A function of the public health services aimed at preventing reintroduction of malaria .Vigilance consists of close monitoring for any occurrence of malaria in receptive areas, and application of the necessary measures to prevent the re-establishment of transmission.
Vulnerability	The frequency of influx of infected individuals or groups and/or infective anophelines. *Note:* Also referred to as importation risk. The term can also be applied to introduction of drug resistance to a specific area.

References – Surveillance

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Vector control

aestivation	A process by which mosquitoes at one or several stages (eggs, larvae, pupae, adult) survive by means of behavioural and physiological changes during periods of drought or high temperature.
age, physiological	Adult female mosquito age in terms of the number of gonotrophic cycles completed: nulliparous, primiparous, 2-parous, 3-parous et seq. *Note:* assessed by age-grading, instead of days.
Age-grading of mosquito female adults	Classification of female mosquitoes according to their physiological age (number of gonotrophic cycles) or simply as nulliparous or parous (parity rate). *Note:* Age-grading of vectors is performed mainly to assess impact of environmental changes (natural or intended for control) on vector populations. In epidemiological studies, age-grading of vectors is used to estimate their mean probability of survival – a key variable to calculate the basic reproduction number R_0 and vectorial capacity.
Age-grading of mosquito larvae	classification of mosquito larvae as instars (development stages) 1, 2, 3, 4
Anopheles, infected	Female Anopheles with detectable malaria parasites.
Anopheles, infective	Female Anopheles with sporozoites in the salivary glands.
Anopheline density	Number of female anophelines in relation to the number of specified shelters or hosts (e.g., per room, per trap, or per person) or to a given time period (e.g., overnight or per hour), specifying method of collection. *Note:* Strictly the population density or abundance of adult female Anopheles mosquitoes. Anopheline density is a very insensitive measure of malaria transmission
Anthropophilic	Descriptive of mosquitoes that show a preference for feeding on humans, even when non-human hosts are available. *Note:* A relative term requiring quantification to indicate the extent of preference for anthropophily, versus zoophily. Usually expressed as the human blood index (proportion of mosquitoes that have fed on humans out of total fed).

Bioassay	In applied entomology, the experimental testing of the biological effectiveness of a treatment (e.g. infection, insecticide, pathogen, predator, repellent) by deliberately exposing insects to it. *Note:* When bioassays are employed for periodically monitoring the continued efficacy of residual insecticide deposits on sprayed surfaces in houses (as for IRS), attention should be given to the environmental conditions and possible adverse factors (e.g. washing, re-plastering, soot) affecting the intertidal deposits on treated surfaces; these factors may reduce effectiveness of the treatment differently from the intrinsic rate of decay of the insecticide.
Capture site	Site selected for periodic sampling of the mosquito population of a locality for various evaluation purposes.
Diapause	Condition of suspended animation or temporary arrest in development of immature mosquitoes.
Endophagy	Tendency of mosquitoes to blood-feed indoors. *Note:* Contrasted with exophagy.
Endophily	Tendency of mosquitoes to rest indoors. *Note:* Contrasted with exophily; usually quantified as proportion resting indoors versus outdoors, for purposes of assessing IRS impact and vector potential.
Exophagy	Tendency of mosquitoes to feed outdoors. *Note:* Contrasted with endophagy; usually quantified as the proportions biting hosts outdoors versus indoors, conveniently assessed by comparative human landing catches (HLC) outdoors and indoors, or by observation of biting rates on non-human hosts outdoors.
Exophily	Tendency of mosquitoes to rest outdoors. *Note:* Contrasted with endophily; usually quantified as proportion resting outdoors versus indoors, for estimating outdoor transmission risks.
Experimental huts	For vector investigations: simulated house with entry and exit traps for sampling mosquitoes entering and exiting, blood-feeding indoors (when host present), surviving or dying in each sub-sample, per day or night. *Note:* Experimental huts are employed for standard protocols to evaluate indoor treatments (IRS and ITNs) against endophilic mosquitoes.

Gonotrophic cycle	Each complete round of ovarian development in the female mosquito, usually after ingestion of a blood meal, to yield a batch of eggs. Gonotrophic harmony is when every blood meal results in one batch of eggs from the gonotrophic cycle. *Note*: Temperature and other environmental factors affect duration of the gonotrophic cycle, taking a few days or weeks, strongly influencing vectorial capacity. Before completion of the first gonotrophic cycle, the adult female mosquito is nulliparous; after laying eggs she is parous; after successive gonotrophic cycles she is primiparous, 2-parous, 3-parous, 4-parous, et seq.
Gonotrophic discordance (gonotrophic dissociation)	Female mosquitoes taking more than one bloodmeal per gonotrophic cycle.
hibernation	Process by which mosquitoes at one or several stages (eggs, larvae, pupae, adult) survive by means of behavioural or physiological changes during cold periods.
House-spraying	Application of liquid insecticide formulation to specified (mostly interior) surfaces of buildings.
Human Landing Catches (HLC)	A method for collecting vectors as they land on individuals. *Note:* Purpose is to monitor exposure of the human population to vector populations. Employed for estimating the 'human biting rate' a basic factor to calculate R_0 and vectorial capacity in epidemiological studies.
Index, host preference	Proportion of blood-fed female Anopheles that fed on the host species and/or individual of interest. *Note:* Blood-fed female Anopheles are sampled from representative resting sites and each blood meal is identified to host species or individual. The methods include 'precipitin testing' and molecular assays.
Index, human blood (HBI)	Proportion of mosquito blood meals from humans.
Indoor residual spraying (IRS)	Operational procedure and strategy for malaria vector control: spraying interior surfaces of dwellings with a residual insecticide to kill or repel endophilic mosquitoes
Indoors	Inside any shelter likely to be used by humans or animals, where mosquitoes may feed or rest. *Note:* Where indoor-resting mosquitoes can be targeted for indoor residual spraying.

Insecticide	Chemical product (natural or synthetic) that kills insects: ovicide kills eggs; larvicide (larvacide) kills larvae; pupacide kills pupae; adulticide kills adult mosquitoes; residual insecticide remains active for prolonged time. *Note:* For malaria vector control, insecticides are approved by the World Health Organization Pesticides Evaluation Scheme (WHOPES) – see http://www.who.int/whopes/
Insecticide cross-resistance	Resistance to one insecticide by a mechanism that also confers resistance to another insecticide, even where the insect population has not been selected by exposure to the latter.
Insecticide discriminating dose, or diagnostic dose for resistance	Amount of an insecticide (usually expressed as the concentration per standard period of exposure) which, in a sample of mosquitoes containing resistant individuals, distinguishes between susceptible or resistant phenotypes and determines their respective proportions. *Note:* Where the genetic factor for resistance is either dominant or recessive, only one discriminating dose operates. Where it is semi-dominant, two such doses may operate: a lower discriminating dose killing susceptibles only and an upper diagnostic dose killing both susceptibles and heterozygous (but not homozygous) resistant individuals.
Insecticide dosage	Amount of active ingredient insecticide applied per unit area of treatment (mg/m^2) as in indoor residual spraying or treated bednets or per unit of space (mg/m^3) as in space spraying.
Insecticide mixture	Insecticide product consisting of two or more active ingredients mixed as one formulation so that, when applied, the mosquito will contact both simultaneously.
Insecticide mosaic	Strategy for mitigating resistance, whereby insecticides with different modes of action are applied in different parts of an area under coverage (usually in a grid pattern), so that parts of the mosquito populations are exposed TO one while others are exposed to another. *Note:* ideally combined with insecticide rotation whereby the treatments are periodically switched between parts of the mosaic

Insecticide resistance	Property of mosquitoes that can survive exposure to a standard dose of insecticide that may be the result of physiological or behavioural adaptation. *Note:* The emergence of insecticide resistance in a vector population is an evolutionary phenomenon caused either by behavioural avoidance (e.g. exophily instead of endophily) or by physiological factors whereby the insecticide is metabolised, not potentiated, or absorbed less compared to susceptible mosquitoes.
Insecticide rotation	Strategy involving sequential applications of insecticides with different modes of action to delay or mitigate resistance.
Insecticide tolerance	Less than average susceptibility to insecticide, but not inherited as resistance.
Insecticide, contact	Insecticide that exerts a toxic action to mosquitoes when they rest on a treated surface and the insecticide is absorbed via the tarsi (feet).
Insecticide, fumigant	Insecticide which acts through the release of vapour from a volatile substance.
Insecticide, residual	Insecticide which, when suitably applied on a surface, maintains for a considerable time its insecticidal (residual) activity by either contact or fumigant action.
Integrated Vector Managment (IVM)	A rational decision-making process for the optimal use of resources for vector control. *Note:* IVM aims to improve efficacy, cost-effectiveness, ecological soundness and sustainability of vector control activities against vector-borne diseases.
Larval Source Management	Management of aquatic habitats (water bodies) that are potential larval habitats for mosquitoes, in order to prevent the completion of development of the immature stages. *Note:* There are four types of LSM: 1) Habitat modification: a permanent alteration to the environment, e.g. land reclamation; 2. Habitat manipulation: a recurrent activity, e.g. flushing of streams; 3. Larviciding: the regular application of biological or chemical insecticides to water bodies; and 4. Biological control: the introduction of natural predators into water bodies.
Larvicide	Substance used to kill mosquito larvae. *Note:* Larvicides are applied in the form of oils (to asphyxiate larve and pupae) or emulsions, or as small pellets or granules of inert carrier impregnated with insecticide, which is released gradually when they are placed in water.

Net, Insecticide-treated (ITN); **Long-lasting insecticidal net (LLIN)**	Mosquito net that repels, disables or kills mosquitoes that come into contact with the insecticide on the netting material. There are two categories of ITN: − Conventionally treated net: a mosquito net that has been treated by dipping it in a WHO- recommended insecticide. To ensure its continued insecticidal effect, the net should be re-treated periodically. − Long-lasting insecticidal net (LLIN). A factory-treated mosquito net made of netting material with insecticide incorporated within or bound around the fibres. The net must retain its effective biological activity without re-treatment for at least 20 WHO standard washes under laboratory conditions and 3 years of recommended use under field conditions. *Note:* Untreated bednets can also provide substantial protection against mosquito bites, but they have less impact on vectorial capacity and transmission rates.
Oocyst	The stage of malaria parasite developing from the ookinete: the oocyst grows on the outer wall of the midgut in the female mosquito.
Oockine	Motile stage of malaria parasite following fertilization of macrogamete and preceding oocyst formation.
Rate, biting	Average number of mosquito bites received by a host in unit time, specified according to host and mosquito species (usually measured by HLC). *Note:* For human malariology we are mainly interested in the 'human biting rate' of vectors.
Rate, entomological inoculation (EIR)	Number of infective bites received per person in a given unit of time, in a human population. *Note:* It is the product of the "human biting rate" (the number of bites per person per day by vector mosquitoes) and the sporozoite rate (proportion of vector mosquitoes that are infective). At low levels of transmission, the EIR estimates may be less reliable and alternative methods should be considered to evaluate transmission risk.
Rate, oocyst	Percentage of female Anopheles with oocysts on the midgut.
Rate, sporozoite	Percentage of female Anopheles with sporozoites in the salivary glands.
Repellent	Anything causing avoidance by mosquitoes, especially deterring them from settling on skin of the host (topical repellent) or entering an area or room treated with the repellent substance (area repellent, spatial repellent, excito-repellent)

Spray round	Implementation of spraying of all sprayable structures in an area designated for coverage in an IRS programme during a discrete period of time. *Note:* According to the residual activity of the insecticide, but also to the dynamics of transmission one or more spray round a year may be required in the same area.
Sprayable	In malaria vector control program context: a unit (dwelling, house, room, shelter, structure, surface) suitable for spraying, or required to be sprayed. *Note:* Usually in context of house-spraying operations implemented by indoor residual spraying (IRS).
Spraying cycle	Repetition of spraying operations at regular intervals; often designated in terms of the interval between repetitions, e.g., six-month spraying cycle when spraying is repeated after a six-month interval. *Note:* Not to be confused with spray round.
Spraying frequency	Number of regular insecticide applications per house per year, usually by IRS.
Spraying interval	Time elapsing between successive applications of insecticide.
Spraying, focal	Spray coverage by indoor residual spraying and/or space spraying of houses or habitats in a limited geographic area.
Spraying, residual	Spraying interior walls and ceiling of dwellings with a residual insecticide to kill or repel endophilic mosquito vectors of malaria.
Transmission, residual	Persistence of transmission after achieving good coverage with high quality vector control interventions to which local vectors are fully susceptible. *Note:* A combination of human and vector behaviours are responsible for this remaining transmission, for example when people stay outdoors during the night or when local mosquito vector species exhibit one or more behaviours that allow them to avoid the core interventions.
Trap hut	Structure adapted for trapping mosquitoes attracted by bait (human or animal) placed inside it. *Note:* Its purpose is to collect a representative portion of the incoming mosquitoes, and/or to test the effectiveness of an insecticide. It is usually a hut of simple design, often built of the same material as the local habitations, provided with trapping devices-usually one or more window traps so that mosquitos may be trapped as they enter or leave.

Vector	In malaria, female adults of any mosquito species in which Plasmodium undergoes the sexual cycle (therefore, the mosquito is the definitive host of the parasite) to the infective sporozoite stage (completion of extrinsic development) ready for transmission when biting a vertebrate host. *Note:* Malaria vector species are usually implicated (incriminated) by field collection and dissection to prove infection with sporozoites in salivary glands; PCR assays may be applied to detect and identify circum-sporozoite protein, especially where infection rates are low.
Vector competence	For malaria, the ability of the mosquito to support completion of malaria parasite development after zygote formation and oocyst formation, development and release of sporozoites that migrate to salivary glands, allowing successful transmission of viable sporozoites when the infective female mosquito feeds again. *Note:* Human malarias are exclusively transmitted by competent species of Anopheles mosquitoes; other malarias are transmitted by competent species of various genera of mosquitoes (*Aedes, Anopheles, Culex*) or other haematophagous Diptera.
Vector control	Measures of any kind against malaria-transmitting mosquitoes intended to limit their ability to transmit the disease. *Note:* Ideally, malaria vector control results in reduction of malaria transmission rates, due to limitation of vectorial capacity, to the point where transmission is interrupted.
Vector susceptibility	The degree to which the mosquito population is susceptible (i.e. not resistant) to insecticides. *Note:* Not to be confused with vector competence (see definition)
Vector trap	Device designed to capture mosquitoes, using appropriate lures (light, CO_2, living baits, suction) in order to sample their densities or to study effects of attractants, repellents, control interventions; mosquito trapping may also be intended for their control.
Vector, principal	Species of Anopheles mainly responsible for transmitting malaria in any particular circumstances. *Note:* Principal vectors may overlap seasonally or alternate in importance.
Vector, secondary or subsidiary	Species of *Anopheles* thought to play a lesser role in transmission than the principal vector; capable of maintaining malaria transmission at a reduced level.

Vectorial capacity	Number of new infections that the population of a given vector would induce per case per day at a given place and time, assuming the population is and remains fully susceptible.

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6. Indoor residual spraying: an operational manual for indoor residual spraying for malaria transmission control and elimination. Geneva: World Health Organisation; 2013.
7. Larval Source Management --operational manual. Geneva: World Health Organisation; 2013.
8. Manual for indoor residual spraying. Geneva: World Health Organisation; 2007 (WHO/CDS/NTD/WHOPES/GCDPP/2007.3).
9. Silver JB. Mosquito Ecology Field Sampling Methods. Third Edit. 2008.
10. Test Procedures for Insecticide Resistance Monitoring in Malaria Vector Mosquitoes. Geneva: World Health Organisation; 2013.

Archived terms

Biting-capture, biting collection, human bait collection (HBC)	sampling of population of mosquitoes and other haematophagous insects by capture when they bite on human bait, or other hosts. *Note:* Discouraged for ethical reasons, to prevent human exposure to risks of transmission of vector-borne diseases (VBDs); human landing collection (HLC) is the recommended alternative.
Breeding site, breeding place	Obsolete term for larval habitat: site where developmental stages of mosquitoes (eggs, larvae, pupae) are found; including sites appearing ecologically suitable for particular species.
Cure, clinical	Relief of symptoms of a malaria attack (e.g., by chemotherapeutic action against asexual erythrocytic parasites) without complete elimination of the infection.
Cure, suppressive	Complete elimination of the parasite from the body by means of continuous suppressive treatment.
Discharge register	List of patients who leave inpatient hospital care. Discharge registers should contain the date of admission, patient's name, residence, age, sex, diagnosis, length of stay and reason for leaving (discharged, died, transferred, absconded). This information should be abstracted from the patient file by appropriately trained staff.
Drug failure	Absence or insufficiency of drug action after administration of a normally effective dose. It is important to discriminate between such causes of drug failure as deficient absorption, unusual rate of degradation or excretion of the drug, and resistance of the parasite.
Infection interval	Period elapsing from the time an individual is infected until he himself becomes infectious to others. In malaria the infection interval is the period from the inoculation of a human being with sporozoites until the appearance of gametocytes potentially infective to mosquitos. To be distinguished from incubation interval and incubation period.
Malaria baseline	The malaria burden that would be present in a specific area if no control activities existed. This is also termed 'intrinsic malaria transmission level'.
Malaria, refractory	Term used by some authors to describe persistence or slow and gradual reduction of the amount of malaria despite total-coverage spraying.
Malaria, responsive	Term used by some authors to describe malaria that is rapidly reduced in amount by total-coverage spraying soon after the beginning of the attack phase.

Malaria, sporadic	Term applied to malaria when autochthonous cases are too few and scattered to cause any appreciable effect on the community. These cases are often due to relapses of a previous infection: for purposes of epidemiological classification by origin of infection, the term "relapsing " is then preferred.
Mass blood examination	Examination of the blood of all persons in a unit of the population, which may be repeated at certain intervals. Blood specimens are commonly obtained during house-to-house visits. Unlike other case-detection methods, mass blood examinations are used to discover all persons harbouring malaria parasites, even those who have no clinical symptoms; they thus supplement the routine methods in special problem areas and are useful in demonstrating the proportion of asymptomatic carriers present in the community examined. They form a part of case-detection activities and must be distinguished from malariometric surveys, which are carried out on a sampling basis in selected groups.
Mass primaquine preventive treatment	Administering primaquine anti-relapse therapy to every individual in a defined population or geographical area during the low transmission season for the elimination of long-latency hypnozoites in infected persons with the aim of reducing P. vivax malaria transmission during the next transmission season *Note:* For safety reasons, G6PD testing of the recipients would be required prior to the intervention.
Outbreak	A case or number of cases of locally transmitted infection greater than would be expected at a particular time and place. *Note:* Used instead of epidemic.
Outpatient register	List of patients seen in consultation in a health facility; the register may include the date of consultation; patient's age, place of residence and presenting health complaint; tests performed; and diagnosis.
Phase, attack	In malaria eradication terminology, the phase during which antimalarial measures applicable on a large scale and aiming at the interruption of transmission are applied on a total-coverage basis in an operational area. This phase is sometimes called the period of total coverage spraying
Phase, consolidation	In malaria eradication terminology, the phase that follows the attack phase; it is characterized by active, intense and complete surveillance with the object of eliminating any remaining infections and proving the eradication of malaria. It ends when the criteria for eradication have been met.

Phase, maintenance	In malaria eradication terminology, period which begins when the criteria of malaria eradication have been met in an operational area and which will continue until world-wide eradication has been achieved. During this period vigilance is exercised by the public health services to prevent the spread of malaria imported from across the borders of the area concerned.
Phase, preparatory	In malaria eradication terminology, time devoted to preparation for the attack operations. It ends when the epidemiological and geographical reconnaissance in the operational area are completed, the central and peripheral stations and essential services established, the staff recruited and trained, and the logistic and reporting systems organized.
Population, vulnerable	Groups of people who are particularly vulnerable to malaria infection in certain situations or contexts, such as mobile workers. Each country should define the specific populations that are particularly vulnerable based on the epidemiological and social context.
Population-based blood survey	Survey in which a blood smear taken on one of more occasions from every individual in a given population (i.e. irrespective of history of fever) to assess the prevalence of malaria parasitaemia (both symptomatic and asymptomatic) in the population. These surveys may also be used to provide supportive evidence of the interruption of transmission.
Pre-eradication programme	Preliminary operation undertaken in a country whose general administrative and health services have not yet reached a level which would enable it to undertake a malaria eradication programme.
Pre-eradication survey	Operation aimed at the collection of accurate data on the malaria situation, preliminary to drafting a complete plan of operations for a malaria eradication programme. The undertaking of the survey presupposes the existence of evidence that transmission can be interrupted by the use of methods commonly employed in malaria eradication and the existence of basic operational facilities. The pre-eradication-survey period ends when the plan of operations has been prepared.
Prophylaxis, absolute	Absolute prevention of infection would imply destruction of inoculated sporozoites before they could fix themselves in the tissues.

Prophylaxis, clinical	Clinical prophylaxis implies prevention of clinical symptoms by early destruction of erythrocytic parasites. It is said to suppress malaria when it permits the continued existence of exoerythrocytic forms or of some erythrocytic forms which will permit subsequent multiplication of the para site after discontinuation of the drug. All blood schizontocides are clinical prophylactic drugs or suppressants, since they destroy merozoites entering the blood stream before they can establish schizogony. This results in prevention of erythrocytic infection, or at least in its reduction to a sub patent level, while the drug is being taken, but overt attacks may occur after it is discontinued.
Rate, malaria morbidity	Number of recorded clinical cases of malaria per unit of population over a certain period. The malaria morbidity rate is too imprecise to be of value in malaria eradication.
Rate, parasite	Percentage of persons in a defined age group showing, on a given date, microscopically detectable parasites in the peripheral blood. The parasite rate should always be defined in terms of the age group examined.
Sub-perennial	Transmission occurs throughout the year with peaks of markedly greater intensity in some months.
Surveillance, active	Surveillance where public health officers seek reports from participants in the surveillance system on a regular basis, rather than waiting for the reports (e.g. telephoning each participant monthly). *Note:* A surveillance system in which public health workers seek reports on a regular basis from participants in the surveillance system, rather than waiting passively for the reports to be submitted).
Surveillance, case-based	Every case is reported and investigated immediately and also included in the weekly reporting system. *Note:* Surveillance based on investigating all cases included in the regular reporting system.
Surveillance, community	Surveillance where the starting point for the notification is from community level, normally reported by a community worker. It can be active (looking for cases) or passive (reporting cases). This may be particularly useful during an outbreak and where syndromic case definitions can be used (the active identification of community cases of Ebola virus infection in Kikwit was an example of active community surveillance). *Note:* Surveillance where the starting point for notification is the community level, usually from a community worker. community surveillance can be either active or passive.

Surveillance, hospital-based	Surveillance where the starting point for notification is the identification by a hospital of a patient with a particular disease or syndrome. *Note:* Surveillance where the starting point for notification is the identification by a hospital of a patient with a particular disease or syndrome.
Surveillance, passive	Surveillance where reports are awaited and no attempt are made to seek reports actively from the participants in the system. *Note:* A system in which no attempts are made to seek reports actively from the participants in the system.
Surveillance, sentinel	of data from a sample (random or non-random) of collecting sites as indicator data for the rest of the population, in order to identify cases* of a disease early or to obtain indicative data about trends of a disease or health event*. Examples are the use of a few hospitals to monitor the composition of influenza virus and check that the vaccine includes the right components, or the use of a network of general practitioners to monitor diseases or health events (e.g. attempted suicide, requests for HIV testing). One instance of sentinel surveillance is the use of a particular population group (e.g., monitoring the serology of syphilis among pregnant women as an indicator of syphilis trends in the general population). Sentinel surveillance is inappropriate for those situations where every case requires public health action, e.g., poliomyelitis. Commentary: Collection and use of data from a random or non-random sample (random or non-random) of collecting sites as an indicator data for the rest of the population as a whole, in order to identify cases of a disease early or to obtain indicative data about trends of a disease or health event not malaria specific.
Treatment, suppressive	Treatment aimed at preventing or eliminating clinical symptoms and/or parasitaemia by early destruction of erythrocytic parasites. It does not necessarily prevent or eliminate the infection, and overt malaria may develop after drug withdrawal.
Treatment, targeted	Group-level application of anthelminthic drugs where the group eligible for treatment may be defined by age, sex, or other social characteristics irrespective of infection status (exclusion criteria may apply).
Vector efficiency	imprecise way of ranking vector species or populations as relatively more or less important in transmission Commentary: less calculable than vectorial capacity

Vector potential	Value of vectorial capacity for competent vector species or population. Note: c.f. *potential vectors* are species with vector competence and appreciable vectorial capacity

GLOBAL MALARIA PROGRAMME

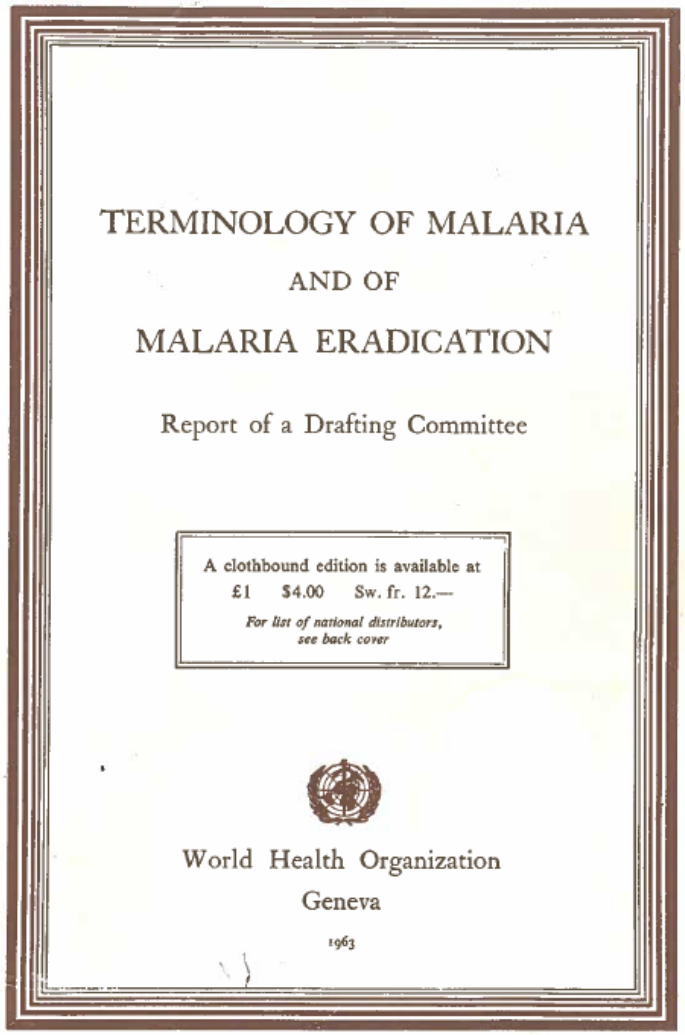
World Health Organization

Report of the WHO Drafting Committee on Malaria Terminology

Malaria Policy Advisory Committee
Geneva, Switzerland
16-18 September 2015

Rick Steketee
Chairperson, WHO Drafting Committee
on Malaria Terminology

TERMINOLOGY of MALARIA and of MALARIA ERADICATION
Report of a Drafting Committee (1963)



TERMINOLOGY OF MALARIA

AND OF

MALARIA ERADICATION

Report of a Drafting Committee

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World Health Organization
Geneva
1963

DRAFTING COMMITTEE

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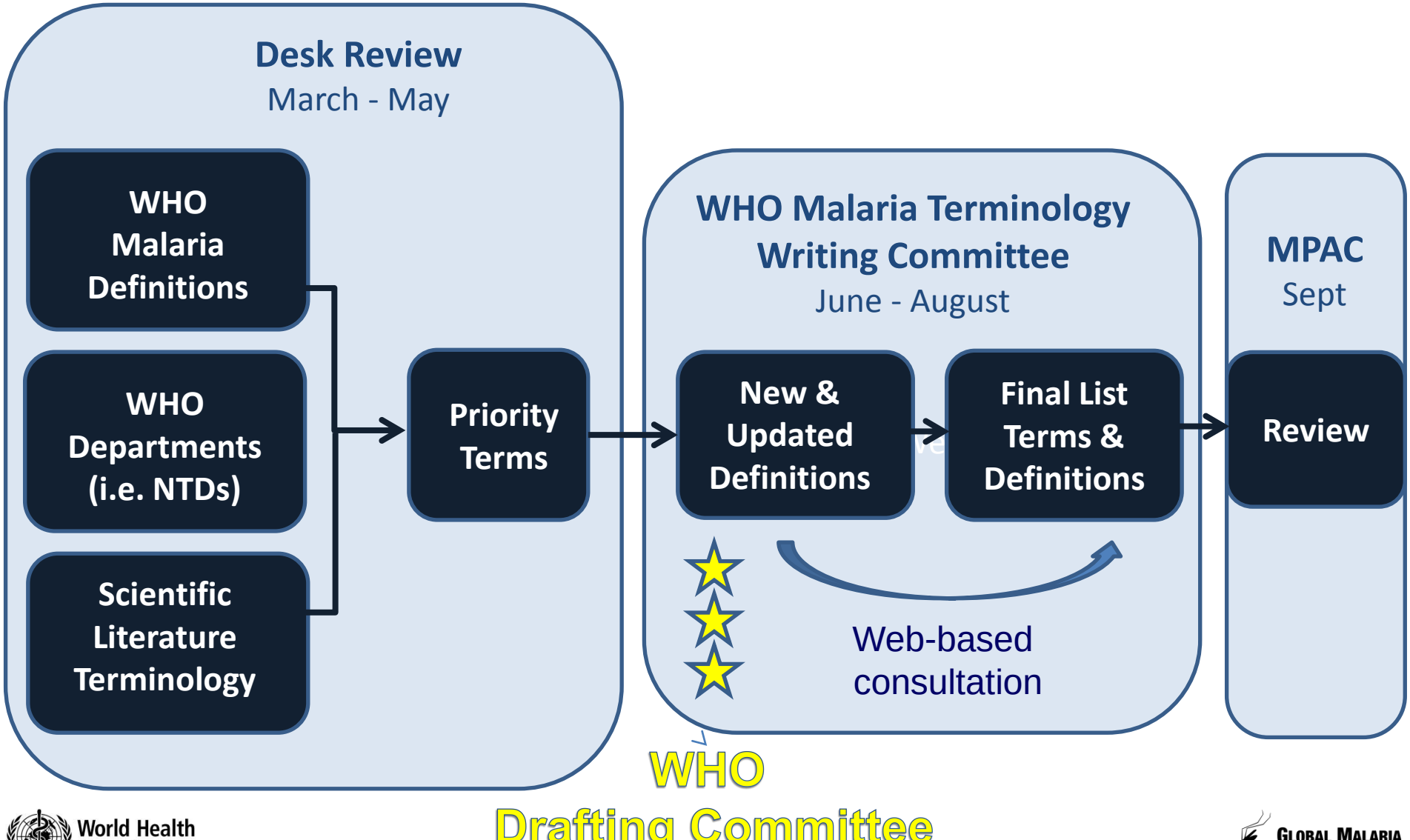
Background

- In recent years there has been a proliferation of new terms in relation to malaria in the scientific literature, media and technical reports, and an increase in the number of terms that have a new or modified use and meaning (e.g. hotpops, hotspots, malaria sources and sinks, proactive infection detection, reactive infection detection, reactive targeted parasite elimination, network testing, time-location testing, dry season vector control HiFSAT – highly focused screening and treatment).
- To complicate matters further:
  - sometimes term are used to mean different things (e.g. case, screening);
  - sometimes, several similar terms are used to mean similar things (e.g. MSAT, MTAT and MSTAT, FSAT and FTAT, MDA and Targeted Malaria Elimination or Targeted Parasite Elimination or Targeted Chemo-Elimination, mass primaquine preventive (or prophylactic) treatment);
  - some terms are used with different meanings by different public health programmes (e.g. elimination, certification, preventive chemotherapy).

Phased Approach in Updating Terminology

- Terms that were and are still relevant and properly described – each definition or description can be reviewed for any need to update the language, but generally these terms could be considered “good as they stand”.
- Terms that have been used in the past and have value in an historical perspective, but are not really in current use (e.g. the endemicity categories and some of the spraying terminology); these terms may be important to keep for historical purposes, and could simply be updated in language.
- Terms that are relevant today but may have taken on a new and modified use and meaning – these terms need to be reviewed and possibly redefined, or at least updated so that the language of the definition reflects their current use, as well as new terms that have come into use and may need to be included and clearly defined.

Process & Timelines



Phase 1 – desk Review (April-May)

a. compile all WHO definitions of terms used in WHO malaria publications since 1995, in addition to those contained in the glossary of “WHO Terminology of malaria and of malaria eradication, 1963”;

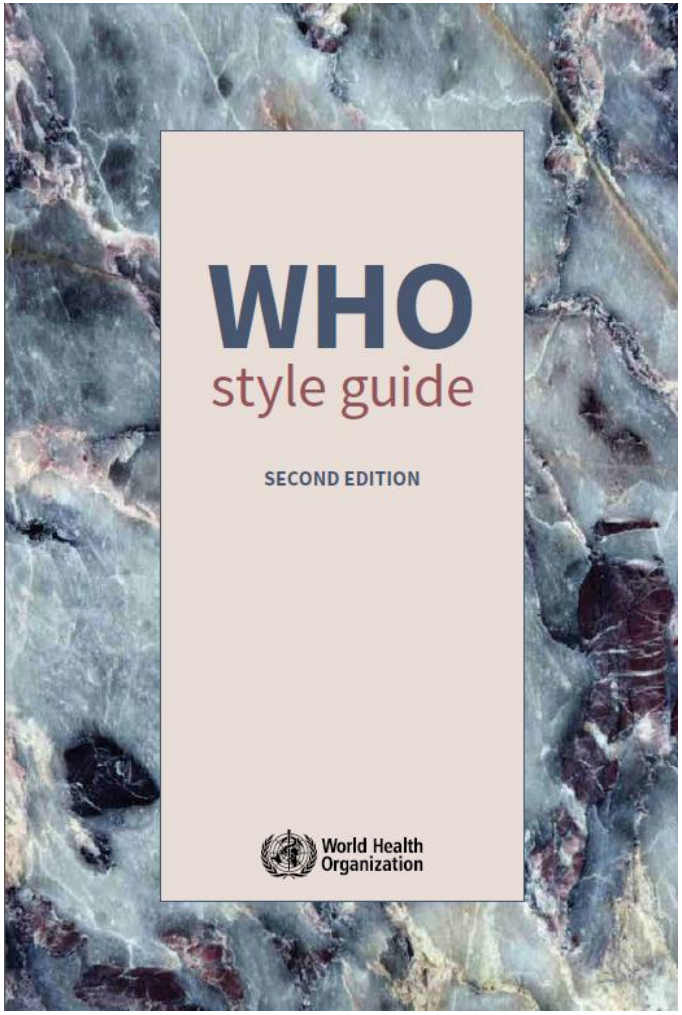
b. compile the specific WHO definitions used by other WHO departments for the same terms (e.g. preventive chemotherapy for NTDs);

c. identify from systematic literature research over the past 10 years recurrent terms that are similar but with different meanings, and multiple different with similar meanings;

As a result of the desk review a total of 292 terms were identified and draft definitions proposed. Terms were divided in four groups related to elimination (50), vector control (69), surveillance (85) and diagnosis and treatment (88) - many relevant to both surveillance and elimination.

Members, Secretariat & Style

- Desk Review
  - Mar Velarde
- Drafting Committee
  - Andrei Beljaev,
  - Graham Brown, Kamini Mendis,
  - José Najera,
  - Trenton Ruebush
  - Rick Steketee
  - Graham White
- WHO Secretariat
  - Andrea Bosman



Drafting Committee: Meeting on 2-3 June 2015

Objectives of the meeting

- To revise priority terms that need to be updated or given new definitions based on the relevance to malaria elimination and eradication, current programmatic use and conflicting definitions in malaria and other public health programs;
- To define the process for finalisation of identified terms in order to be presented at the MPAC meeting in September;
- To develop a system for reviewing and incorporating new terms; and
- To agree on mechanisms for dissemination and promotion of uptake of new terms

Drafting Committee: Meeting on 2-3 June 2015

Decision Principles

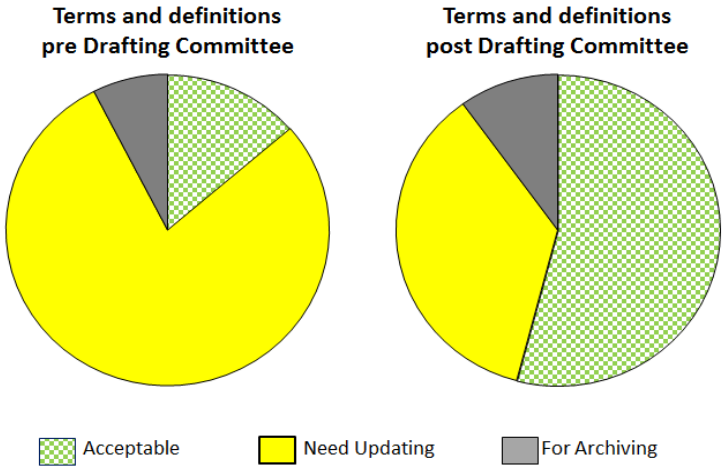
- Keep definitions short and crisp with a balance between technically correct and user-friendly language;
- Use “comments” linked to the definitions to provide relevant context and additional information;
- Generally avoid trendy and cute terms including acronyms and abbreviations;
- Highlight problematic terms for specific additional discussion

Phase 2 - WHO Drafting Committee

a. Identify the priority terms that need to be updated or given new definitions, based on the following criteria:
   - i. terms relevant to malaria elimination and eradication
   - ii. terms with programmatic relevance
   - iii. terms with conflicting definitions.

b. Develop updated or new definitions for priority terms

c. Outcome of the review by the Drafting Committee:

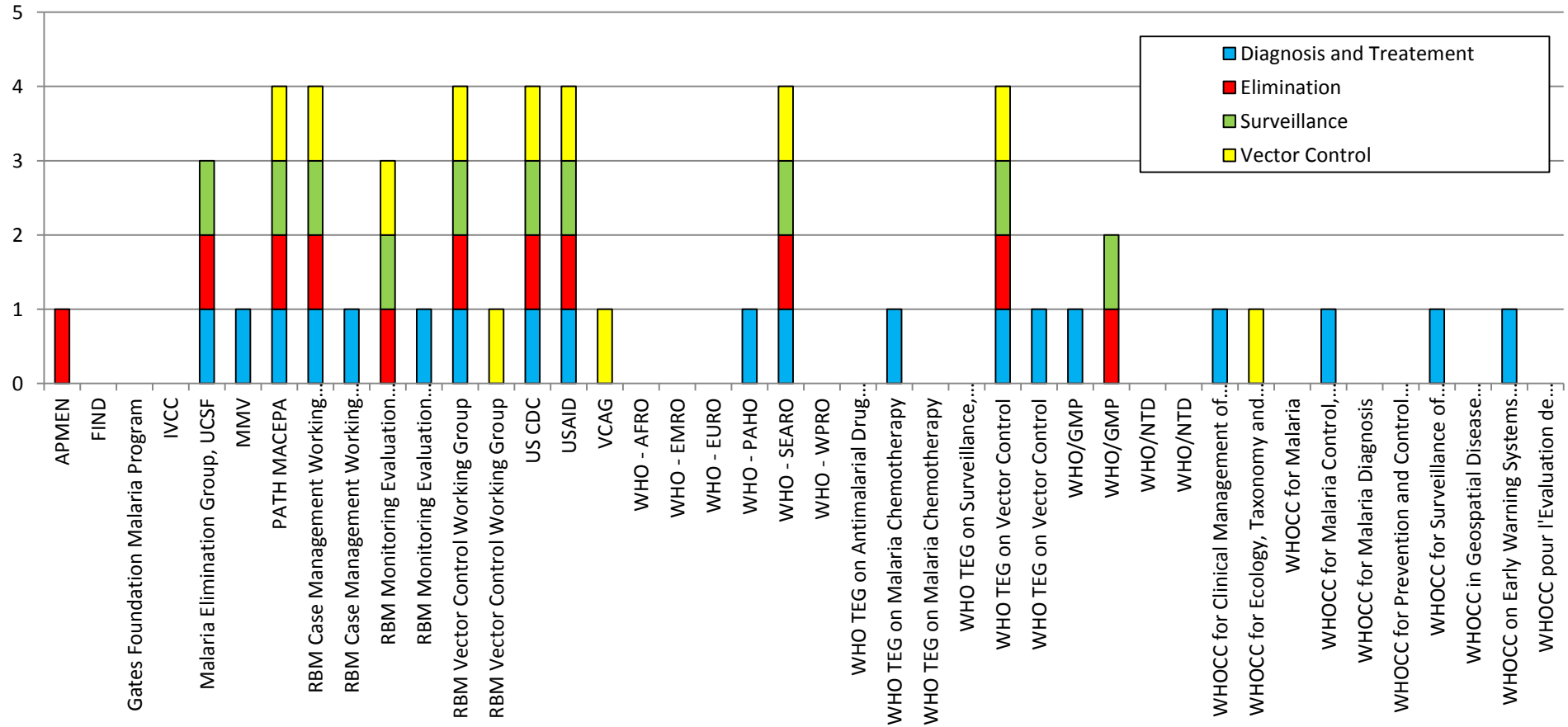


External Survey

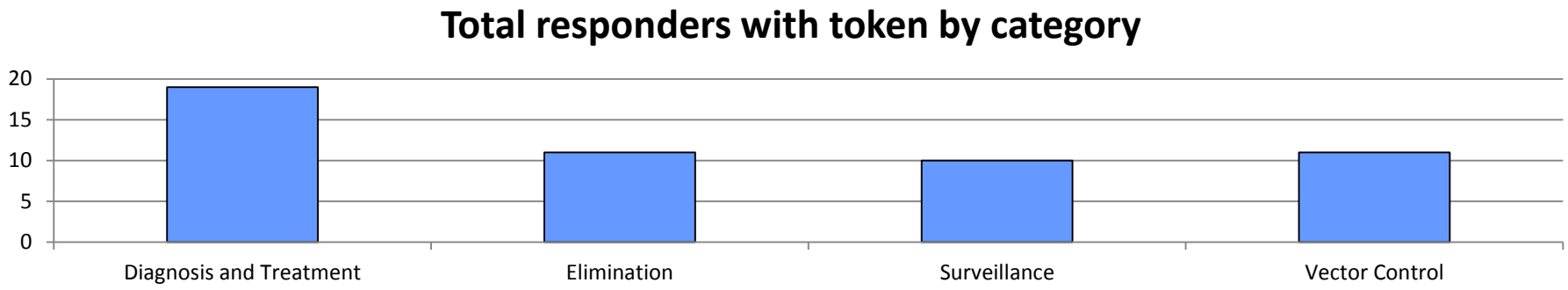
- 101 terms in 4 categories included in the survey:

  Diagnosis and treatment (32), Elimination (28), Surveillance (21), Vector control (20)

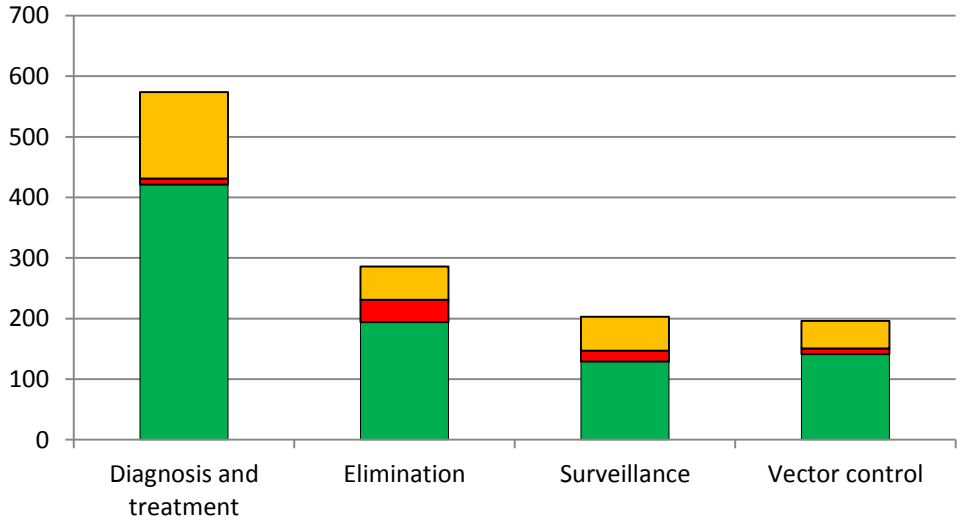
- Responses: 25 tokens by 20 institutions/groups



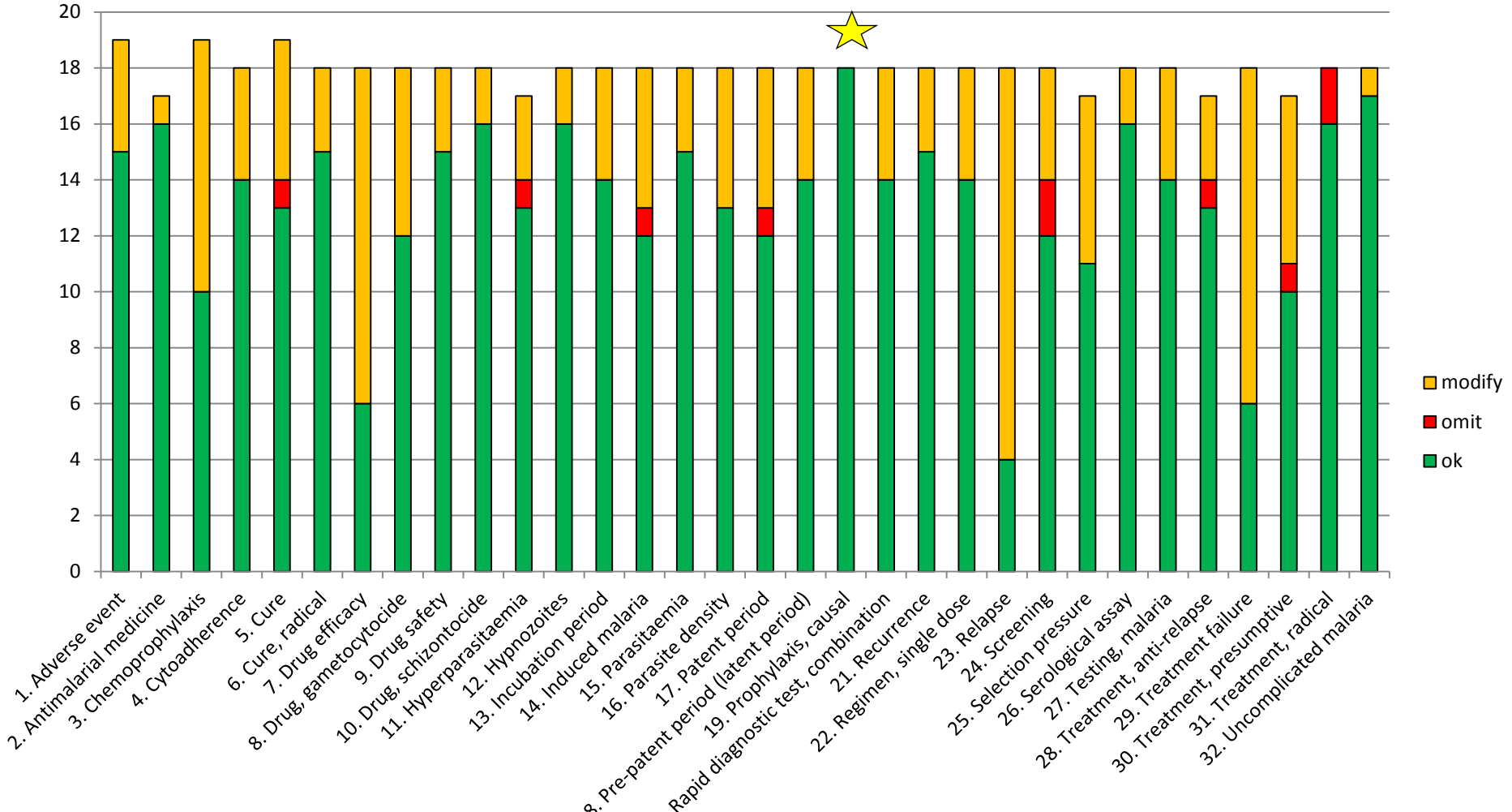
Survey statistics (III)



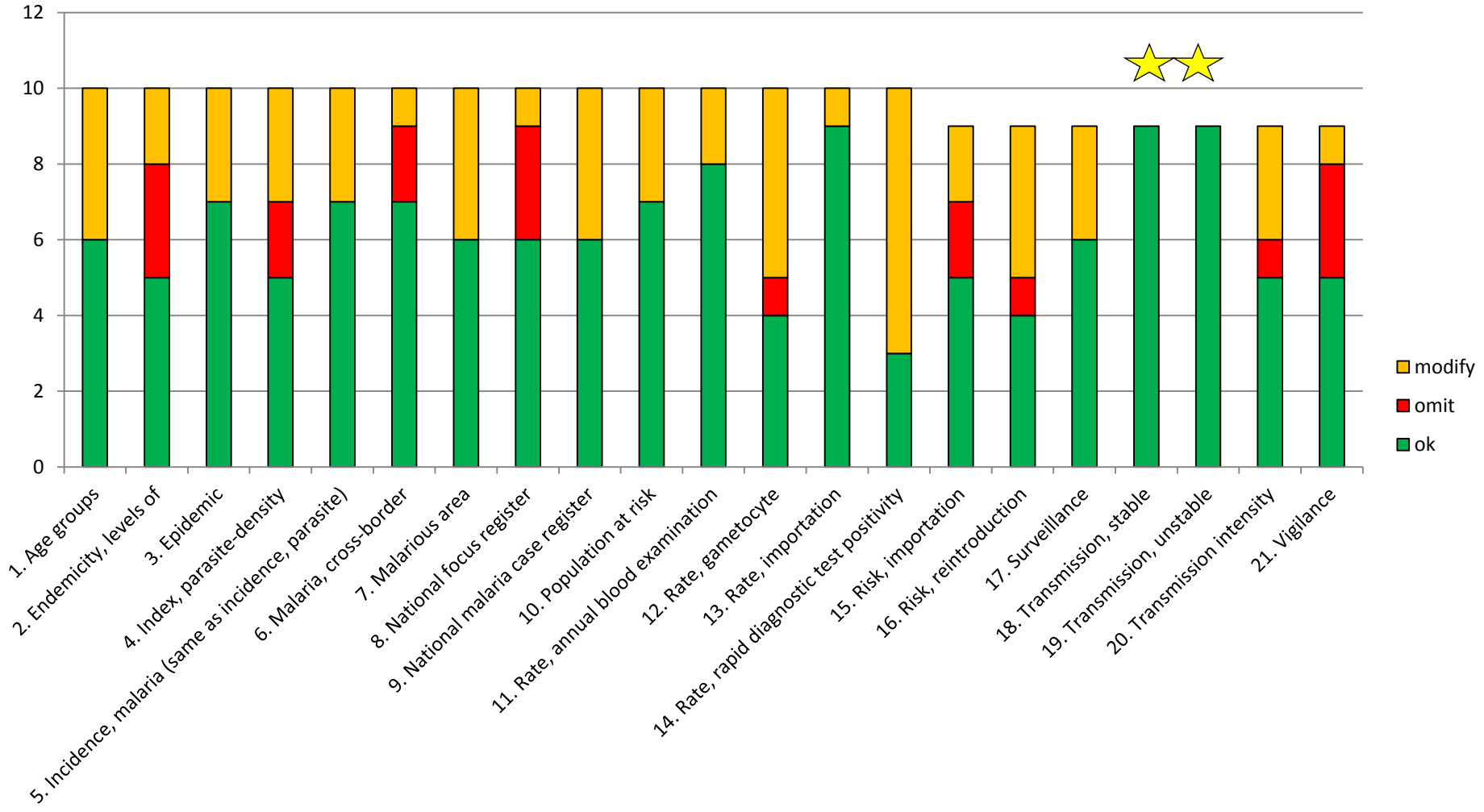
- A total of 1260 entries was received
  - (884 ok, 75 omit, 301 modify)
- 5 terms marked ok by all reviewers



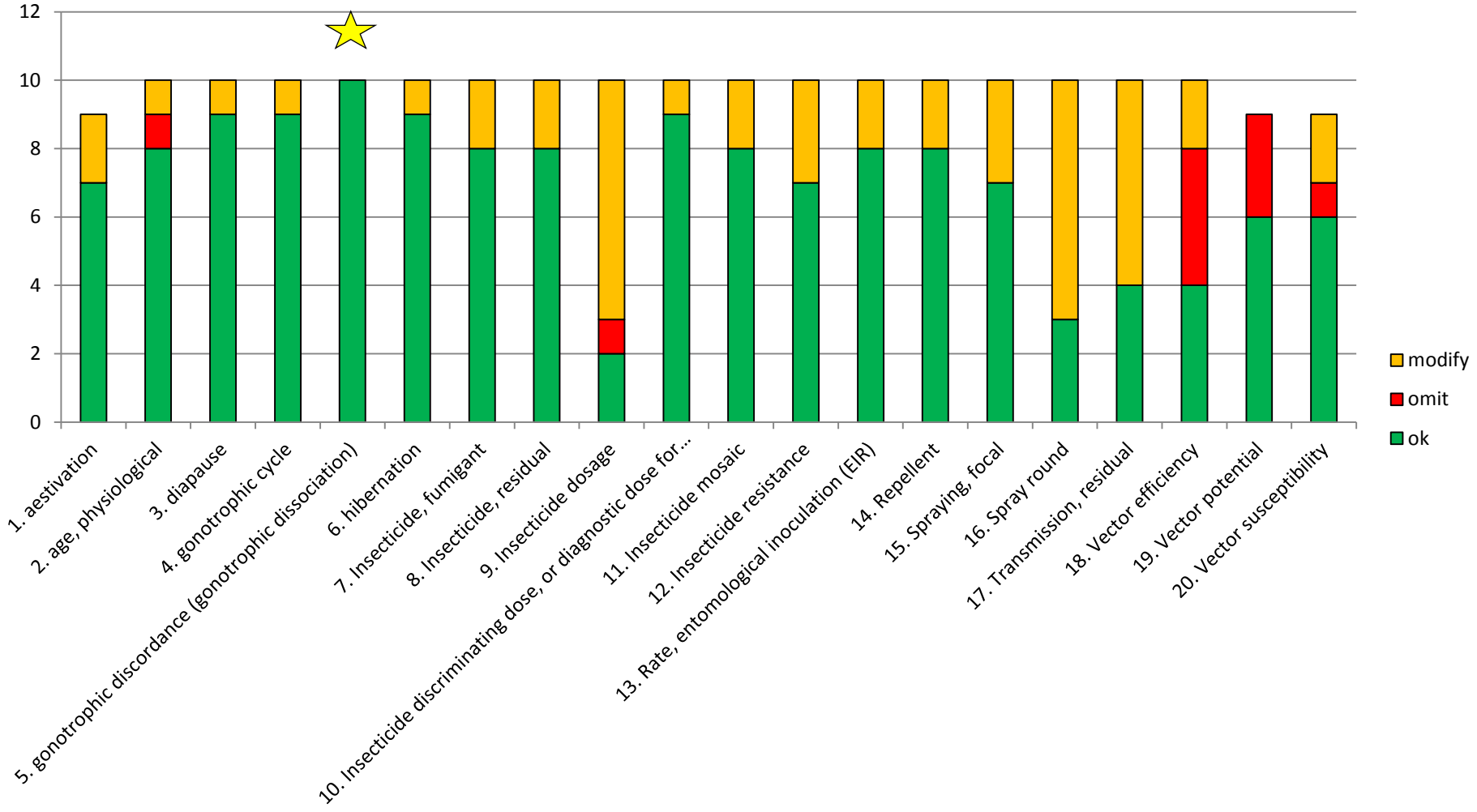
Responses per Category (I): Diagnosis and Treatment



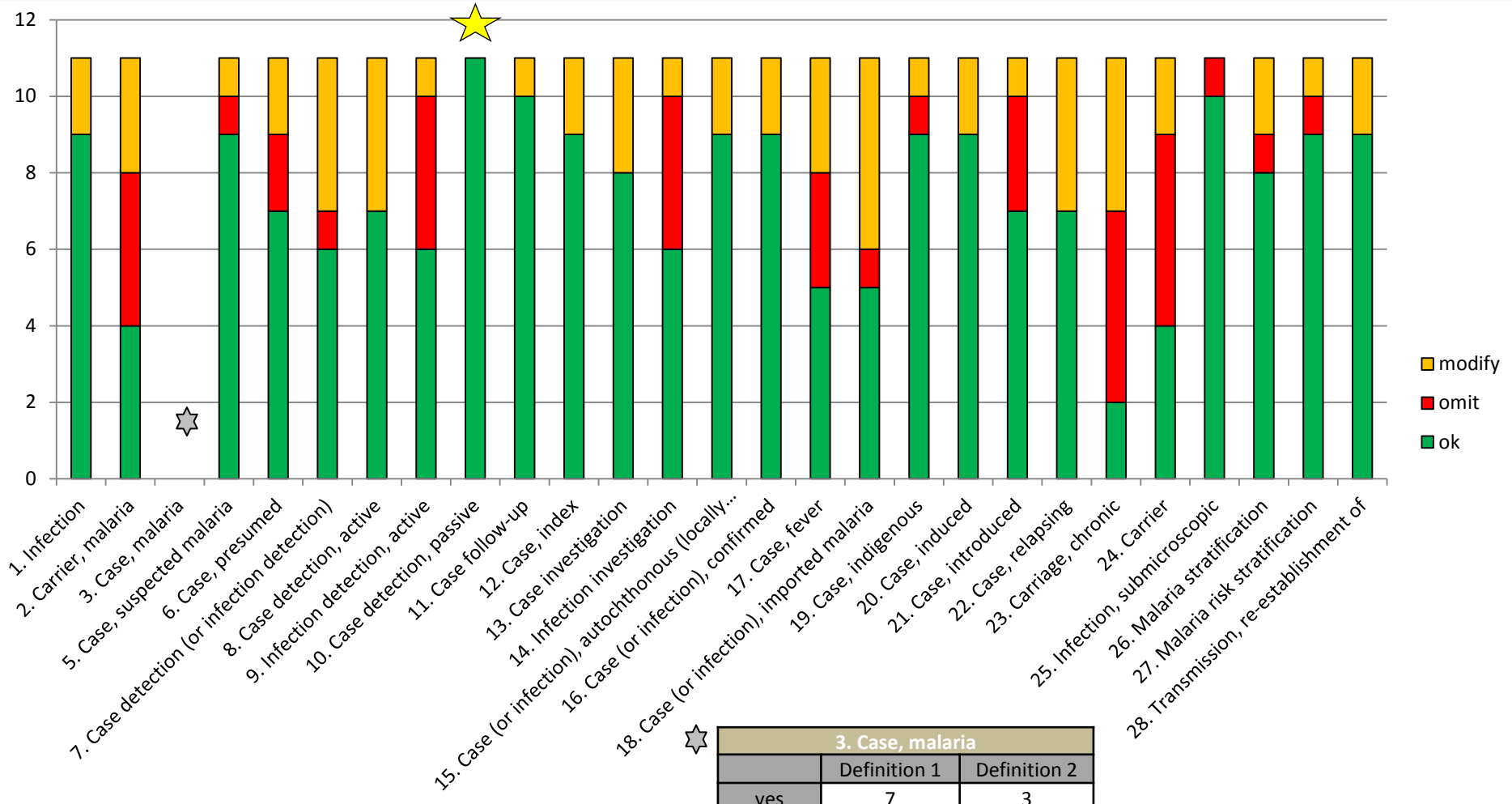
Responses per Category (III): Surveillance



Responses per Category (IV): Vector Control



Responses per Category (II): Elimination



3. Case, malaria		
	Definition 1	Definition 2
yes	7	3
uncertain	2	4
no	2	3

The Changes in WHO Definition of "Malaria Cases"

- **WHO Terminology of malaria and of malaria eradication, 1963**

Malaria case. In malaria eradication terminology, occurrence of **malaria infection in a person in whom, regardless of the presence or absence of clinical symptoms**, the presence of malaria parasites in the blood has **been confirmed by microscopic examination**. During surveillance, every malaria case detected is classified, according to the origin of the infection, as indigenous or as imported, introduced, relapsing or induced. (WHO Malaria Terminology, 1963)

The Changes in WHO Definition of "Malaria Cases"

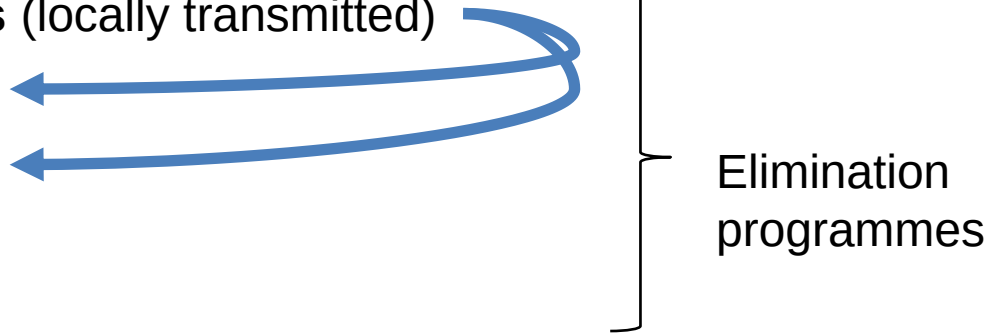
- **WHO Terminology of malaria case, 1998**

Malaria cases: We concentrate here on **parasitologically confirmed**, **symptomatic cases** on the grounds that, wherever malaria is an important disease, microscopic diagnosis 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 detection activities) should be presented separately as these represent malaria infection, but not malaria cases. Where most persons with symptoms plus parasitemia 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):**

$$\text{API} = \frac{\text{No. parasitologically confirmed cases/year}}{\text{Population at risk}} \times 1000$$

The Changes in WHO Definition of "Malaria Cases"

- WHO **Disease surveillance for malaria control: an operational manual**, 2010
  - **Confirmed malaria**
  - **Presumed malaria**
  - **Suspected malaria**
  - **Autochthonous** (locally transmitted)
  - **Indigenous**
  - **Introduced**
  - **Induced**
  - **Imported**



- **Malaria Case.** Any case, in which, regardless of the presence or absence of clinical symptoms, the presence of malaria parasites in the blood has been confirmed by quality-controlled malaria laboratory diagnosis

Two Definitions for Malaria Case in Current Glossary

Definition #1:

- Occurrence of **malaria illness/disease** in a person in whom the presence of malaria parasites in the blood has been **confirmed by parasitological testing**. Note: A malaria case can be classified as suspected, presumed, confirmed (based on the level of confirmatory diagnosis) and as indigenous, induced, introduced, imported, relapsing (based on the origin of infection). *(Assumes that we would introduce an alternative definitional term for asymptomatic infections identified by active processes)*

Definition #2:

- Occurrence of **malaria infection (symptomatic or asymptomatic)** in a person in whom the presence of parasites in the blood has been **confirmed by parasitological testing**. Note: A malaria case can be classified as indigenous, induced, introduced, imported, relapsing (based on the origin of infection).

Lack of Consensus by Drafting Committee/Reviewers

Those preferring definition #2:

- Advantage of continuity with the past GEP
- Single all encompassing definition may be better for surveillance; exchangeable with “infection”
- Aligned with malaria elimination actions (seeking both symptomatic and asymptomatic infections) that are increasingly adopted by countries; already adopted by countries in final steps to elimination
- Affirms parasitological confirmation
- Not all infections are cases (e.g. hypnozoite carriers are infected, but are not cases)
- All malaria data sets and reports should include the definition used of "malaria case"

Those preferring definition #1:

- Advantage of continuity for surveillance reporting of “cases” as a program transitions from control to elimination
  - consistent/same case definition for control/elimination: case counting, SPR (slide positivity rate), API (annual parasite incidence), CFR (case fatality rate) remain stable measures.
- Many countries remain in transition between control and elimination and current case definition comes from the control program
- Permits/forces the differentiation between detection/identification of symptomatic and asymptomatic infections
- Affirms parasitological confirmation
- Assumes use of an alternative term/ definition for asymptomatic infection

Lack of Consensus by Drafting Committee/Reviewers

Those preferring using different definitions (#1 and #2), in different phases of malaria control and elimination:

- Malaria surveillance reports both confirmed and presumed malaria cases - parasitological confirmation is “mandatory” only in elimination settings.
- Surveillance can evolve as part of programme transitions.
- Case definitions for surveillance can change based on operational setting. -- also assumes that measures of progress in higher transmission “control” areas may differ from measures of progress in very low transmission “elimination” areas.

Lack of Consensus by Drafting Committee/Reviewers

Caveats on “opinions” of drafting committee and reviewers:

- Drafting committee is small
- Number of external reviewers is modest
- Additional engagement of program managers and regional leadership in malaria may be particularly relevant

Requested Advice from MPAC

- Advise WHO on malaria case definition
- Feedback on the Glossary with proposed terms and definitions
- Advice on process for reviewing and incorporating new terms
- Mechanisms for dissemination and promoting uptake following MPAC review

GLOBAL MALARIA PROGRAMME

World Health Organization

Update on artemisinin resistance and ACT efficacy

Malaria Policy Advisory Committee
Geneva, Switzerland
16-18 September 2015

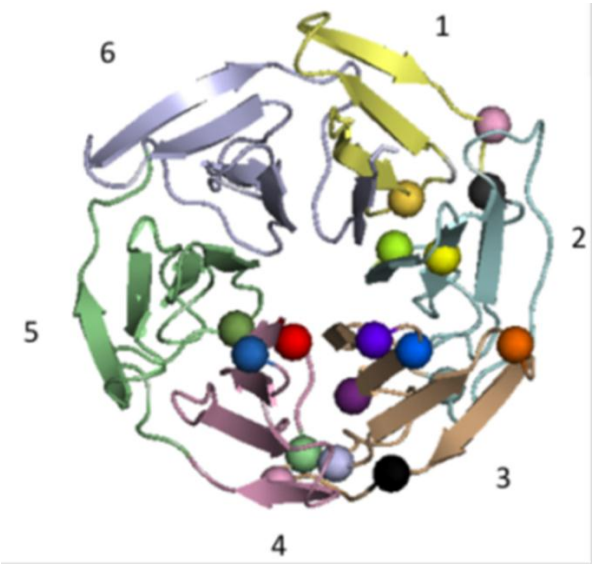
P. Ringwald
Drug Resistance and Containment Unit

Outline

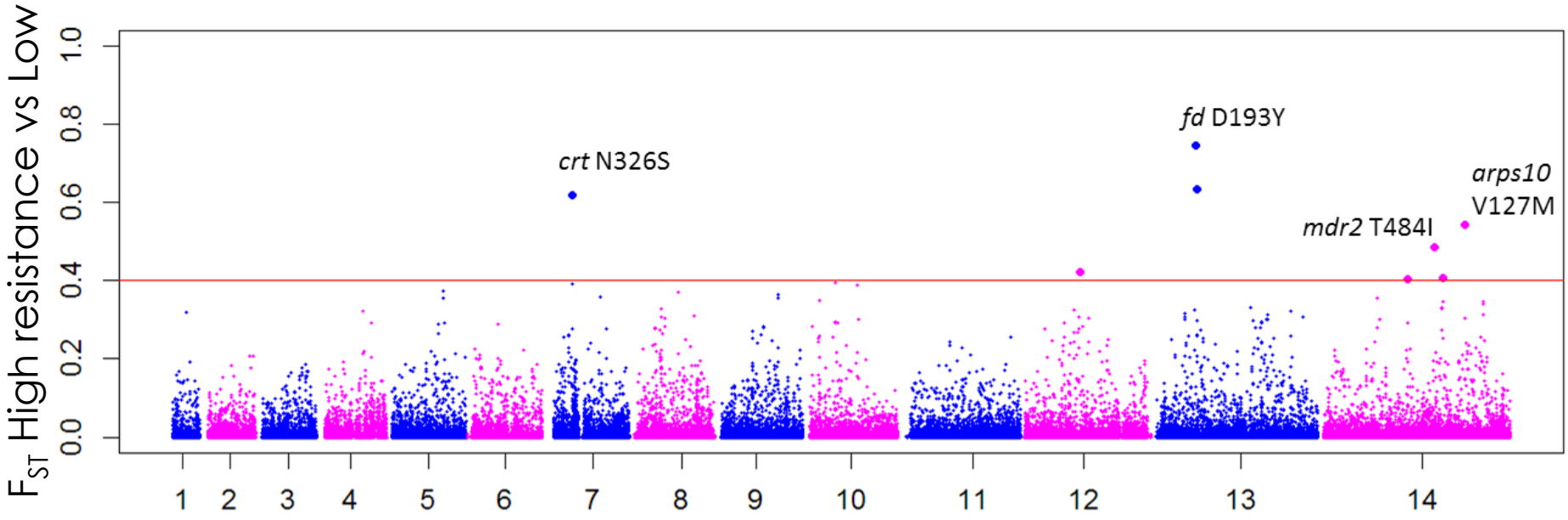
- Definition of artemisinin resistance
- KARMA project
- Efficacy of AL and ASAQ
- Efficacy of AS+SP
- Efficacy of DHA-PIP in Cambodia
- Efficacy of DHA-PIP in GMS outside Cambodia

Definition of artemisinin resistance

- Artemisinins resistance is defined as delayed clearance = <u>partial resistance</u>
- Prolonged treatment with artemisinin are highly effective in SEA:
  - 7-day artesunate > 95% efficacy in Cambodia, China, Myanmar and Viet Nam;
  - 3-day artesunate + ACT 100% efficacy;
- Mutations in the Kelch 13 (K13)-propeller domain were shown to be associated with delayed parasite clearance in vitro and in vivo;
- Artemisinin emerged independently is multiple foci in South-East Asia;
- Patients with a delayed parasite clearance response are still cured by ACTs, provided that the partner drug remains effective even in area of high prevalence of K13 mutant (China, Myanmar and Viet Nam).



GWAS confirms key role for K13 and possible "permissive" or compensatory background mutations



Mutation	BD	WSEA	ESEA		
			HR	IR	LR
kelch13	0%	33%	79%	27%	2%
arps10 V127M	0%	61%	92%	42%	12%
fd D193Y	2%	81%	95%	35%	3%
mdr2 T484I	6%	78%	88%	46%	23%
crt N326S	31%	100%	94%	38%	10%

Note: differentiation is on both sides of SEA! E.g.

- W. Thailand vs. Bangladesh
- W. Cambodia vs. Laos

Miotto O et al. (2015) *Nature Genetics*

KARMA project

Objectives

•Provide data (worldwide mapping) on the current distribution of artemisinin resistant parasites (mutant K13 allele parasites) using blood samples already collected (after 2012) from both symptomatic patients or asymptomatic individuals, with a minimum of standard parameters (sample location, year of collection, age, sex, etc..)

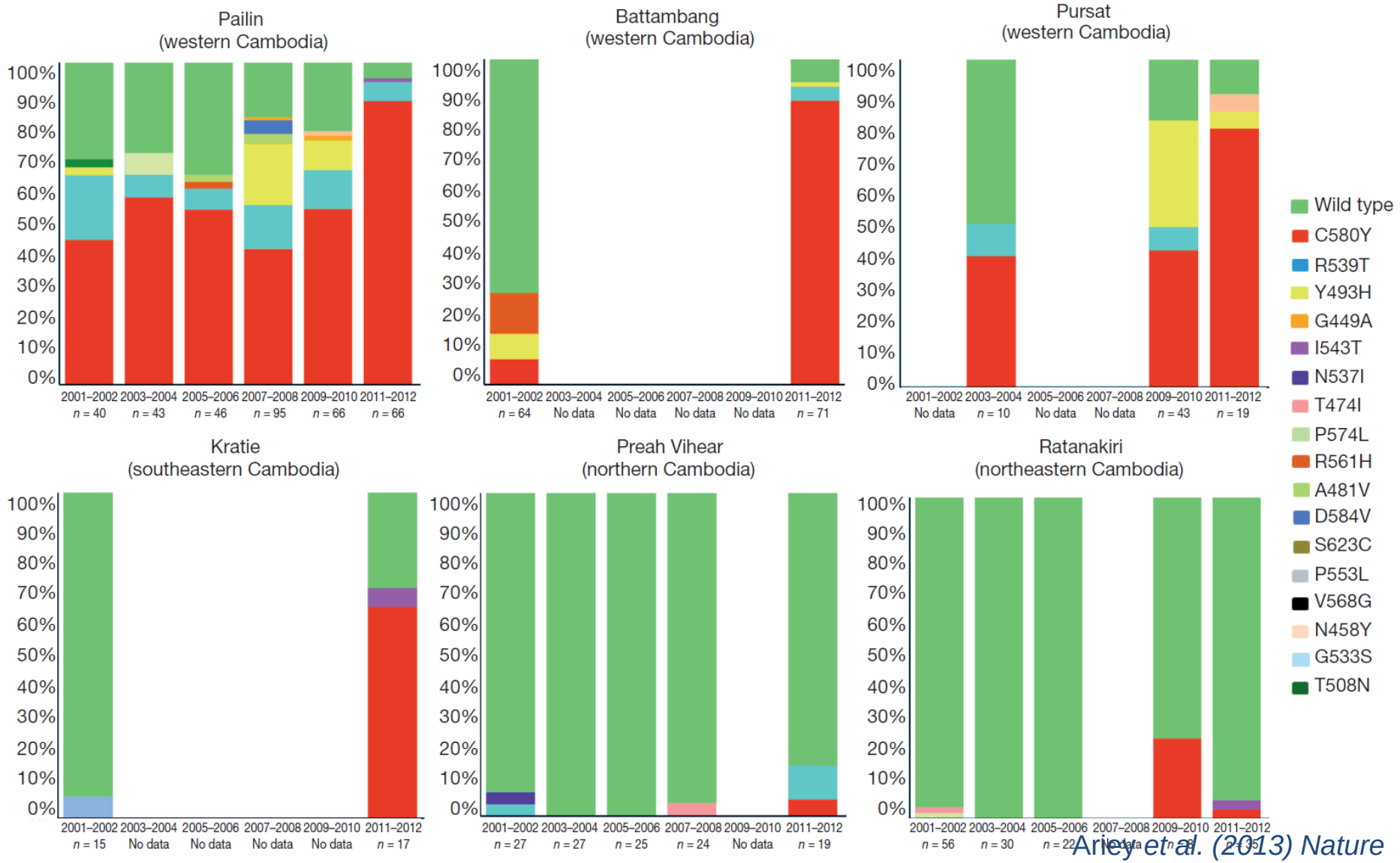
•Provide capacities and expertise (capacity building) to each participant to monitor the over-time trend of the artemisinin resistance by using IP molecular approach (prevalence of the K13).

Expected results

•Snapshot mapping of the geographical distribution of K13 allelles polymorphism and the prevalence of artemisinin resistant parasites (K13 mutant alleles)

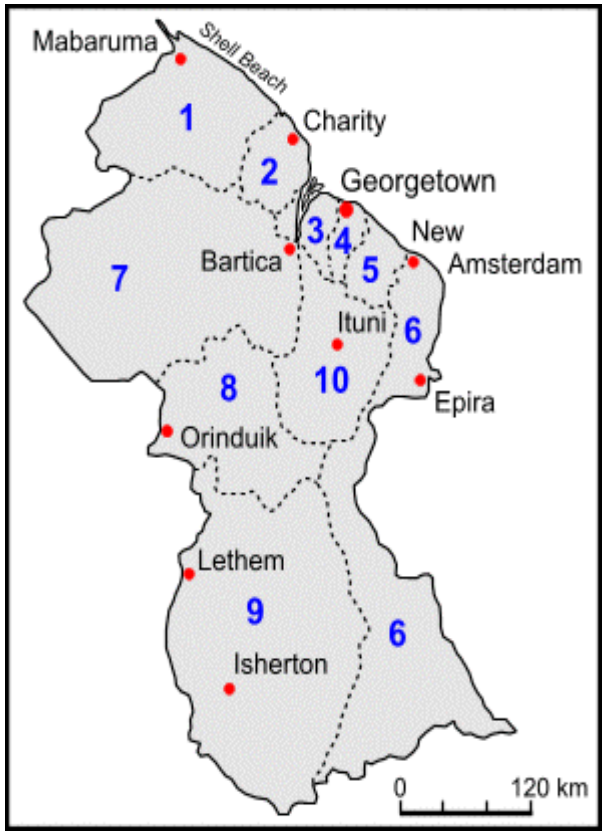
•Support to participants through training to monitor overtime the detection of artemisinin resistance.

Frequency of K13-propeller SNPs in 886 parasite isolates in six Cambodian provinces in 2001–2012



Ariey et al. (2013) Nature

Guyana

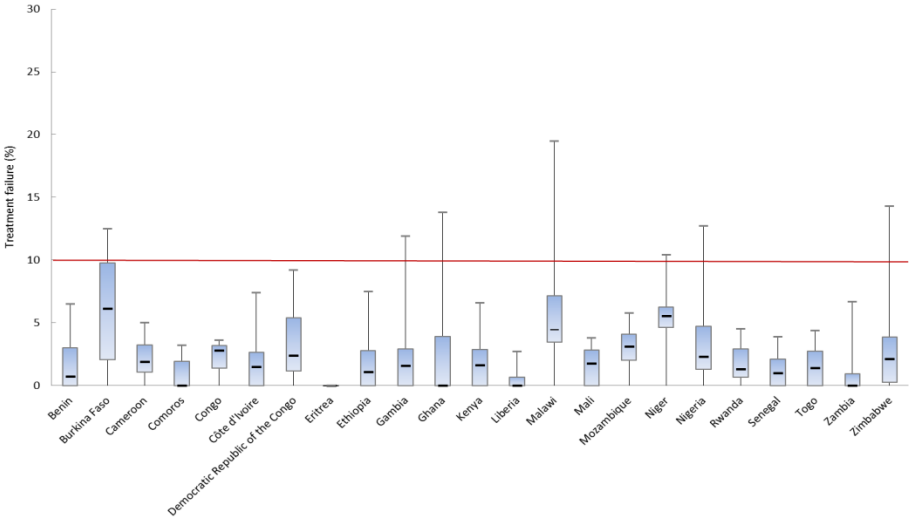


- Sample collected in 2010 for HRP2 survey;
  - 5 samples carried the mutant C580Y (4/5 from zone 7)
  - All five samples had similar K13 flanking microsatellite profiles and were different to the ones observed in Southeast Asia
- June-Nov 2014: 7-day artesunate trial (4 mg/kg/day) + primaquine single dose;
  - 2% day-3 positivity rate; 100% efficacy; 100% of K13 wild type
  - 50% from zone 7
- Next step: survey conducted in zone 7 (800 samples);
- No C580Y reported in other countries (Brazil, Fr Guiana, Suriname).
  - ,

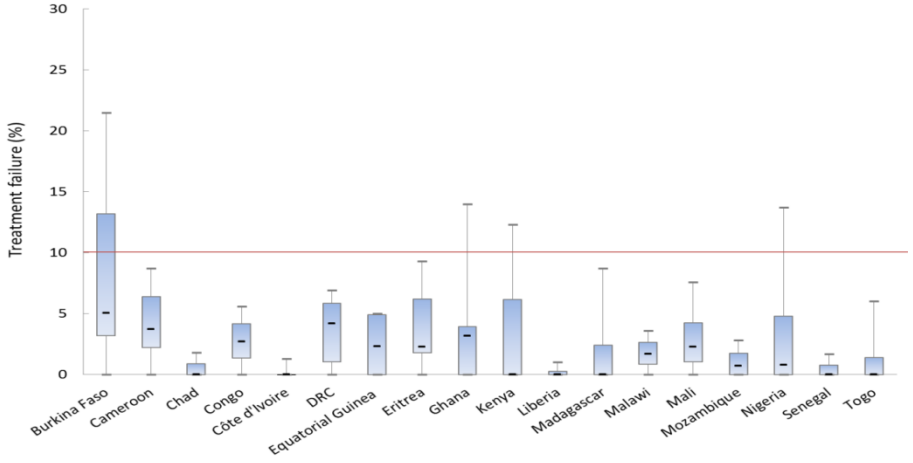
Associated and validated K13 resistance mutations

K13 mutation	Classification
441L	Associated
446I	Associated
449A	Associated
458Y	Associated
493H	Confirmed
539T	Confirmed
543T	Confirmed
553L	Associated
561H	Associated
568G	Associated
574L	Associated
580Y	Confirmed
675V	Associated

ACT efficacy in Africa

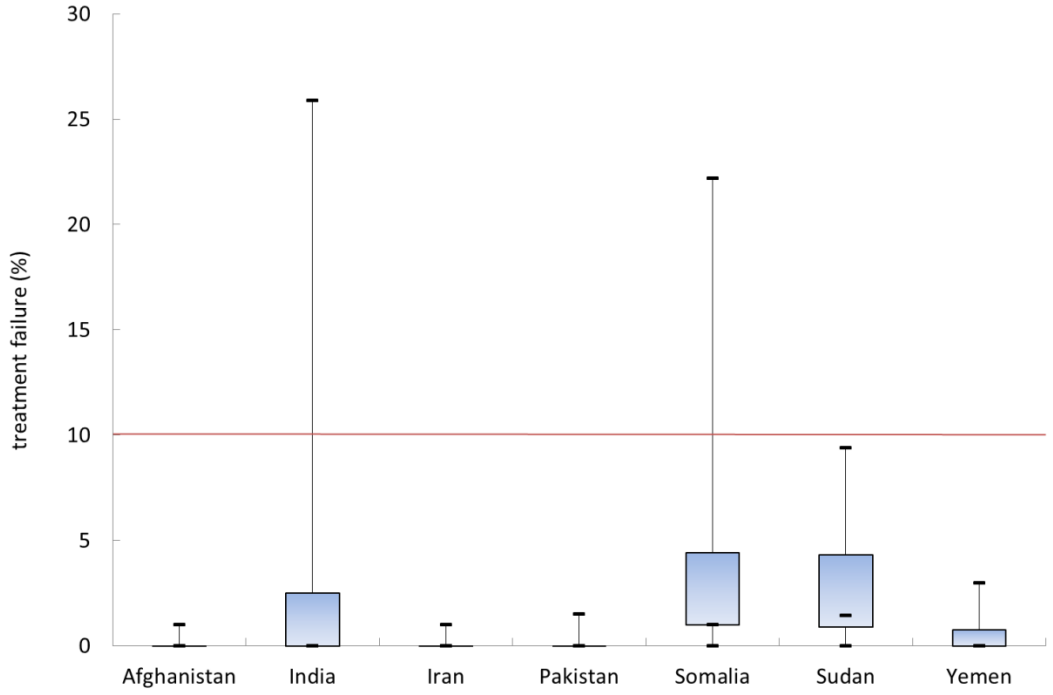


AL



ASAQ

Efficacy of AS+SP

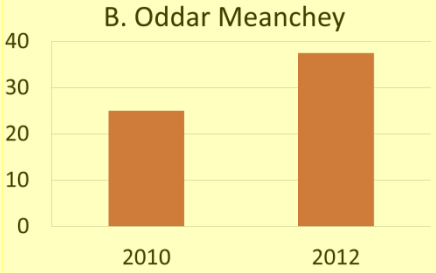


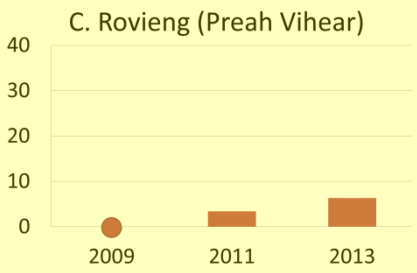
- In India, Somalia and Sudan, treatment failure failures are associated with *Pfdhfr* and *Pfdhps* quadruple and quintuple mutants;
- These mutations are still rare in Afghanistan, IR Iran and Pakistan.

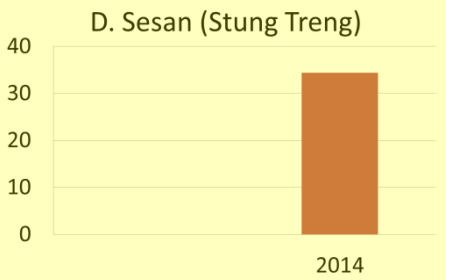
Pipearquine: history

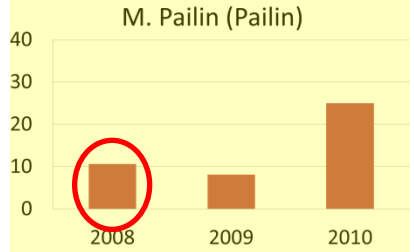
- Piperaquine developed in 1960s (Rhône Poulenc, France and Shanghai Pharmaceutical Industry Research Institute, China);
- Massive use late 60s in China for large scale prophylaxis and treatment including MDA in Yunnan and Hainan provinces (214 metric tonnes = 140,000,000 adult doses)
- Resistance to piperaquine confirmed both in vivo and in vitro in 1985 (Hainan island);
- Piperaquine was introduced in 1976 in Cambodia;
- Piperaquine donation from China to Cambodia from 1978 to 1986;
- DHA-PIP was used in clinical trials in Cambodia as early as 1999 (Artecom®) and 2002 (Artekin®).

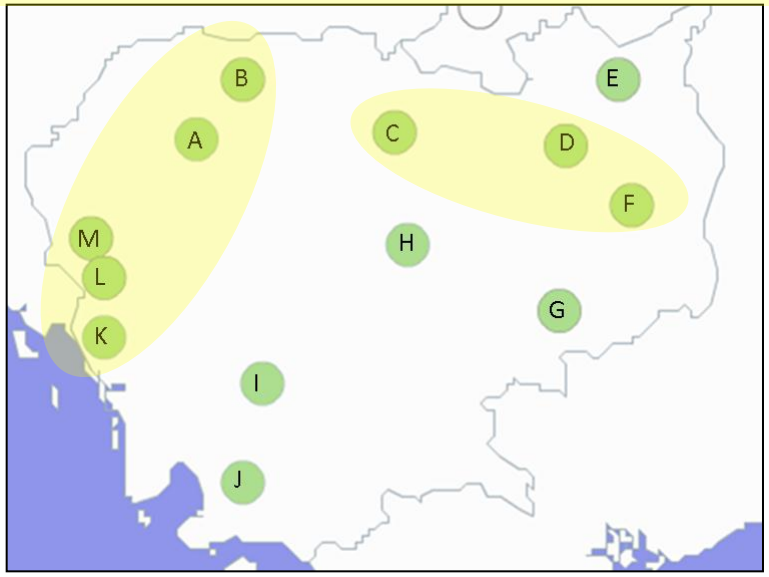
Treatment failure after treatment with DHA-PIP, Cambodia (2008–2014)

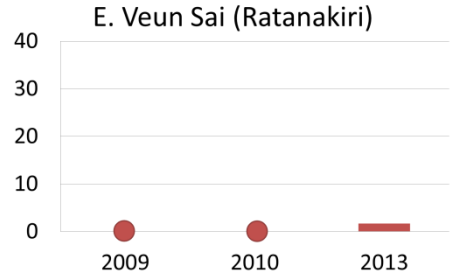


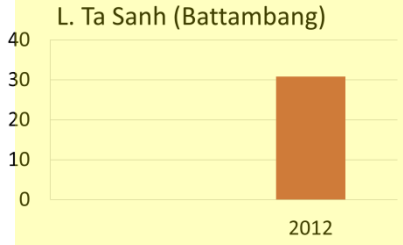


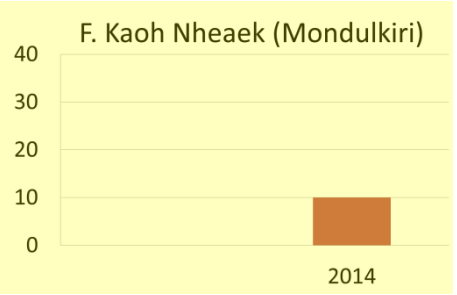


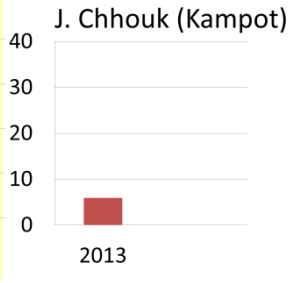


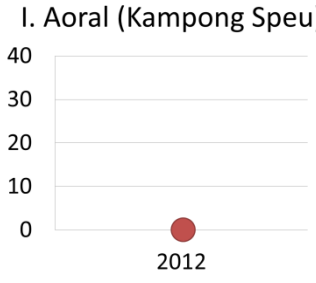


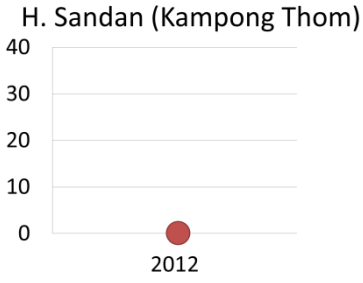


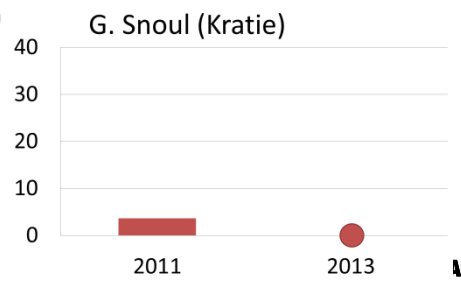






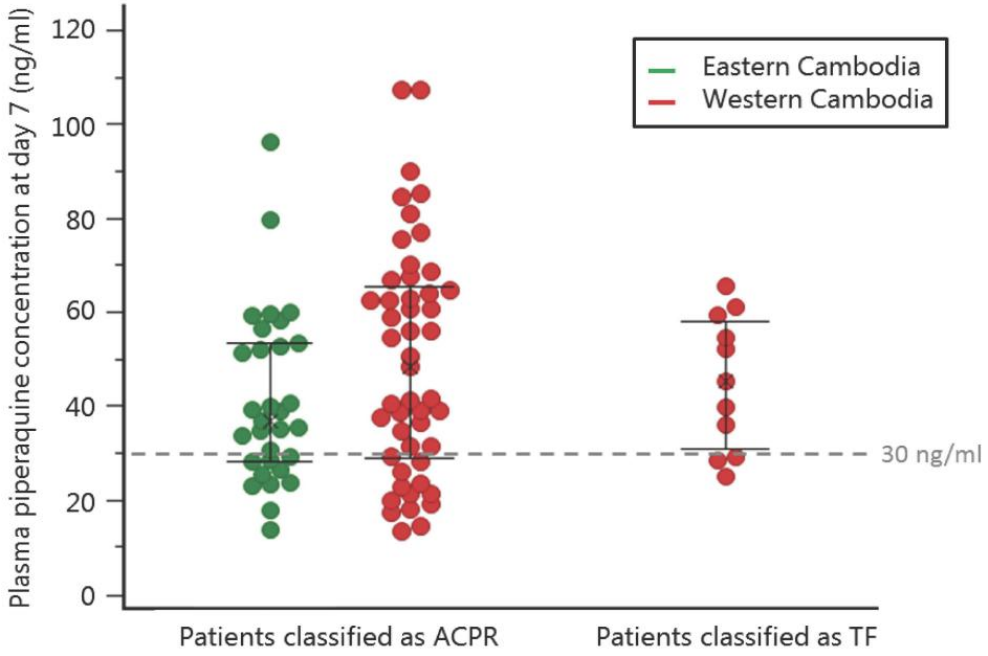






Pharmacokinetic

- Study conducted as part of TES studies in 2011-2012 (Kratie and Preah Vihear) and 2012-2013 (Kampong Speu, Pursat and Battambang)



Therapeutic efficacy tests with DHA-PIP in GSM

	China	Lao PDR	Myanmar	Viet Nam
Year	2007-2014	2005	2008-2014	2004-2014
Follow-up	28 d (2007-11) 42 d (2012-14)	42 d	28 d (2008-10) 42 d (2011-14)	28 d (2004-10) 42 d (2010-14)
n (N) studies	5 (10)	1 (1)	6 (26)	15 (29)
Treatment failure (%)	2.3-6.0	0.0	0.0-4.8	0.0-4.3
Day 3 + (%)	2.4-3.7	0.0	0.0-20.2	0.0-36.0

Relation between K13 mutations and DHA-PIP treatment outcome in GMS countries

China	ACPR	TF	2012-14
K13 mutants*	56	3	59
K13 WT	64	2	66
	120	5	125

* F446I (71.2%)

Cambodia	ACPR	TF**	2011-14
K13 mutants*	258	70	328
K13 WT	213	1	214
	471	71	542

* C580Y (89.6%); C580Y, R539T, Y493H (98.7%)

** *Pfmdr1* copy number: 94.7% single copy

p<0.001

Myanmar	ACPR	TF	2014
K13 mutants*	34	1	35
K13 WT	47	1	48
	81	2	83

* F446I, R561H (77.1%)

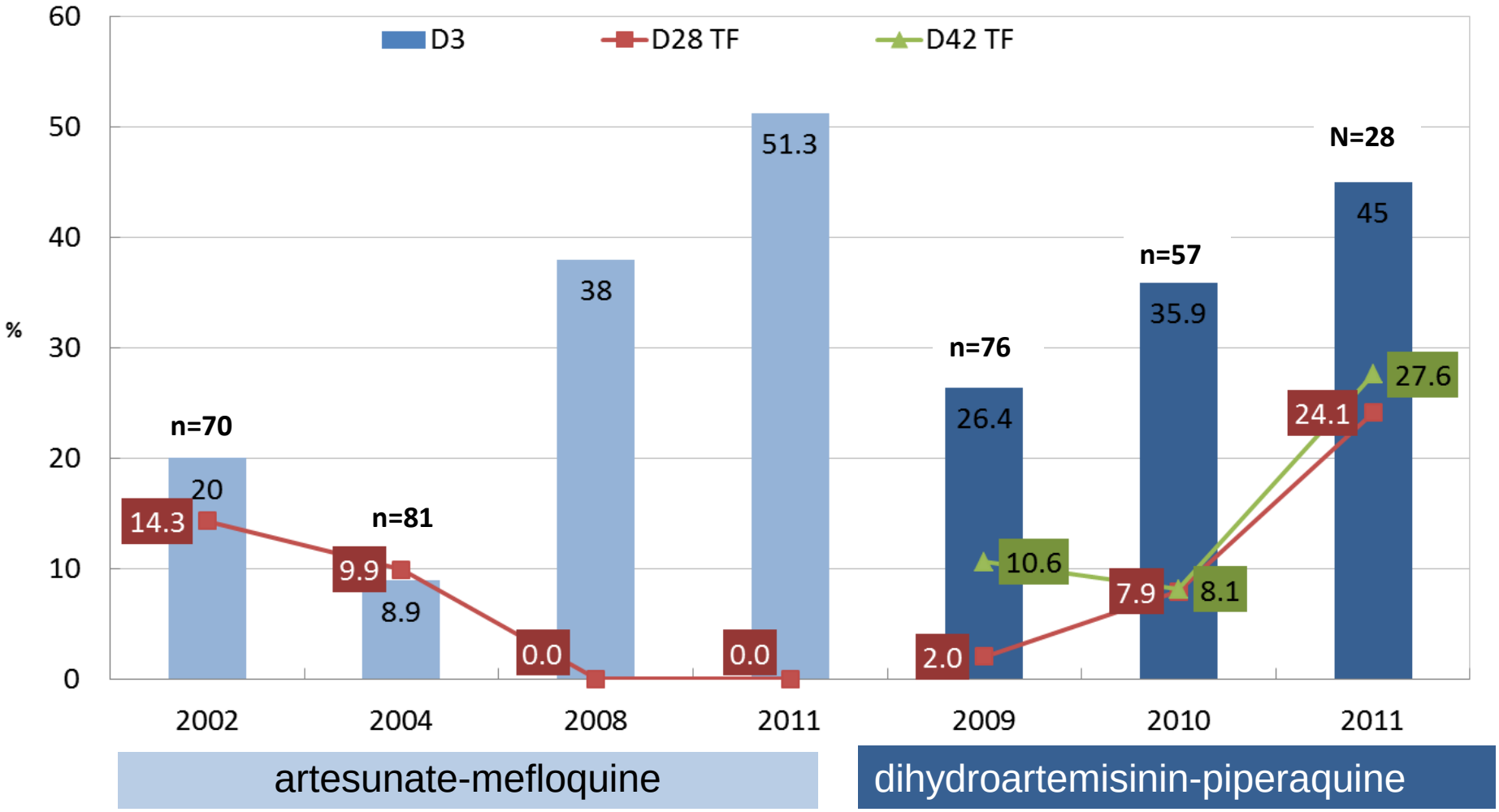
Viet Nam	ACPR	TF	2014
K13 mutants*	48	0	48
K13 WT	91	0	91
	139	0	139

* C580Y, Y493H (64.5%)

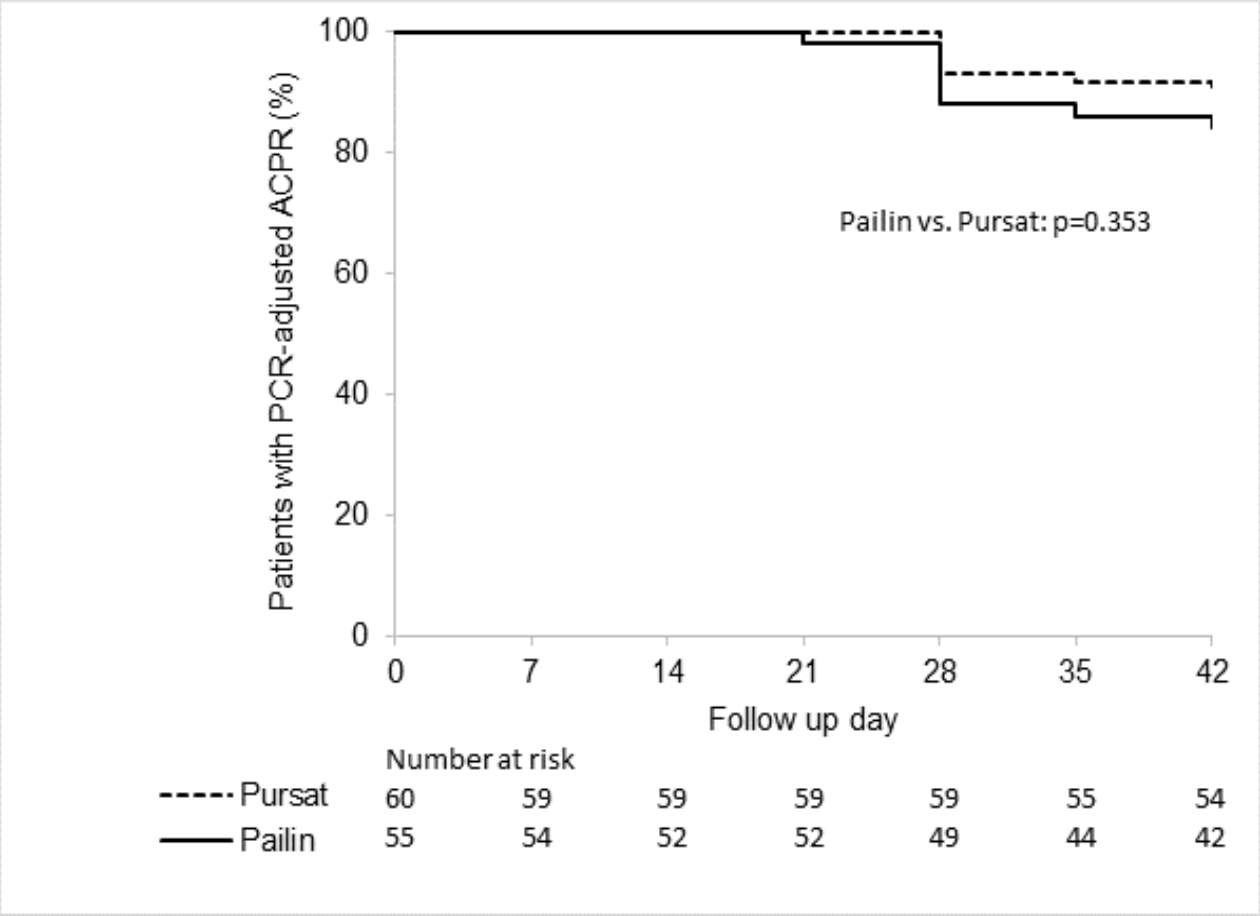
Relation between partner drug efficacy and K13 mutations

Year	Site	ACT	N	Efficacy 42 days (%)	K13 mutant (%)	*Pfmdr1* copy number (n > 1) (%)
2011	Pailin, Cambodia	Artesunate-mefloquine	29	100	75.9 (C580Y)	6.9
2012-2013	Dak Nong, Viet Nam	Dihydro-piperaquine	33	100	72.7 (C580Y; Y493H)	N/A
2014	Yingjiang county, Yunnan	Dihydro-piperaquine	23	100	91.3 (F446I)	N/A

ACT efficacy in Pailin, Cambodia (2002-2011)



Efficacy of artesunate-pyronaridine in Cambodia 2014



Treatment policy in GMS

	artemisinin resistance		containment activities started	AL		AS-MQ		DHA-PPQ	
	suspected year of emergence	detected		D3+	TF	D3+	TF	D3+	TF
Cambodia	2001*	2006	2009	♦	♦	♦	♦	♦	♦
Laos	2013	2013	2014	♦	-				
Myanmar	2001*	2008	2011	♦	-	♦	-	♦	-
Thailand	2001*	2008	2009	♦	♦	♦	♦		
Viet Nam	2009	2009	2011					♦	-

first-line treatment

*detected retrospectively using molecular markers or retrospective data; ♦ observed to be > 10%; '-' = observed to be < 10%, blank = undetermined

Clinical outcome after ACT treatment according to resistance pattern of each component

Artemisinin	Partner drug	Treatment outcome
S	S	TS (ACPR)
R Delayed clearance	S	TS (ACPR) China, Laos, Myanmar, Viet Nam
S 3-day AS = 50% TS	R	TS → TF (ASSP, India; AL, Africa)*
R	R	TF Cambodia (DP), Thailand (ASMQ)

* If resistance to partner drug increases: > 20-30% for AQ or SP

World Health Organization

GLOBAL MALARIA PROGRAMME

Status report on artemisinin and ACT resistance

September 2015

Key messages

1. Artemisinin resistance[1] is defined as delayed parasite clearance following treatment with an artesunate monotherapy, or after treatment with an artemisinin-based combination therapy (ACT). Such resistance represents partial resistance.
2. Delayed parasite clearance will not necessarily lead to treatment failure. In the Greater Mekong subregion (GMS), a high treatment failure rate following treatment with an ACT has only been observed where there is resistance to the partner drug, regardless of the presence of artemisinin resistance. However, artemisinin resistance could facilitate the selection of partner drug resistance.
3. A molecular marker for artemisinin resistance has been identified and will help to improve the global surveillance of artemisinin resistance.
4. Emergence of multidrug resistance, including ACT resistance, and independent emergence of artemisinin resistance in the GMS have led to the recommendation of elimination of malaria in this region.

Background

Artemisinin resistance

Artemisinin resistance is defined as delayed parasite clearance; this represents a partial resistance that so far affects only ring-stage parasites. Most patients who have delayed parasite clearance following treatment with an artemisinin-based combination therapy (ACT) clear their infections. However, this is not the case in Cambodia and Thailand, where there is concomitant resistance to the partner drugs such as mefloquine and piperaquine.

It is not clear whether artemisinin resistance has precipitated the emergence of piperaquine resistance, or whether it has helped to further select parasites that are already piperaquine resistant. Resistance to piperaquine may have emerged independently from resistance to artemisinin, because of the long half-life of piperaquine and its previous use as a monotherapy (similar to the use of mefloquine). Further research is needed to evaluate the exact role of artemisinin resistance in the development or selection of drug resistance to partner drugs.

Molecular marker of artemisinin resistance

A molecular marker of artemisinin resistance was recently identified. Mutations in the Kelch 13 (K13) propeller region are associated with delayed parasite clearance both in vitro and in vivo. The identification of **the** K13 marker for artemisinin resistance has allowed for a more refined definition of resistance that includes information on the genotype. However, as the list of mutations associated with artemisinin resistance is still evolving, so the definition of artemisinin resistance will continue to evolve. The current definition of artemisinin resistance is divided into:

1. Artemisinin refers to artemisinin and its derivatives.

- *suspected artemisinin resistance* – defined as a high prevalence of the delayed parasite clearance phenotype, or high prevalence of K13 mutants; and
- *confirmed artemisinin resistance* – defined as a combination of delayed parasite clearance and K13 resistance-associated mutations in a single patient.

Confounding factors in these definitions include the effect of partner drugs, immunity, insufficient levels of drug in the blood and non-validated K13 mutations.

A total of 186 K13 alleles, including 108 non-synonymous mutations,[2] have been reported so far. In South-East Asia, distinct alleles originating from multiple independent events of emergence have been observed. In the eastern Greater Mekong subregion (GMS) – comprising Cambodia, Lao People's Democratic Republic (PDR) and Viet Nam – the mutations C580Y, R539T, Y493H and I543T are frequent. In the western GMS – comprising China, Myanmar and Thailand – mutations F446L, N458Y, P574L and R561H are common. In Africa, non-synonymous mutations are rare but highly diverse. Non-synonymous K13 mutations have been reported in Cameroon, Central African Republic, Chad, Comoros, Democratic Republic of the Congo, Gabon, Gambia, Kenya, Madagascar, Malawi, Mali, Rwanda, Togo, Uganda and Zambia. The most frequent allele observed in Africa is A578S.

Not all non-synonymous propeller-region K13 mutants reported indicate emerging artemisinin resistance. Such mutants can represent "passer-by" genotypes; that is, they do not lead to selection of the mutant K13 genotype. In addition, the position of the mutation affects the clearance phenotype. Validation of a K13 mutation as a resistance marker will require correlation with slow clearance in clinical studies, reduced drug sensitivity in ex vivo or in vitro assays (e.g. the ring-stage assay – $RSA_{0–3h}$), or reduced in vitro sensitivity in transfection studies involving insertion of the mutant K13. Table 1 provides a list (that will have to be updated regularly) of associated K13 propeller mutations (i.e. those correlated with delayed parasite clearance) and confirmed K13 propeller mutations (i.e. those confirmed by in vivo and in vitro data).

Table 1. Associated and validated K13 resistance mutations

K13 mutation	Classification
441L	Associated
446I	Associated
449A	Associated
458Y	Associated
493H	Confirmed
539T	Confirmed
543T	Confirmed
553L	Associated
561H	Associated
568G	Associated
574L	Associated
580Y	Confirmed
675V	Associated

Monitoring therapeutic efficacy of ACTs

Routine monitoring of the therapeutic efficacy of ACTs is essential for making timely changes to treatment policy; it can also help to detect early changes in *Plasmodium falciparum* susceptibility to antimalarial drugs. WHO currently recommends monitoring the efficacy of first-line and second-line ACTs every 2 years in all falciparum-endemic countries. The results of therapeutic efficacy studies (TESs) make it possible to determine the:

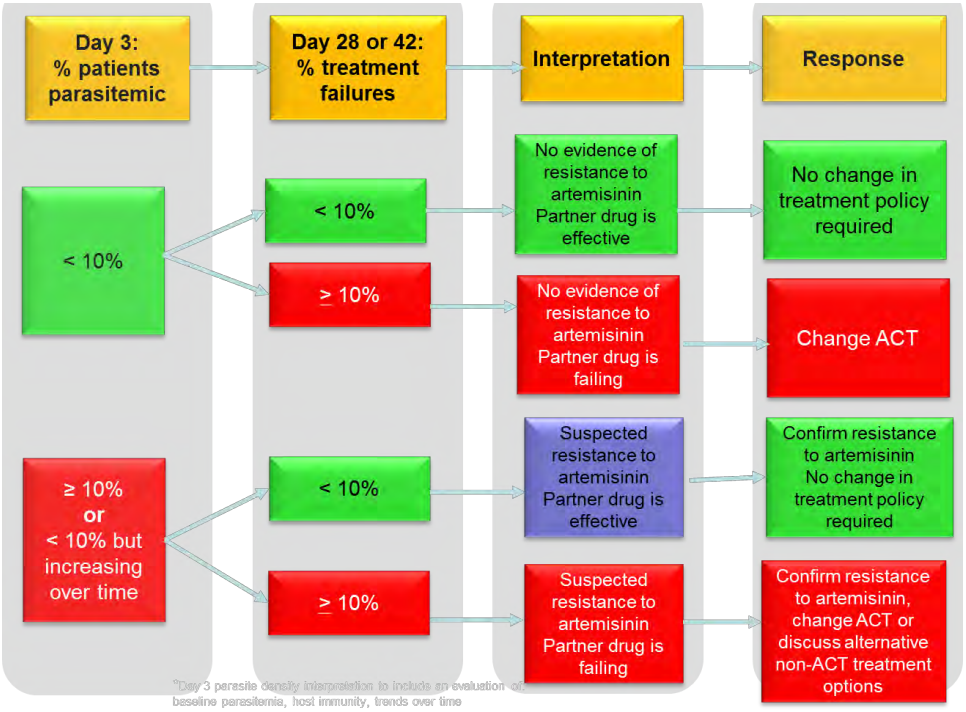
- *proportion of patients who are parasitemic on day 3***,** which is currently the indicator of choice for routine monitoring to identify suspected artemisinin resistance in *P. falciparum*; and

2. A non-synonymous mutation is one that changes the gene expressed and the phenotype of the individual.

- *proportion of treatment failure* by 28-day or 42-day follow-up (depending on the partner drug half-life in the specific ACT); a treatment failure rate exceeding 10% should prompt a change in the national antimalarial treatment policy.

The flowchart in Fig. 1 outlines the recommended steps in the decision-making process for the interpretation of and response to TES findings.

Figure 1. Decision-making process based on TES results



If artemisinin resistance is suspected because of slow clearance in a clinical trial or TES, K13 marker analysis (e.g. from filter-paper blood spots) should be prioritized. If resistance is suspected based on a survey with molecular data only, it should be confirmed by studies that combine information on the clinical phenotype (delayed parasite clearance) and the K13 genotype from the same parasite strain. If necessary, the K13 mutant should be validated as a resistance marker using an in vitro assay such as the $RSA_{0–3h}$.

Possible implications of delayed parasite clearance

Delayed parasite clearance after treatment with an ACT is of great concern. Failure to rapidly clear parasites could compromise the use of artemisinin for the treatment of severe malaria. Also, slow parasite clearance causes more parasites to be exposed to the partner medicine alone, increasing the risk of selection of partner drug resistance, which in turn increases the risk of treatment failure. Currently, most patients with a delayed parasite clearance response are still cured by ACTs, provided that the partner drug remains effective. Finally partial resistance could include development of total artemisinin resistance.

Response to artemisinin resistance and eliminating malaria in the GMS

Emergency response to artemisinin resistance in the GMS

In April 2013, WHO launched the *Emergency response to artemisinin resistance (ERAR) in the GMS* (*1*).The framework urges partners to work in a coordinated manner to provide malaria interventions to all at-risk groups; to achieve tighter coordination and management of field operations; to obtain better information for containment of artemisinin resistance; and to strengthen regional oversight and support.

WHO has received support from the Australian Department of Foreign Affairs and Trade and the Bill & Melinda Gates Foundation to strengthen the coordination of and technical support for activities to contain artemisinin resistance in the GSM. The project is implemented by the WHO Global Malaria Programme, the WHO Regional Office for South-East Asia, the WHO Regional Office for the Western Pacific and WHO country offices. A regional hub has been established in Phnom Penh, Cambodia, to support and help with coordination of activities.

In line with the call to action and recommendations contained in the ERAR, the Global Fund to Fight AIDS, Tuberculosis and Malaria has allocated US$ 100 million to a regional artemisinin initiative, funding activities to contain and eliminate artemisinin resistance in Cambodia, Lao PDR, Myanmar, Thailand and Viet Nam. The regional artemisinin initiative includes a regional component to support cross-border activities.

Malaria elimination in the GMS

The incidence of malaria has been greatly reduced over the past 10–20 years. However, there is concern that falciparum malaria in the GMS is becoming increasingly resistant to antimalarial medicines; at the border between Cambodia and Thailand, falciparum malaria could become untreatable within a few years. In addition, molecular studies have confirmed that artemsinin resistance has emerged independently in many areas of the GMS. Against this background, WHO's Malaria Policy Advisory Committee recommended in September 2014 the adoption of the goal of elimination of *P. falciparum* in the GMS by 2030. Subsequently, at the World Health Assembly in May 2015, WHO launched a *Strategy for malaria elimination in the GMS (2015–2030)* (*2*), which was endorsed by all the GMS countries.

Country updates on ACT efficacy

The information given here is taken from the *Global report on antimalarial efficacy and drug resistance: 2000–2010* (*3*).

South-East Asia

Cambodia

Background

- Artemisinin resistance was first identified in clinical studies in 2006; however, retrospective analysis of molecular markers indicates that artemisinin resistance probably emerged in 2001, before the widespread deployment of ACTs in Cambodia.
- Due to high failure rates with artesunate-mefloquine (ASMQ), the first-line treatment for the treatment of uncomplicated falciparum malaria, was changed from co-blistered ASMQ to fixed-dose dihydroartemisinin-piperaquine (DHA-PPQ) in Pailin in 2008, and then nationwide in 2010.
- After the implementation of this new treatment policy, an increase in treatment failures was quickly identified in TESs using DHA-PPQ in Pailin. Between 2008 and 2014, similar trends were observed in seven provinces, mainly in the western and northern part of the country. The high treatment failure rates observed with DHA-PPQ are related to the presence of piperaquine resistance, which is spreading from western to north-eastern Cambodia.
- A consensus meeting held in November 2011 recommended the use of atovaquone-proguanil delivered as directly-observed therapy for Pailin province as a short-term interim solution, with stringent follow-up for monitoring resistance. Mutations conferring resistance to atovaquone were observed less than a year after the implementation of the drug as first-line therapy, which was sufficient reason to change the recommendation.

Update

- A consensus meeting on the national treatment policy for *P. falciparum* was held in January 2014. ASMQ was re-introduced as first-line treatment, since the proportion of falciparum strains with multiple *Pfmdr1* copy numbers (which confer mefloquine resistance) is currently minimal in the area. Quinine plus doxycycline over 7 days has been adopted as rescue therapy. DHA-PPQ remains the first-line treatment in the rest of the country.

Lao PDR

Update

- In 2013, a trial conducted in Champasack province found that 22.2% of the patients treated with artemether-lumefantrine (AL) were still parasitemic on day 3 after treatment.
- The emergence of artemisinin resistance in southern Lao PDR is supported by the identification in 2013 of the presence of K13 mutants (mainly C580Y and R539T) in the circulating parasite populations.
- The therapeutic efficacy of AL has not been affected, and cure rates have remained high since 2005.
- Containment activities started in 2014, and TESs are now being conducted in Atteupeu, Champasack and Sekong provinces.

Myanmar

Background

- Artemisinin resistance probably emerged at the border between Myanmar and Thailand in 2001, but was not clearly recognized until 2008.
- Since 2009, data show consistently delayed parasite clearance times among a significant proportion of patients treated with ACTs; this trend was observed in all the three first-line ACTs (AL, ASMQ and DHA-PPQ).
- The results showing delayed parasite clearance rates in several parts of the country led to the initiation of the Myanmar Artemisinin Resistance Containment framework, in line with the recommendations described in the *Global Plan for Artemisinin Resistance Containment (GPARC)* (*4*).
- The three first-line ACTs used in the country are still effective, with high cure rates.

Update

- Studies evaluating the presence of K13 mutants have shown that the predominant K13 mutant found in Myanmar is likely to have arisen independently rather than to have spread from Cambodia.
- A new K13 propeller polymorphism (F446I) is potentially associated with delayed parasite clearance. Preliminary results indicate a high prevalence of the K13 F446I mutation along both the China–Myanmar border and the India–Myanmar border. Research is ongoing to validate the role of this new mutant in artemisinin resistance.
- ACT efficacy remains high on both sides of the border between India and Myanmar.

Thailand

Background

- Containment activities on the Thailand side of the border between Cambodia and Thailand began simultaneously with those in Cambodia in 2008.

- Thailand initially used a regimen of 2-day ASMQ as first-line treatment. Despite the change to a 3-day regimen in 2009, treatment failures with ASMQ increased in Kanchanaburi, Ranong, Tak and Ubonratchathani, reaching levels of at least 10%.
- High treatment failure rates observed in Thailand after treatment with ASMQ could be explained by the presence of mefloquine resistance (which has been confirmed countrywide) in addition to artemisinin resistance. Mefloquine drug pressure has been considerable over the last decades, since Thailand has been using different regimens of mefloquine (15 to 25 mg/kg) as monotherapy or in combination with artesunate.

Update

- The efficacy of AL was evaluated in two provinces in 2012; the treatment failure rate was close to or exceeded 10%.
- During a consensus meeting held in 2015, DHA-PPQ became the first-line treatment in the country, and its efficacy is currently being evaluated.

Viet Nam

Background

- Delayed parasite clearance was first detected after treatment with DHA-PPQ in the Bu Dang district of Binh Phuoc province in 2009.
- Routine monitoring of treatment with DHA-PPQ also detected other foci of delayed parasite clearance in Gia Lai province (2010), Dak Nong province (2011), Quang Nam province (2012), and Kon Tum and Khanh Hoa provinces (2014).
- In mid-2011, Viet Nam began containment activities following GPARC recommendations with the support of the WHO Western Pacific Regional Office and the WHO country office.

Update

- TES conducted since 2010 using DHA-PPQ reported a treatment efficacy of more than 95%, despite a day-3 positivity rate of up to 36%.

Summary

The status of artemesinin resistance in the GMS is summarized in Table 2.

Table 2. Summary of the status of artemisinin resistance in the GMS

	Artemisinin resistance		Containment activities started	AL		AS-MQ		DHA-PPQ	
	Suspected year of emergence	Detected		D3+	TF	D3+	TF	D3+	TF
Cambodia	2001[a]	2006	2009	♦	♦	♦	o	♦	♦
Lao PDR	2013	2013	2014	♦	o	ND	ND	ND	NS
Myanmar	2001[a]	2008	2011	♦	o	♦	o	♦	o
Thailand	2001[a]	2008	2009	♦	♦	♦	♦	♦	
Viet Nam	2009	2009	2011	ND	ND	ND	ND	♦	o

AL, artemether-lumefantrine; AS-MQ, artesunate-mefloquine; D3, day 3; DHA-PPQ, dihydroartemisinin-piperaquine; PDR, People's Democratic Republic

Orange shading indicates first-line treatment; ♦, observed to be >10%; o, observed to be <10%; ND, undetermined

[a] detected retrospectively using molecular markers or retrospective data

Africa

- The efficacy of ACTs is being monitored in most malaria-endemic countries. There have been some reports of delayed parasite clearance during routine TES of ACTs conducted in Africa, but these reports have not been consistent over time.
- To date, the K13 mutations observed have not been associated with slow parasite clearance. Currently, Africa appears to be free of the resistance-associated Asian alleles.
- TESs show that, in general, ACTs remain efficacious.

South America

Suriname

- Routine surveillance of ACT efficacy between 2005 and 2006, and in 2011 in gold miners, reported an increase of day-3 positivity rate (from 2% to >20%), with a high cure rate at day 28. In 2013–2014, a study using artesunate and mefloquine did not confirm the high positivity rate at day 3, and sequencing of K13 of strains collected during this study revealed only wild-type K13.

Guyana

- The last TES study evaluating AL was conducted from May 2011 to July 2012; a total of 92 patients were enrolled, with 68 completing the day-28 follow-up. A total of 70.8% of day-3 slides were reported to be positive, but after a review of quality control, this result was considered to be flawed. A new clinical study evaluating 7-day artesunate for uncomplicated falciparum malaria was started in 2014. The efficacy of artesunate was 100% at day 28, whereas only 2% of the patients had persistent parasitaemia at day 3 after treatment. The 47 strains collected all showed K13 wild type.
- A retrospective analysis of blood samples collected in 2010 for a histidine rich protein-2 (HRP2) surveillance study, detected the C580Y mutation. All five C580Y mutant samples detected had a nearly identical haplotype, suggesting that they had a common origin that was distinct from the South-East Asian C580Y haplotype. A survey for K13 sequencing is ongoing in the region where five of the earlier cases originated.

French Guyana

- Between 2009 and 2013, the day-3 positivity rate among patients treated in Cayenne Hospital after treatment with AL was 7.5%, but the treatment was not systematically supervised. So far, no K13 mutant strains have been reported from French Guyana.

Conclusion

Despite the delayed response to artemisinin in some areas of the GMS, ACTs remain the most effective treatment for uncomplicated falciparum malaria. Most patients with delayed parasite clearance are cured, as long as the partner drug remains effective. Routine monitoring must continue to ensure that the recommended ACTs are effective, that changes in national treatment policies can be implemented in a timely manner, and that artemisinin resistance can be detected early. Assessment of K-13 propeller-region mutants will greatly facilitate the tracking of artemisinin resistance as it emerges. Due to the existence of multidrug resistance (including ACT resistance) in the GMS, elimination of falciparum malaria has become a high priority. The role played by artemisinin resistance in the development of partner drug resistance needs to be further evaluated.

Further information

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Please also visit the following WHO website for additional information and data:

http://www.who.int/malaria/areas/drug_resistance/en/index.html

References

1 WHO. Emergency response to artemisinin resistance in the Greater Mekong subregion. Regional framework for action 2013-2015. Geneva, World Health Organization (WHO). 2013 (http://apps.who.int/iris/bitstream/10665/79940/1/9789241505321_eng.pdf, accessed 24 August 2015).

2 WHO. Strategy for malaria elimination in the Greater Mekong subregion (2015–2030). Geneva, World Health Organization (WHO). 2015 (http://www.who.int/malaria/areas/greater_mekong/consultation-elimination-strategy/en/, accessed 08 April 2015).

3 WHO. Global report on antimalarial efficacy and drug resistance: 2000–2010. Geneva, World Health Organization (WHO). 2011 (http://whqlibdoc.who.int/publications/2010/9789241500470_eng.pdf accessed 24 August 2015).

4 WHO. Global plan for artemisinin resistance containment. Geneva, World Health Organization (WHO). 2011 (http://www.who.int/malaria/publications/atoz/artemisinin_resistance_containment_2011.pdf, accessed 08 April 2015).

GLOBAL MALARIA PROGRAMME

World Health Organization

Updates of the Greater Mekong Subregion Elimination Strategy

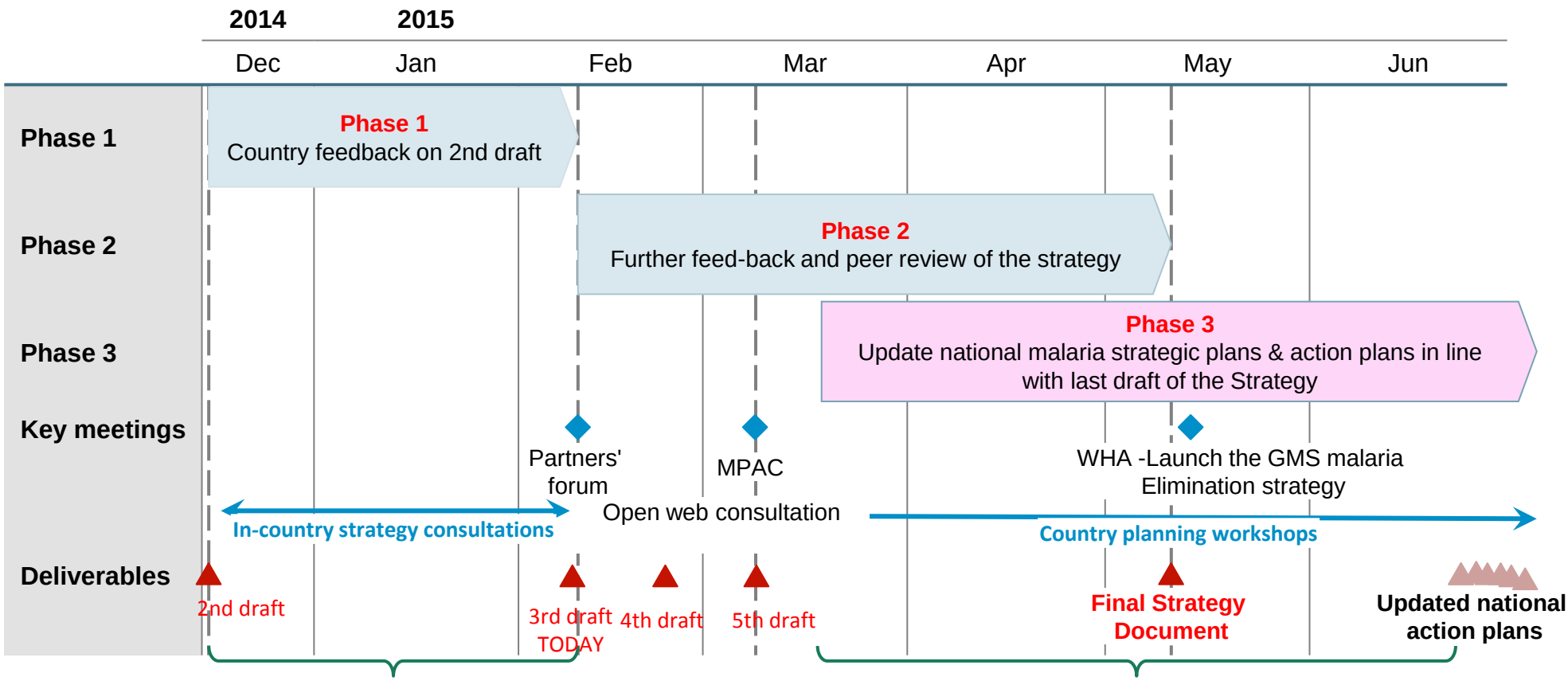
Dr. Walter KAZADI MULOMBO
Coordinator, ERAR & Mekong Malaria Elimination Hub

Malaria Policy Advisory Committee (MPAC), Geneva, September 17 2015

Outline

- **Introduction**: Process, Goals, Objectives, milestones, targets and main interventions
- **Progress with the strategy roll out:** Development/adaptation of national malaria elimination strategies in line with the “Strategy for malaria elimination in the GMS 2015 – 2030”, Governance, Training, SME and other regional functions
- **Tracking progress:** The scorecard indicators and trend analysis for selected indicators
- **Looking ahead:** Refocussing the regional coordination
- **Feedback from MPAC:** Orientations on our future work

The GMS Malaria Elimination Strategy – Finalisation and Roll-out



Country Action

- Participate in 1st GMS consultation (Nov. 2014)
- Organize in-country consultations and provide feedback on 2nd draft
- Discuss cross-border & regional components

Engage in Partners Forum

Provide feedback during open web consulta-tion

- Conduct in-country planning workshops to update national malaria strategic and action plans
- Conduct gap analysis
- Define financial and technical support needs
- Brief minister of health for WHA

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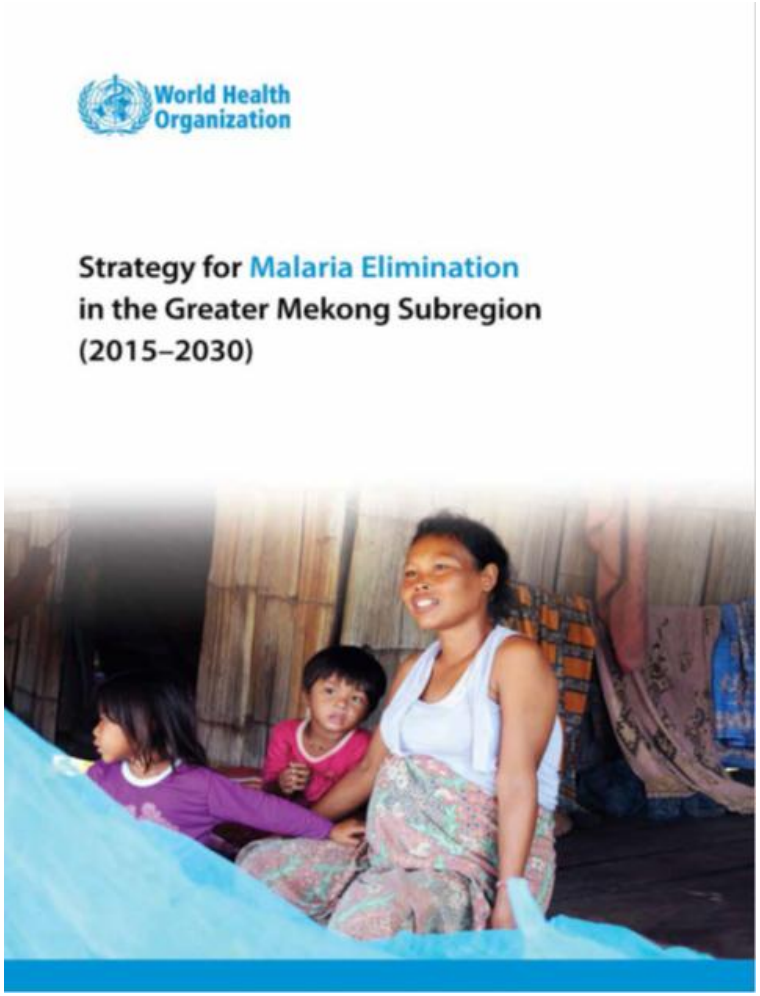
EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

The GMS Malaria Elimination Strategy



Vision:

- A GMS free of malaria and the continual threat posed by antimalarial drug resistance

Goals:

- The ultimate goal of this regional strategy is to eliminate malaria by 2030 in all GMS countries and, considering the urgency of action against multidrug resistance in the GMS, to eliminate *P. falciparum* by 2025.
- In areas and countries where malaria transmission has been interrupted, the goal is to maintain the malaria-free status and prevent reintroduction of malaria.

Objectives

- To interrupt transmission of *P. falciparum* in areas of multidrug resistance, including ACT resistance, by no later than 2020, and in all areas of the GMS by 2025

- To reduce malaria in all high-transmission areas to less than 1 case per 1000 population at risk and initiate elimination phase activities by 2020

- To prevent re introduction of malaria in areas where transmission has been interrupted

Prioritization

- **Regional level priorities:**
  - Urgently and aggressively interrupt transmission in areas with multidrug resistance in the border areas between Cambodia and Thailand;
  - Reduce transmission in the high transmission areas in Myanmar;
  - Control malaria in areas of resurgence.
- **Country level priorities:**
  - Eliminate malaria in areas of multidrug resistance;
  - Flatten the epidemiological landscape by reducing transmission in areas of high transmission;
  - Local analysis may identify additional priorities such as measures targeting certain mobile populations.

The prioritization does not mean that efforts to eliminate malaria in low transmission areas should be put on hold

Strategic Interventions

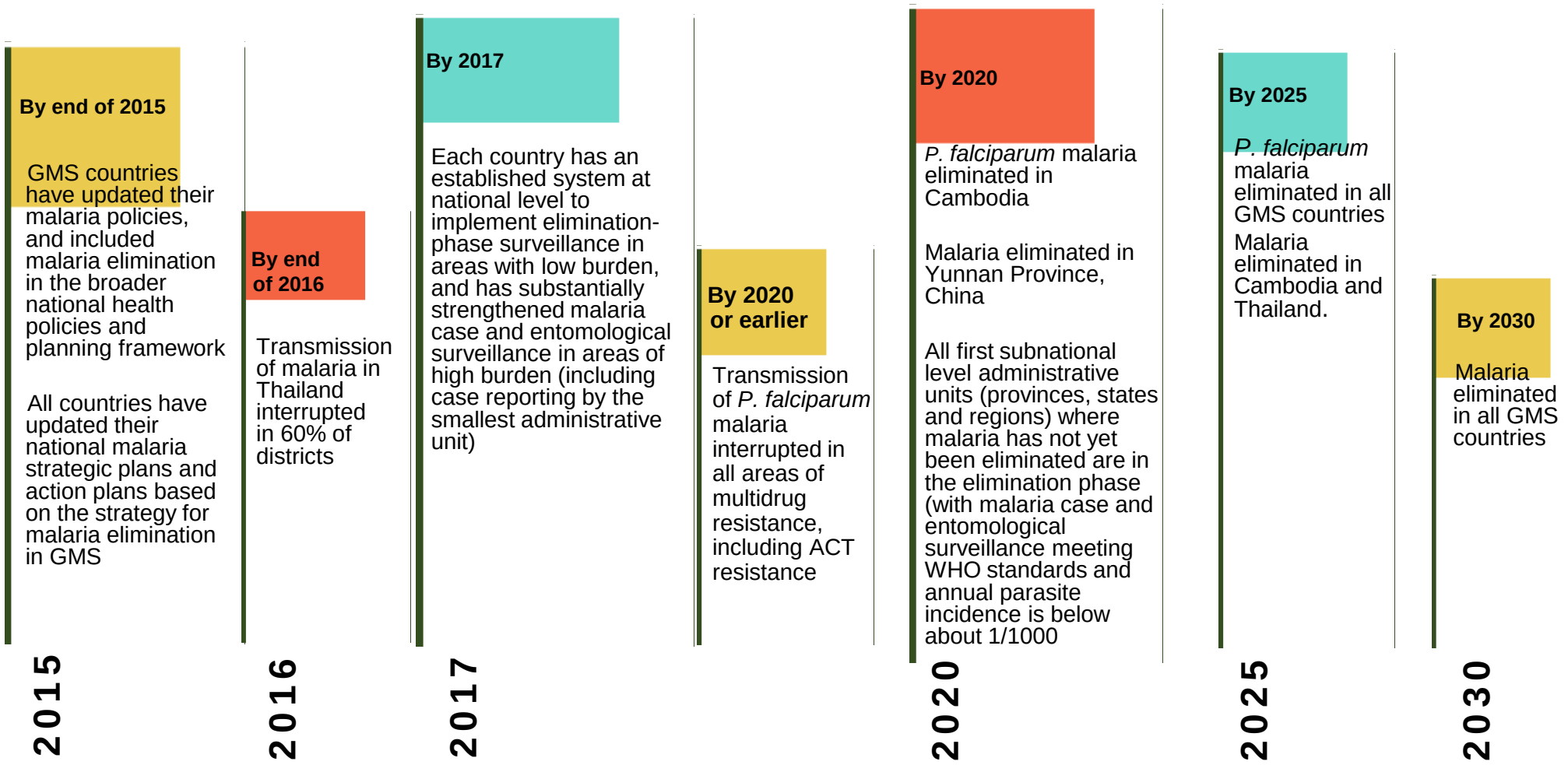
- **Case detection and management**
  - Universal access to quality diagnostics and treatment in public, private sector and in the community
  - Detection of asymptomatic carriers
  - ACTs, Primaquine for both *P. falciparum* (single dose) and *P. vivax* (anti-relapse therapy)
- **Disease prevention**
  - Vector control
  - Drug based approaches
- **Malaria case and entomological surveillance**
  - Mandatory notification
  - Case based malaria surveillance;
  - Case, foci investigation and response
  - Entomological surveillance
  - Outbreak detection and response
  - Vigilance

Interventions are to be customized to prevailing local conditions

Governance Needed in the GMS

- Ensuring engagement and buy-in of appropriate partners
- Shared oversight of implementation of the agreed strategy
- Optimal use of available resources - prioritization
- Tracking of achievements and identification of bottlenecks and “failures”
- Review together regularly a common set of milestones/indicators -> reallocate resources if necessary
- This is needed at REGIONAL and COUNTRY level

GMS Malaria Elimination Milestones and Targets



National Level Coordination & Governance

	Country	Status	Issues
1	Cambodia	• National Malaria Elimination Committee to be reinvigorated • Planning Donor conference once Action Plan fully costed	• Funding to reactivate National and provincial task forces established during ARCE project
2	China PR	• Multi sectoral High level National Malaria Elimination Committee since 2010	• Fund raising for common areas/cross border coordination activities
3	Lao PDR	• Discussions under way through Dept. for Control of Com. Diseases (DCDC) to establish National Malaria Elimination • Considering Donor conference in Oct 2015	• Ensuring malaria elimination agenda is high on the political agenda
4	Myanmar	• Multi sectoral High level National Malaria Elimination Committee not yet in place • Plans are to complete NSP prior to establishment	• How to generate, maintain momentum for elimination • Timing for setting up the committee
5	Thailand	• National High level malaria elimination committee set up (chaired by Deputy PM - March 2015)	• No specific issue reported
6	Vietnam	• National Multi Sectoral Steering Committee established chaired by Deputy Minister for Health and convened by PM	• No specific issue reported

Review of Malaria Stratification

	Country	Status	Issues
1	Cambodia	• Latest update in 2014 • Next plan for update?	• No specific issue reported
2	China PR	• Done annually	• No specific issue reported
3	Lao PDR	• Passive Case Detection Survey conducted using 2012 – 2014 data (report being finalized)	• Representativeness given current HIS issues
4	Myanmar	• Latest exercise in 2012 – 13 in 180 townships out off 330 target townships	• Representativeness • Guidelines for micro-stratification under review
5	Thailand	• Done annually	• No specific issue reported
6	Vietnam	• Updated in December 2014 (next update due in 4 – 5 years)	• No specific issue reported

Malaria Elimination Strategies and Action Plans

Country	Status	Issues
1 Cambodia	• Current NSP up to 2025 • Revision to Action Framework 2016 – 2020 Initiated since May 2015 • Completion due September 2015	• Micro-planning and costing time consuming and need WHO support
2 China PR	• Developed in 2010, period 2010 – 2020 • Operational plan 2015 – 2020 (now completed)	• Difficulty in assessing transmission risks in certain counties and in border areas with GMS countries
3 Lao PDR	• Initial update in April 2014 (MOH endorsed October for CN GF NFM); period 2016 - 2020 • Further revisions since May 2015 and July 2015 (alignment with GMS Strategy) - completion Sept. 2015 followed by OP	• Updating M&E plan • Surveillance and MIS • Programmatic and management capabilities • High level advocacy & Fund raising
4 Myanmar	• Started June 2015, period 2016 – 2020 • National consultation on NSP, September with launching due November 2015	• National consultation workshop overdue (Disaster and Emergency Relief Operations due to flooding)
5 Thailand	• Current NSP, 2011 – 2016; GMS Strategy and MPR to inform New NSP 2016 – 2020 under development • Completion Q4	• Current NSP loose in term of elimination strategies and approaches
6 Vietnam	• Current NSP up to 2030 endorsed by PM • Fully costed AP 2015 – 2020 (Jan 2015) • OP being updated post GMS Training	• No specific issue reported

GMS Malaria Elimination Country Strategies: Goals, Objectives and Milestones

Year	Elimination goals and objectives in approved national plans	Goals, objectives and priorities identified at Phnom Penh workshop	Proposed milestones based on all goals and objectives
2015-16		Priority of **Cambodia-Thai** border area (5 provinces in each country) and **Myanmar-Thai** border area	
2016	**Thailand**: Eliminate malaria in 60% of districts		**Cambodia**: All areas in elimination phase
2019			**Thailand**: All areas in elimination phase
2020	**Cambodia**: Eliminate Pf **China**: Eliminate malaria **Lao PDR**: Eliminate malaria in 6 provinces in the north **Thailand**: Eliminate malaria in 80% of districts **Viet Nam**: Eliminate malaria in 40 of 63 provinces	**Myanmar**: enter elimination phase	
2024	**Thailand**: Eliminate malaria		
2025	**Cambodia**: Eliminate malaria		**Lao PDR:** All areas in elimination phase **Viet Nam**: All areas in elimination phase
2030		**Lao PDR**: Eliminate malaria **Myanmar**: Eliminate malaria **Viet Nam**: Eliminate malaria	

GMS Regional Level Functions - Snapshot

Domain	Status	Issues
1 Training and technical collaboration	• GMS Malaria elimination training Chiang Mai (started) • Malaria elimination programmers' training course, 12 – 18 Oct 15 in PR China • GMS elimination operation manual started	• Harmonization of guidelines for malaria elimination across the GMS • Cascading at country level
2 Cross border collaboration	• Draft MMPs Strategy developed • Ongoing initiatives: Lao, THA, KHM X-border initiative (Champasak, Ubon and Steung Treng) • China – MMR X border malaria	• Funding and political support
3 Product quality	• Meetings of NRAs and training being organized through ERAR Hub, ASEAN, APLMA • New Drug Policies	• Harmonization and alignment across Governments and Partners
4 High priority research	• Priority research agenda defined (December 2013 through ERAR) and several research projects going on • Regional Research Coordination group established (November 2014)	• Ensuring ongoing research responds to country needs • Capacity strengthening for OR • Translation: Evidence – Policy- Practice
5 Surveillance, M& E	• ERAR Score card • SME capacity assessment done • Draft SME Strategy for elimination • Regional Data Sharing Platform	• Adaptation of SME Frameworks Based on Regional Guidance
6 Governance and coordination	• WHO ERAR Hub coordinating discussions on a possible model in consultation with APLMA	• How take forward the model and ensure buy in by all Stakeholders

Tracking Progress – Strategic Information, Planning and Management

Scorecard indicators

S/No.	Indicator
1	Malaria funding (USD) available for malaria program activities
2	Artesunate monotherapy ban in place and implemented
3	Number of planned drug efficacy studies implemented using WHO latest protocol
4	Number of studies of insecticide efficacy (resistance) completed according to WHO protocol
5	Completeness of reporting by due date
6	Percentage of suspected malaria cases that have had a diagnostic test
7	Percentage of the population at risk potentially covered by nets distributed.
8	Percentage of health facilities without stock-outs of first-line antimalarial medicines and diagnostics, during the past 12 months (by month)
9	Proportion of confirmed malaria cases that received appropriate antimalarial treatment by specie according to national policy
10	Number of people in the at risk population groups especially mobile and migrant populations reached with specific malaria interventions.
11	Availability of drug quality control and regulatory mechanisms
12	Number of confirmed malaria cases by species
13	Number of in-patient malaria deaths (or) Number of parasitological diagnosed malaria deaths
14	Percentage of administrative units in a country with an TPR <5%, API <1/1,000, interruption of local transmission compared with baseline year data (ERAR is 2013)

Routine surveillance data submission by country (as of 28 Aug 2014)

Country	Jan_14	Feb_14	Mar_14	Apr_14	May_14	Jun_14	Jul_14	Aug_14	Sep_14	Oct_14	Nov_14	Dec_14
Cambodia	■	■	■	■	■	■						
China (Yunnan)	■	■	■									
Lao PDR	■	■	■	■								
Myanmar	■	■	■									
Thailand	■	■	■	■	■	■	■					
Vietnam	■	■	■	■	■	■						

Routine surveillance data submission by country (as of 14 Sept 2015)

Country	Jan_15	Feb_15	Mar_15	Apr_15	May_15	Jun_15	Jul_15	Aug_15	Sep_15	Oct_15	Nov_15	Dec_15
Cambodia	■	■	■	■	■	■						
China (Yunnan)	■	■	■	■	■	■	■	■				
Lao PDR												
Myanmar	■	■	■	■								
*Thailand	■	■	■	■	■	■	■	■				
Vietnam	■	■	■	■	■	■	■					

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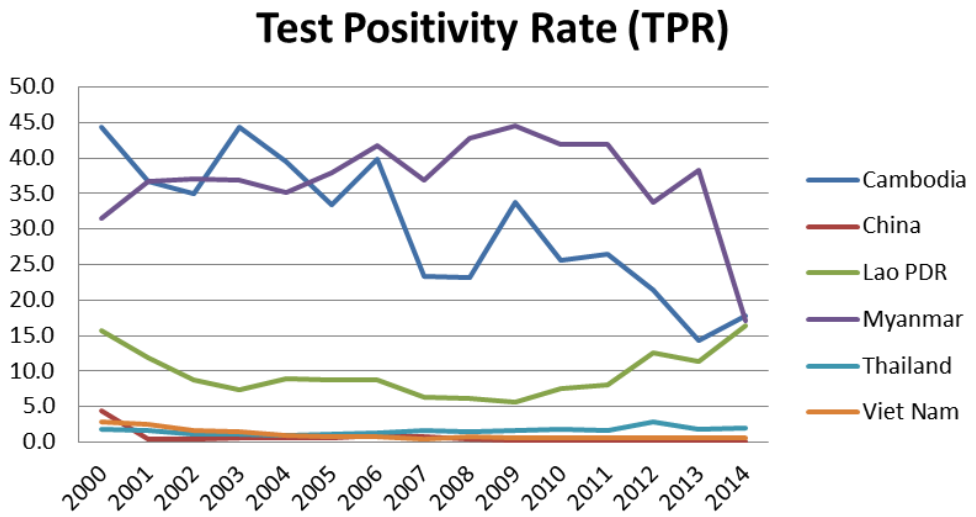
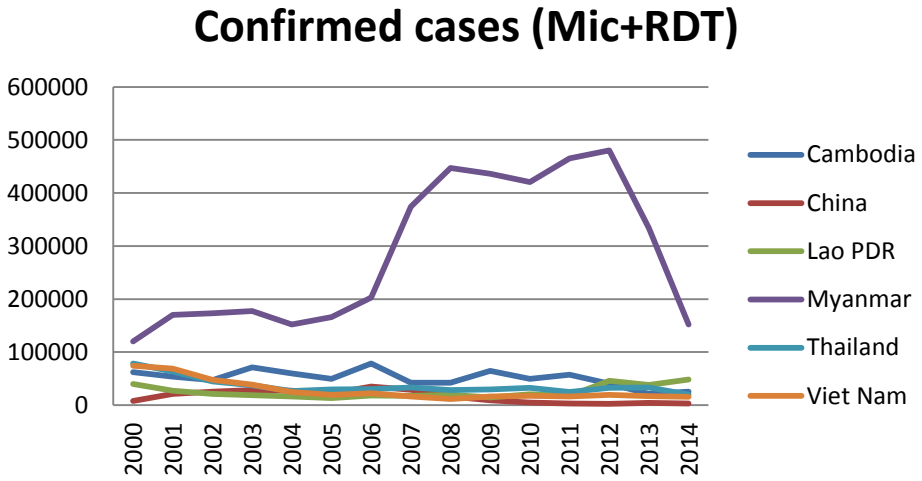
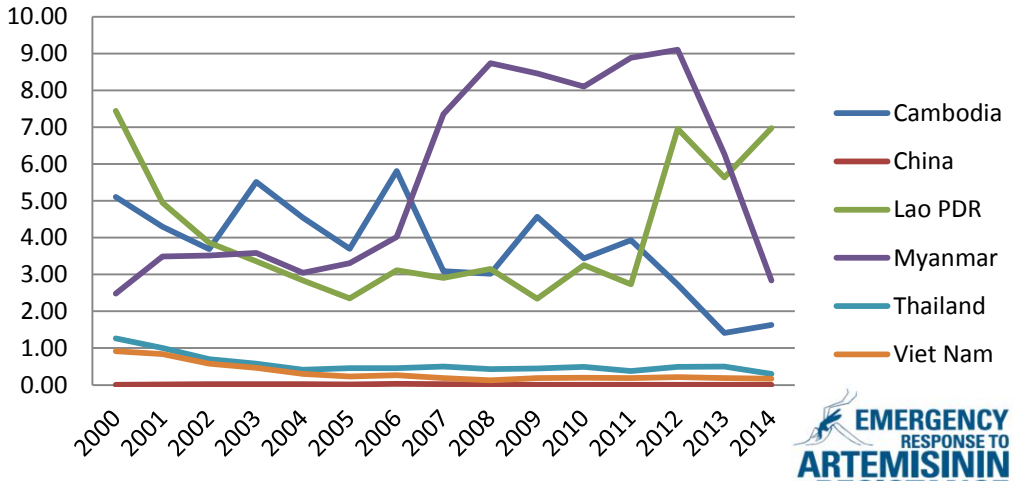
EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

Malaria Trends in the GMS, 2000–2014







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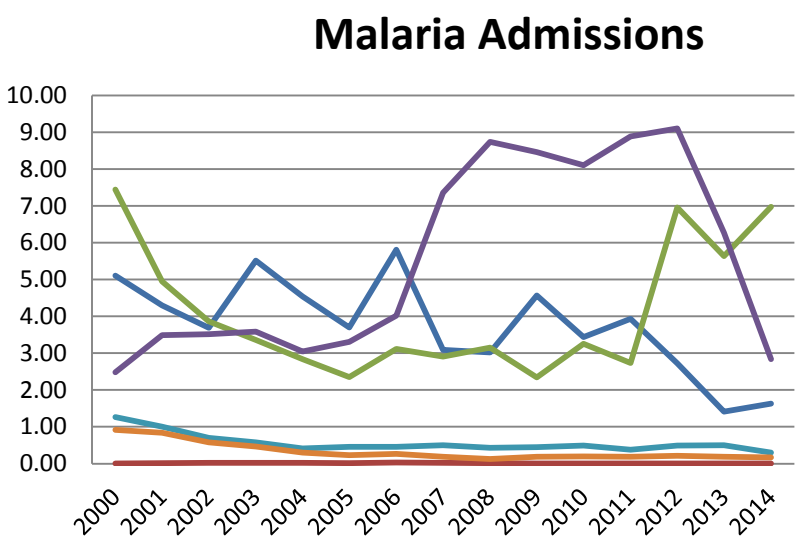
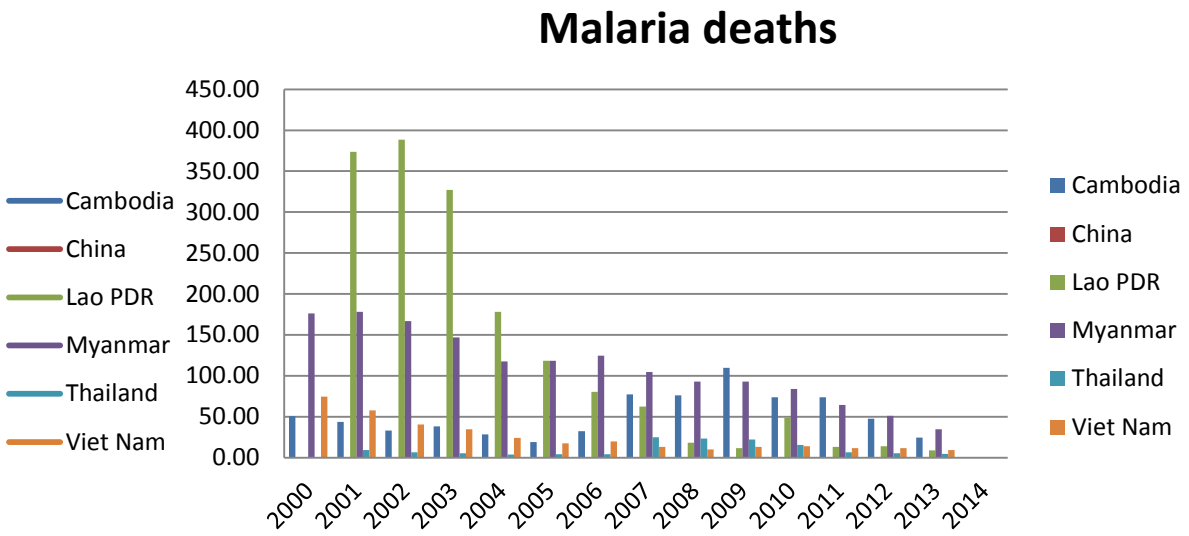
EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

Malaria Trends in the GMS , 2000–2014 (2)





Good case management has resulted in dramatic reduction of malaria related deaths across the Sub Region

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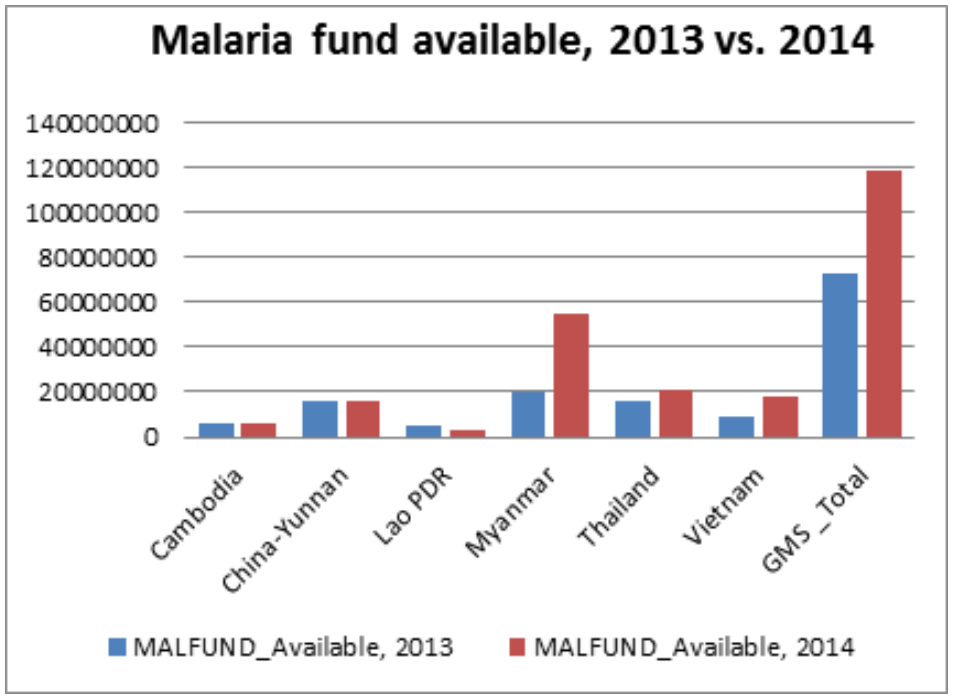
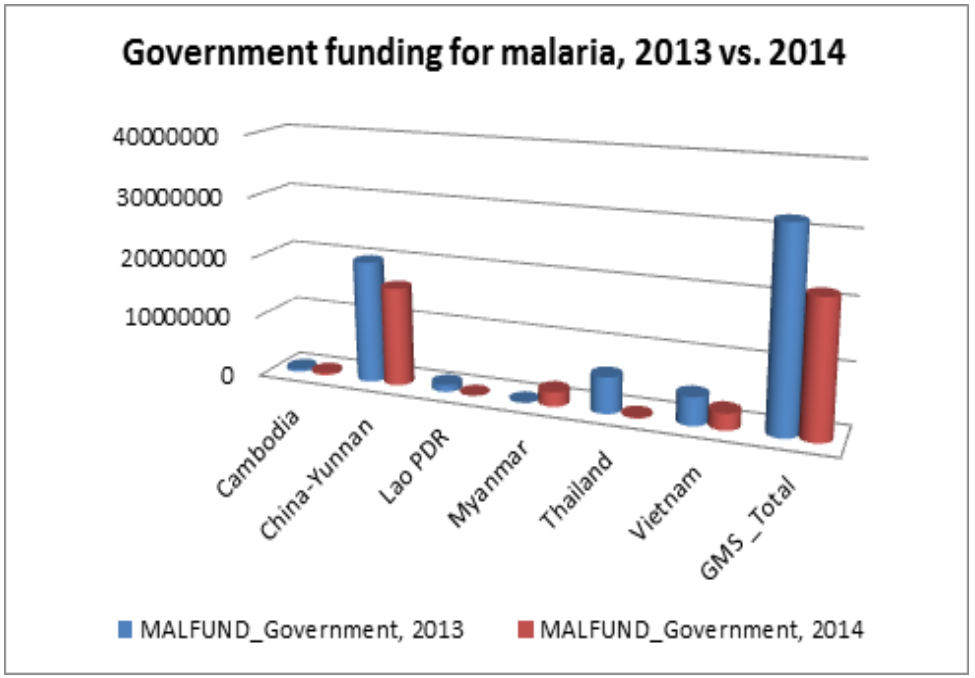
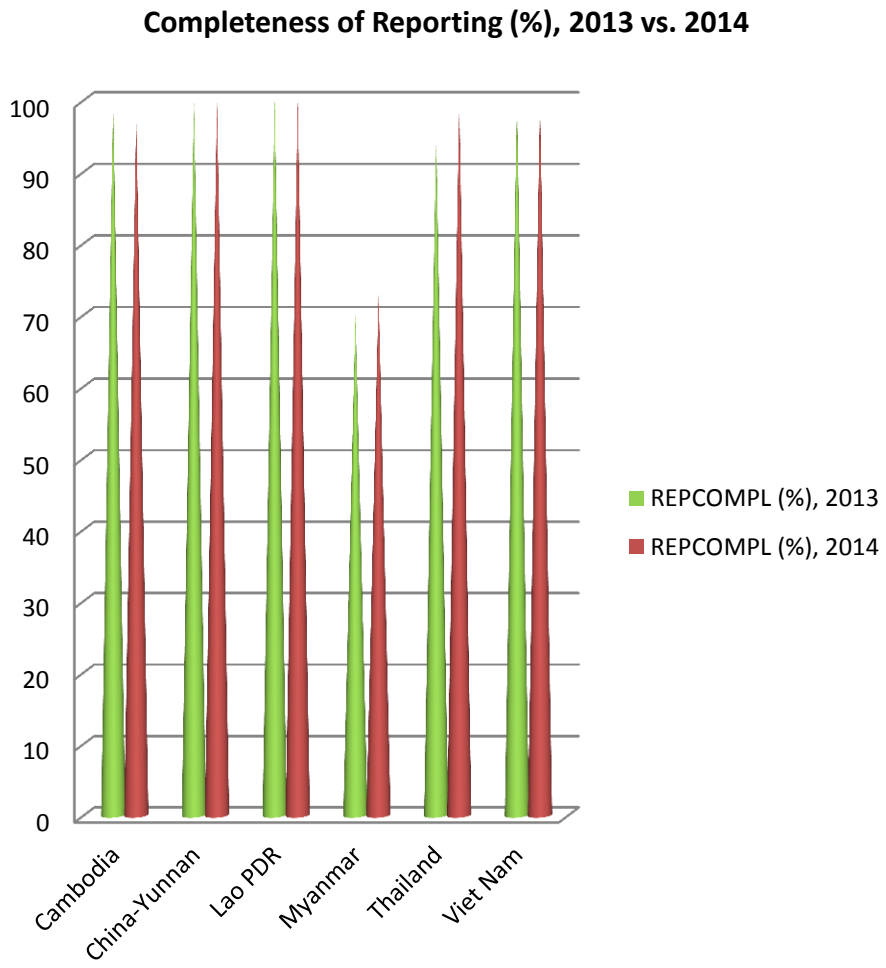
EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

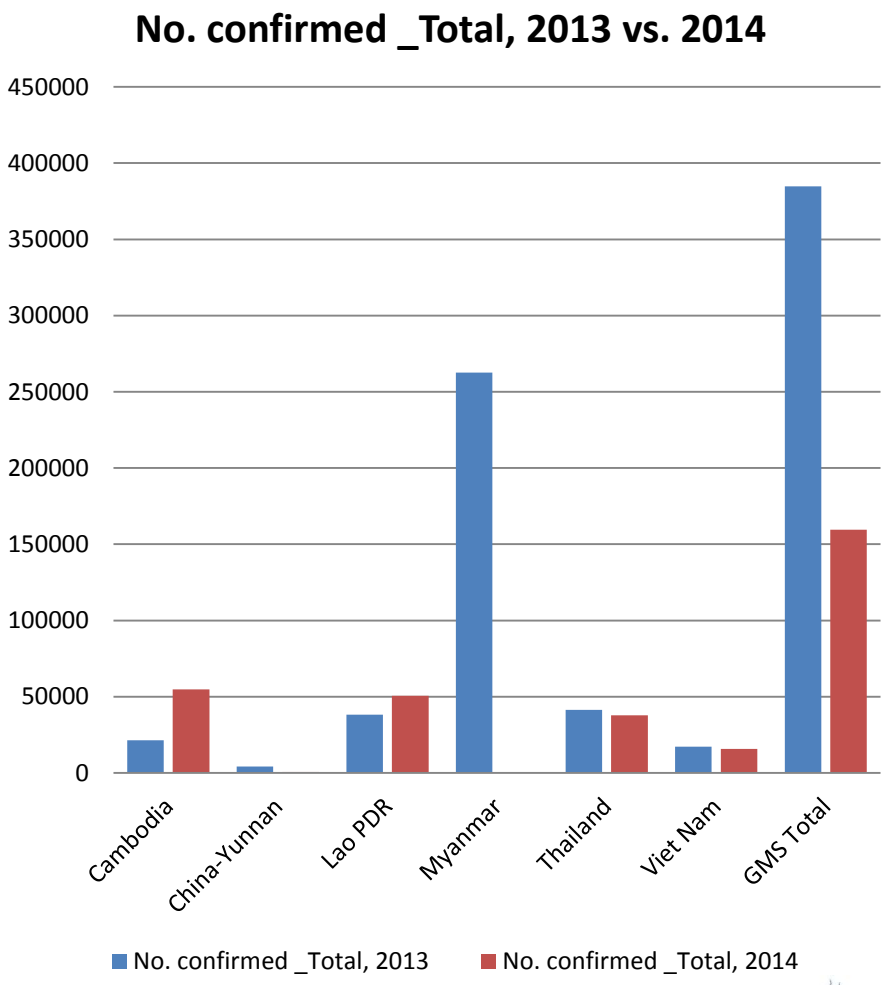
Selected ERAR Scorecard Indicators, WHO ERAR, 2015





Selected ERAR Scorecard Indicators, WHO ERAR, 2015





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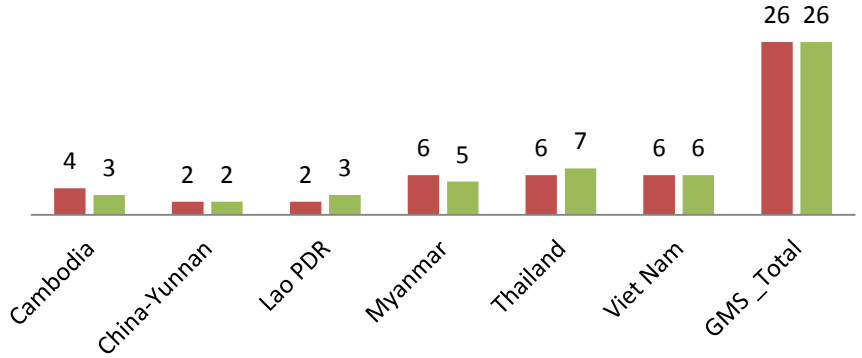
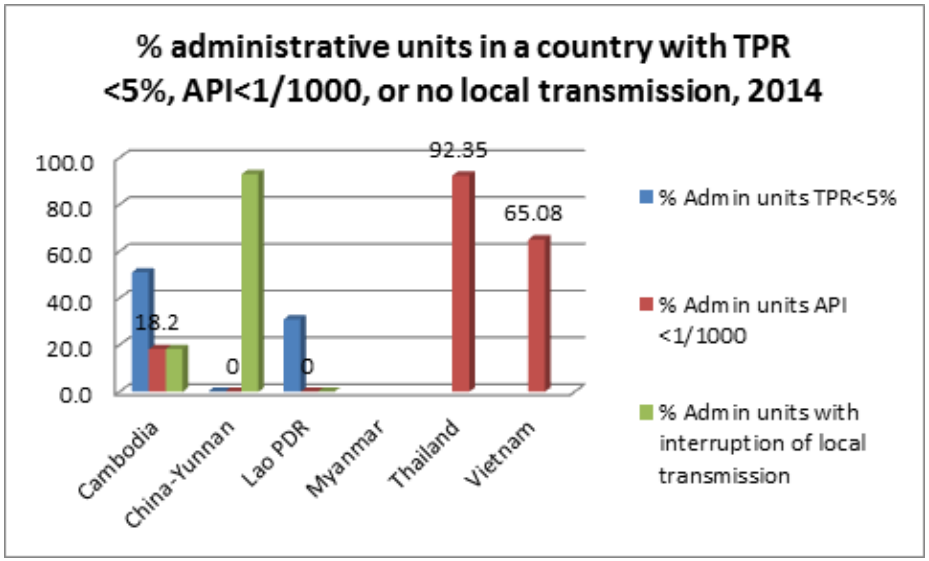
EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

Selected ERAR Scorecard Indicators, WHO ERAR, 2015

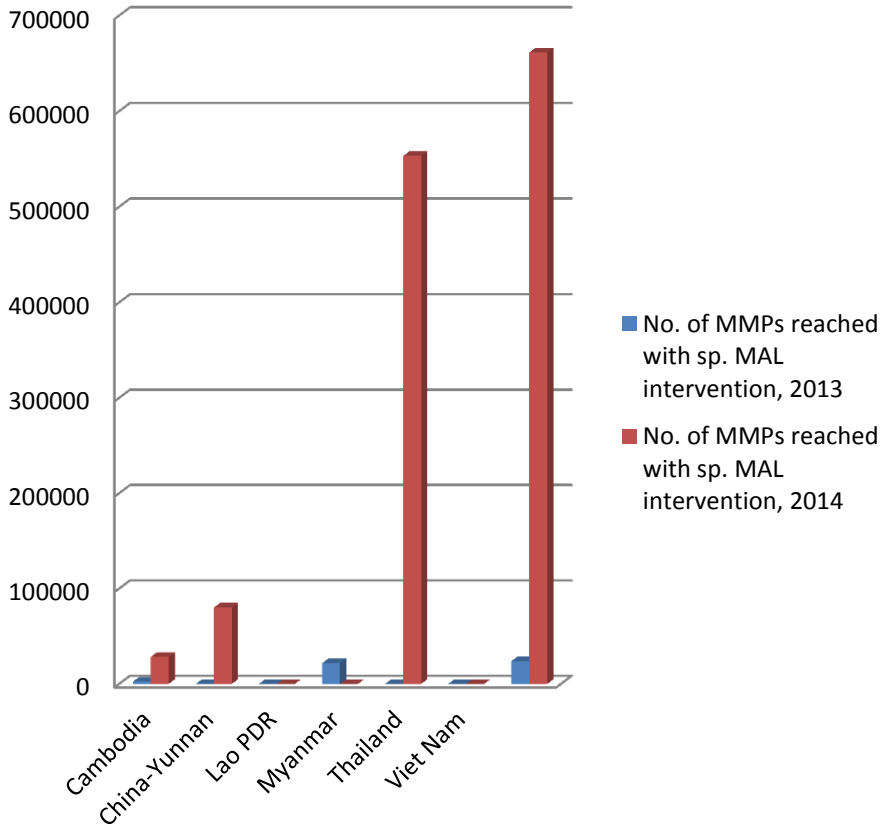
Drug Efficacy Studies conducted, 2013 vs. 2014



% administrative units in a country with TPR <5%, API<1/1000, or no local transmission, 2014



No. of MMPs reached with sp. MAL intervention, 2013 vs. 2014



World Health Organization

EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

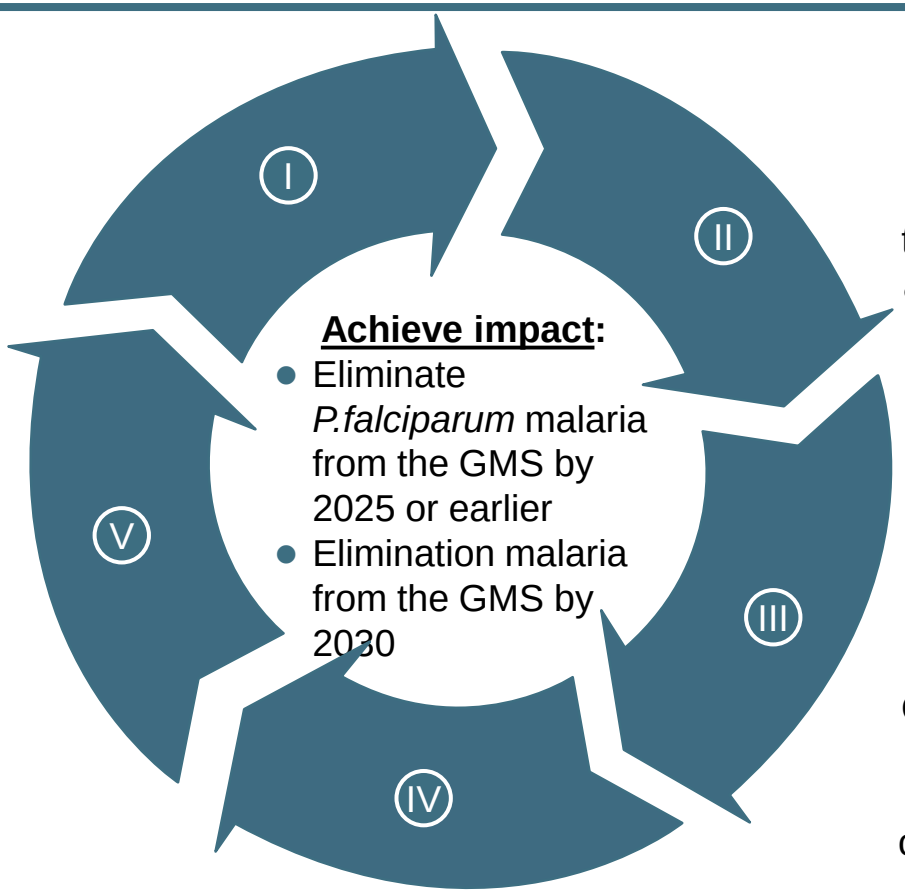
Looking Ahead: Transformation from the ERAR into GMS Malaria Elimination Hub

I

Promote high level and multi stakeholder engagement to keep malaria elimination high on the agenda and ensure mutual accountability

II

Strengthen existing malaria surveillance systems in their transition towards malaria case and entomological surveillance as core intervention



V

Keep an **independent score** of sub regional progress in malaria elimination, including **drug & insecticide resistance**

III

Coordinate and synergize case detection and management, disease prevention and vector control interventions adapted to local context

IV

Plan and implement capacity building activities (training, mentoring and supervision)

World Health Organization

EMERGENCY RESPONSE TO ARTEMISININ RESISTANCE IN THE GREATER MEKONG SUBREGION

Acknowledgment:
Governments, Partners, Stakeholders and Donors

World Health Organization
REGIONAL OFFICE FOR Europe

Organisation mondiale de la Santé
BUREAU RÉGIONAL DE L' Europe

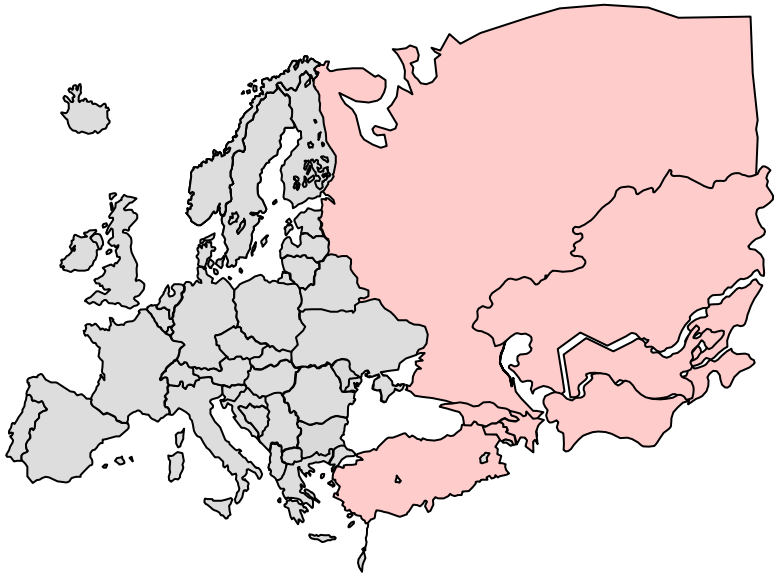
Weltgesundheitsorganisation
REGIONALBÜRO FÜR Europa

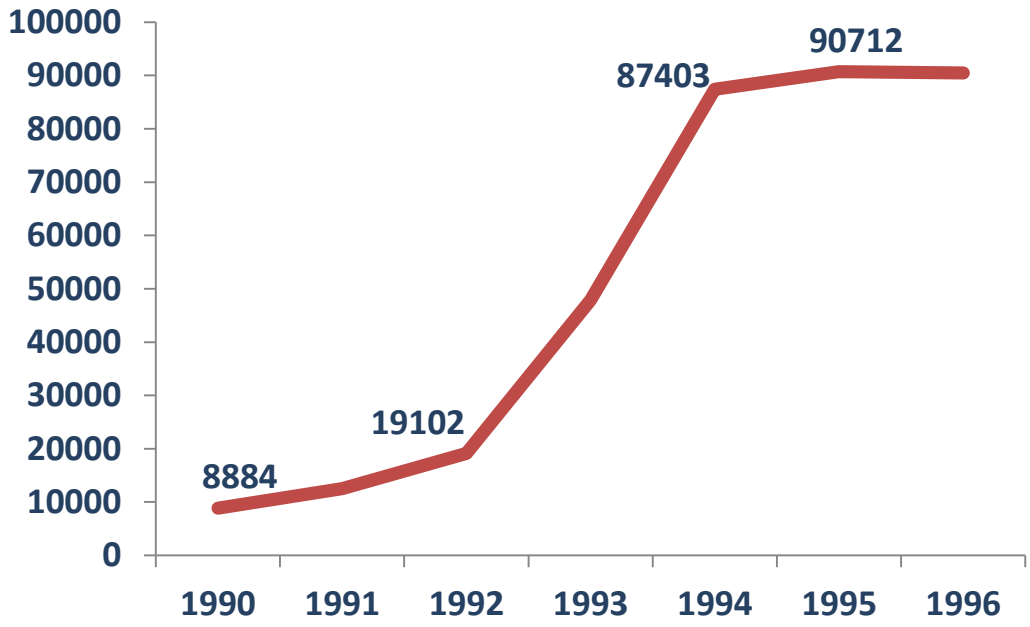
Всемирная организация здравоохранения
Европейское региональное бюро

UPDATE ON MALARIA ELIMINATION IN WHO EUROPEAN REGION

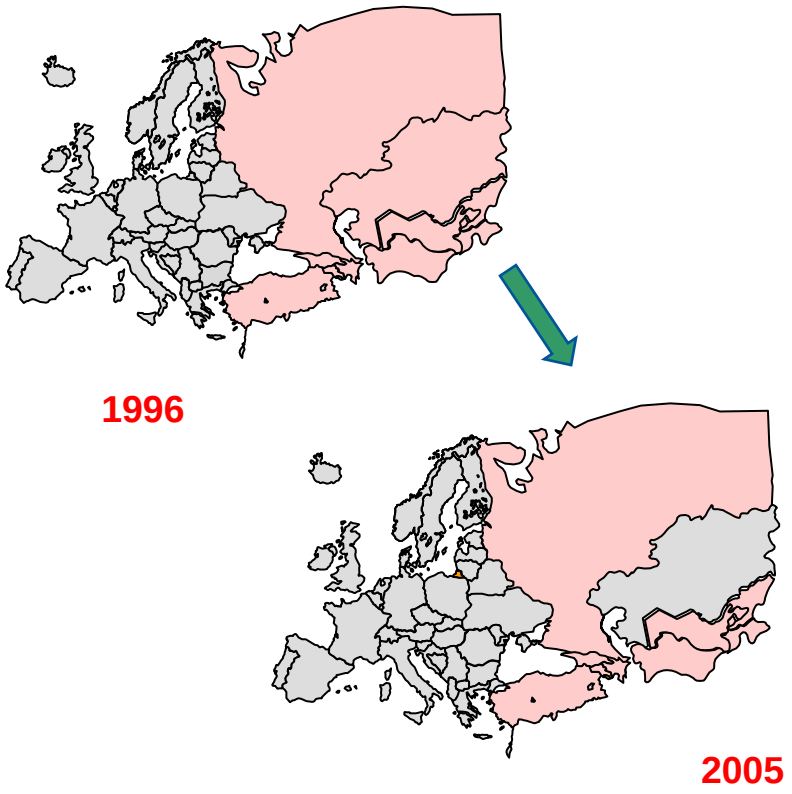
Dr Elkhan Gasimov

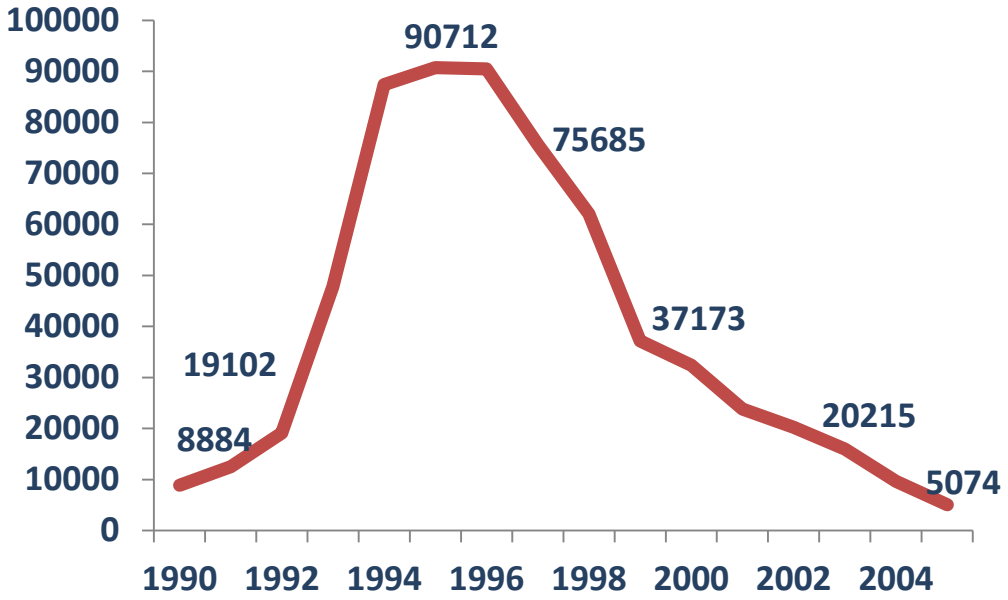
Autochthonous malaria cases in Europe, 1990 - 1996





Autochthonous malaria cases in Europe, 1990 - 2005





Dr Norayr Davidyan,
Minister of Health,
Armenia

Dr Oktay Shiraliyev,
Minister of Health,
Azerbaijan

Dr Vladimer Chipashvili,
Minister of Health,
Georgia

Mr Erbolat A. Dosayev,
Minister of Health,
Kazakhstan

Dr Shailoobek Nyiazov,
Minister of Health,
Kyrgyzstan

Prof. Nusratullo Faizullaev,
Minister of Health,
Tajikistan

Dr Recep Akdag,
Minister of Health,
Turkey

Dr G.M. Berdymukhammedov,
Minister of Health,
Turkmenistan

Prof. Feruz Nazirov,
Minister of Health,
Uzbekistan

World Health Organization
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Web site: www.euro.who.int

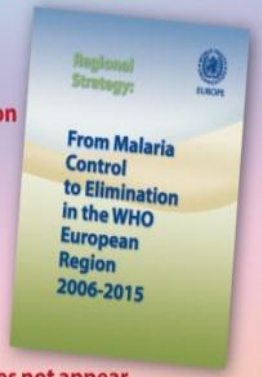
WORLD HEALTH ORGANIZATION
EUROPE

The Tashkent Declaration

"The Move from Malaria Control

Regional Objectives 2006 – 2015

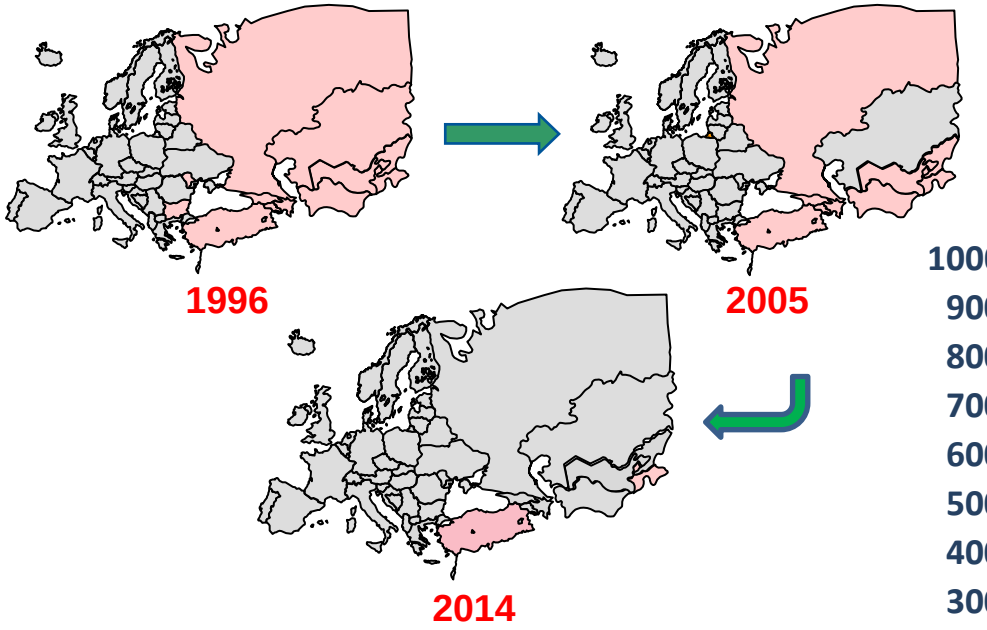
EUROPE



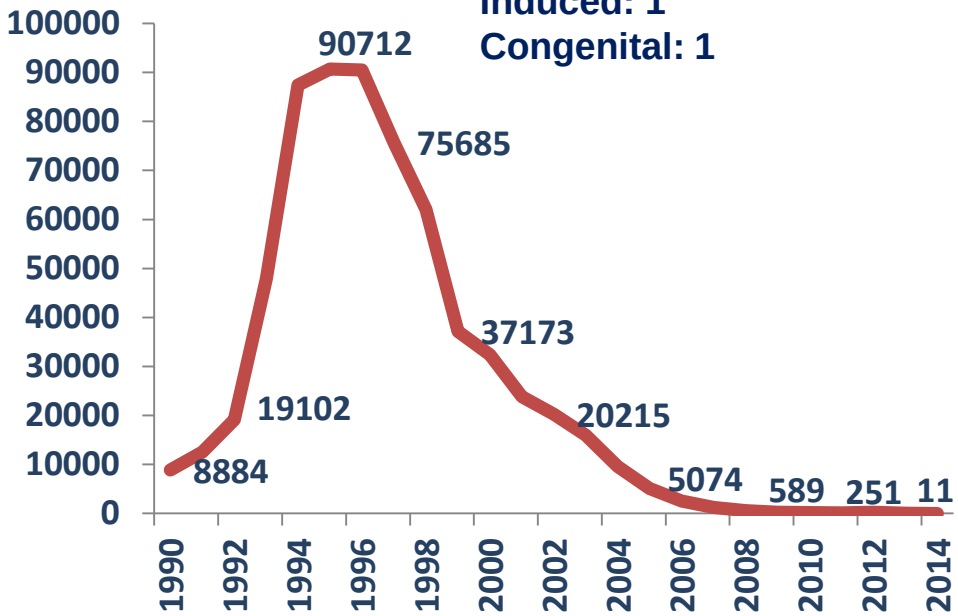
- To interrupt malaria transmission in countries where malaria is a focal problem and there is clear evidence of political support and technical and operational feasibility of elimination
- To reduce further the incidence and prevalence of malaria in countries where elimination does not appear to be feasible at present

- To prevent the re-establishment of malaria transmission and to maintain the malaria-free status in countries and territories where the disease has been eliminated

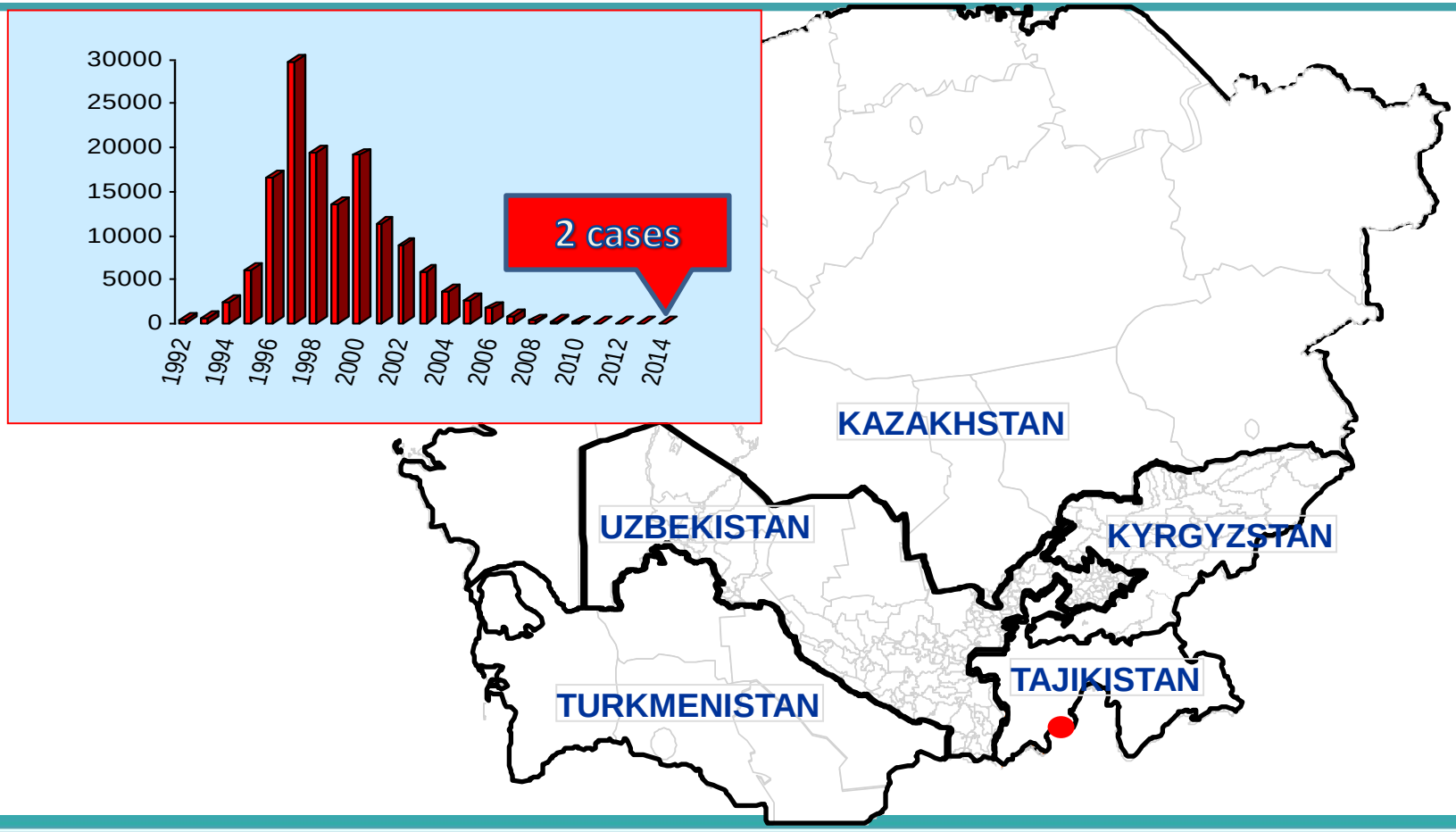
Autochthonous malaria cases in Europe, 1990 - 2014



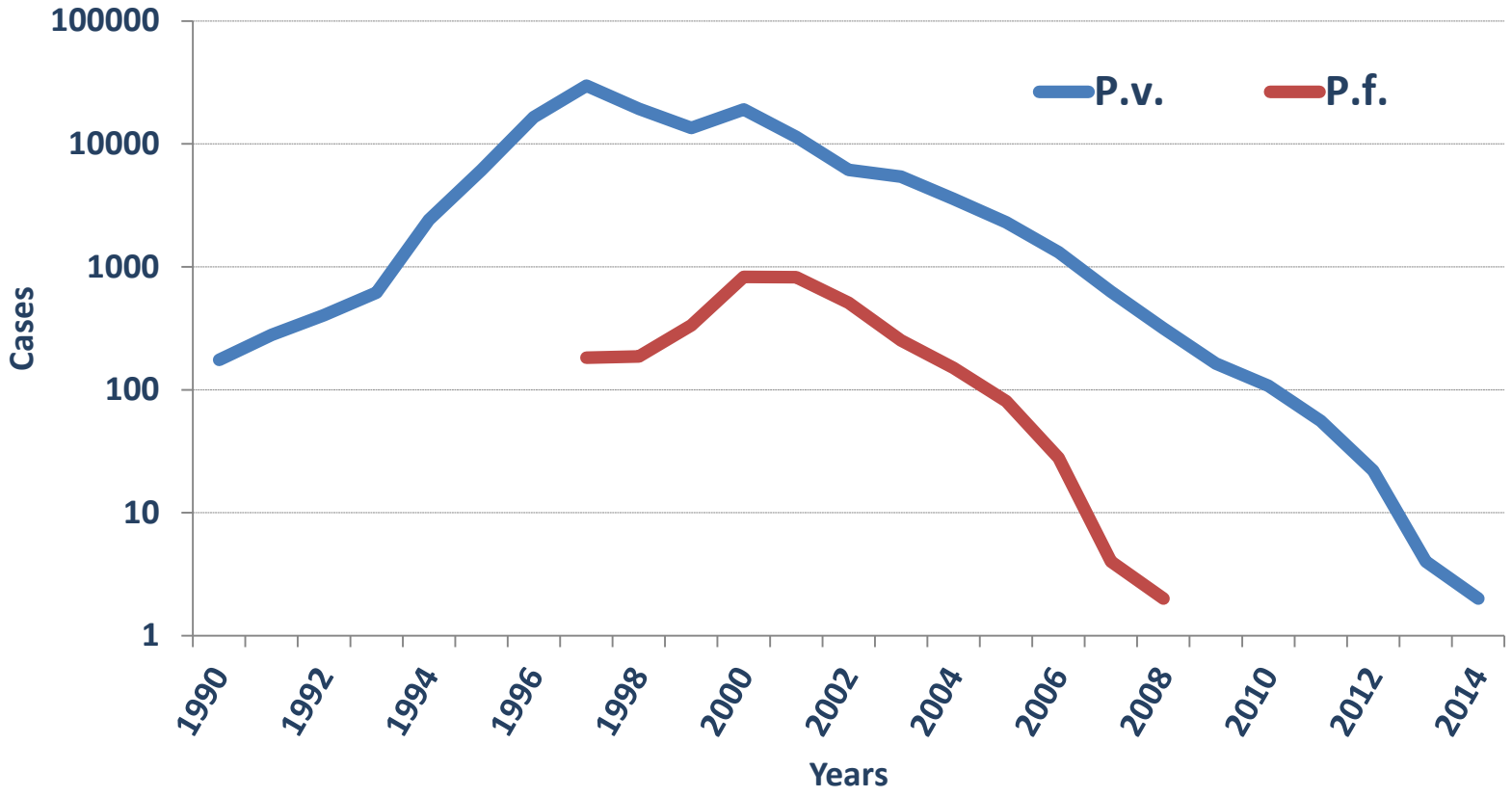
Cases in 2014
Indigenous: 2 (Tajikistan)
Introduced: 7
Induced: 1
Congenital: 1



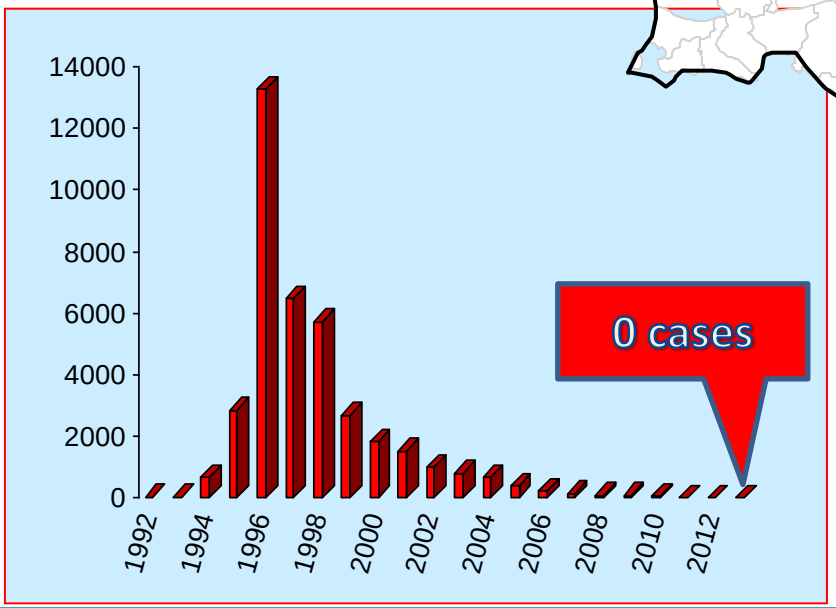
Central Asia, 2014



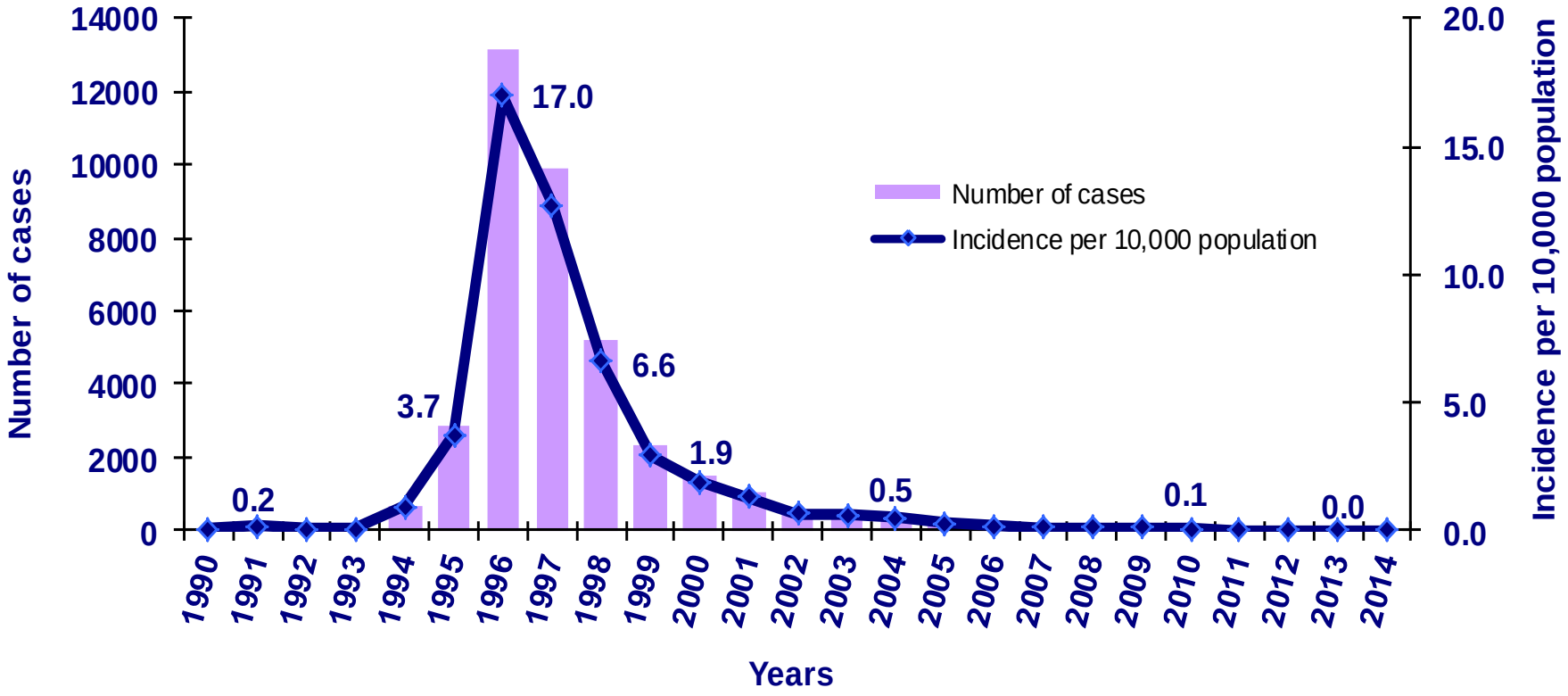
Tajikistan


100000
10000
1000
100
10
1
Cases
P.v.
P.f.
1990
1992
1994
1996
1998
2000
2002
2004
2006
2008
2010
2012
2014
Years

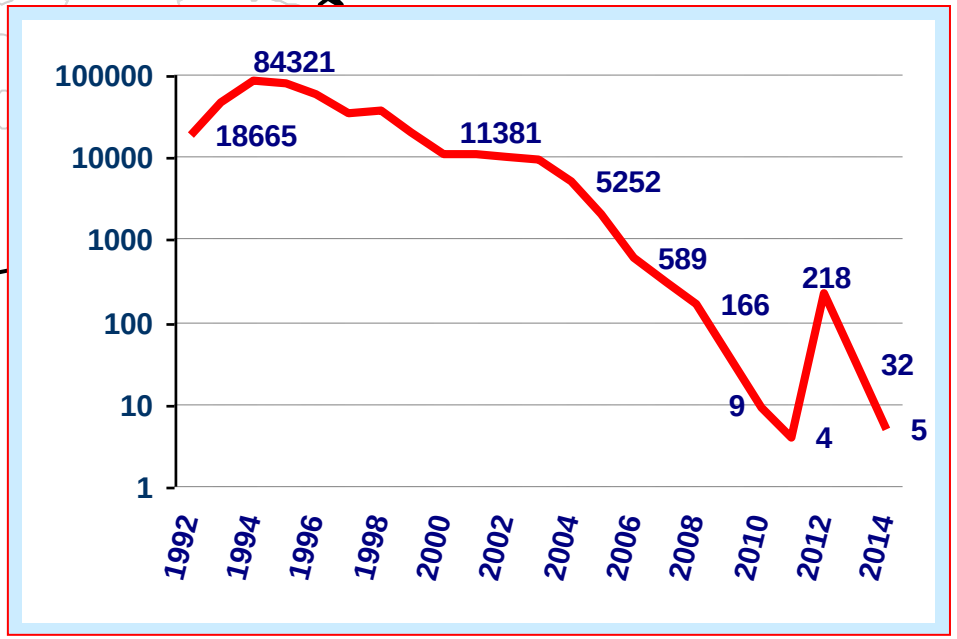
South Caucasus, 2014



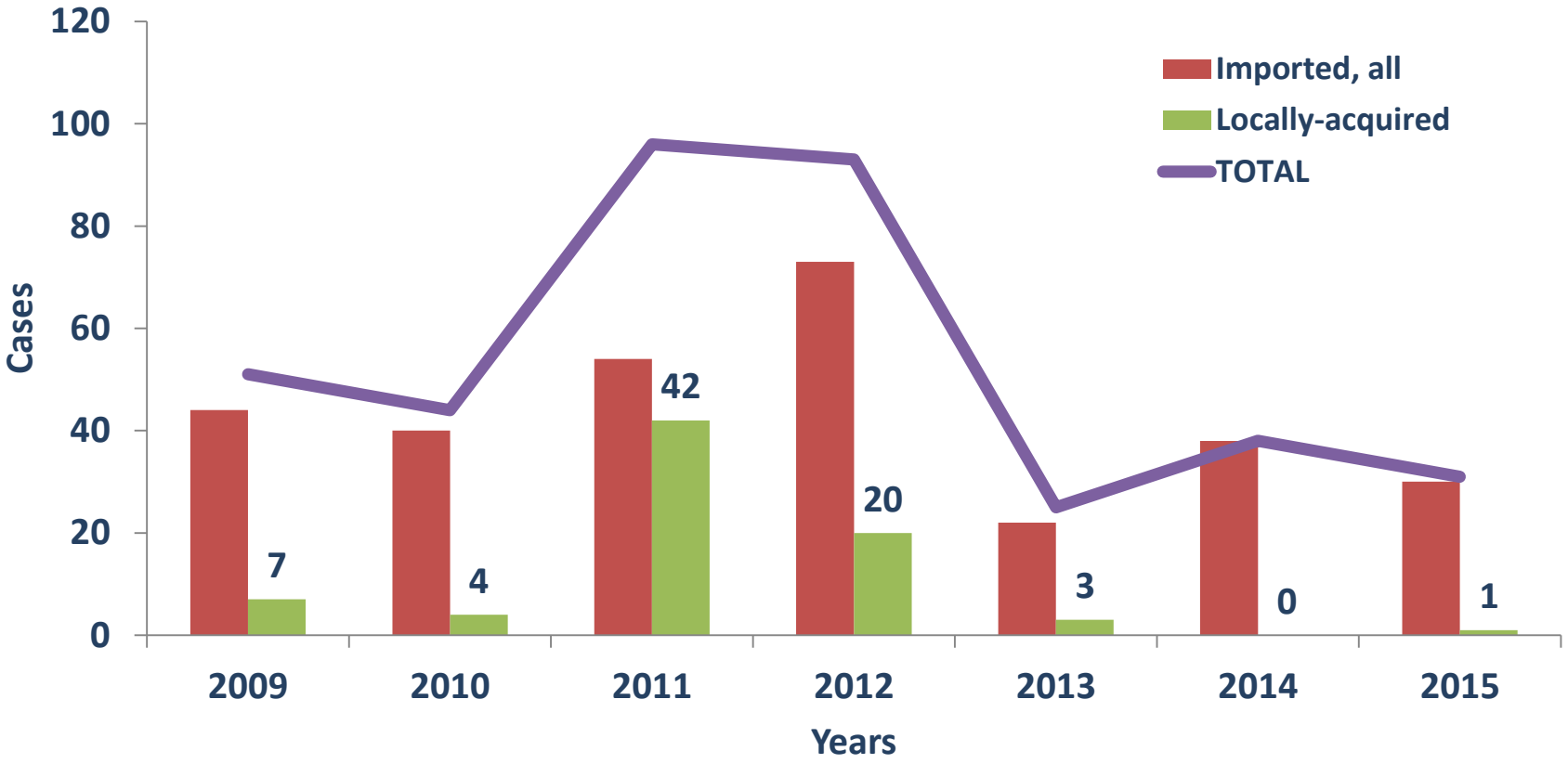
Azerbaijan


Number of cases
Incidence per 10,000 population
Number of cases
Incidence per 10,000 population
Years
0.2
3.7
17.0
6.6
1.9
0.5
0.1
0.0

Turkey, 1992-2014



Greece, 2009 - 2015



2015

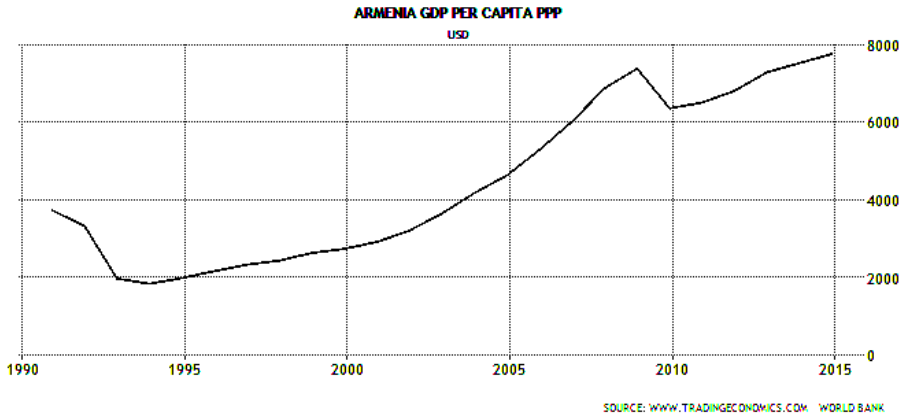
Tajikistan: 1 case, Khatlon province, registered in January (case of 2014)

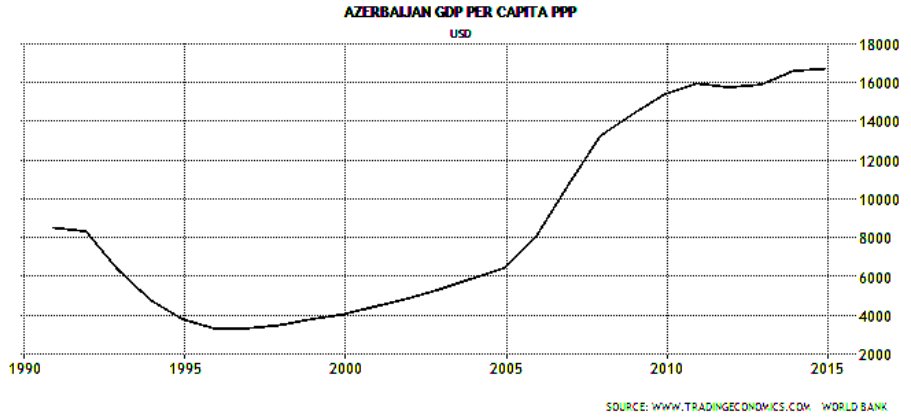
Georgia: 1 induced case

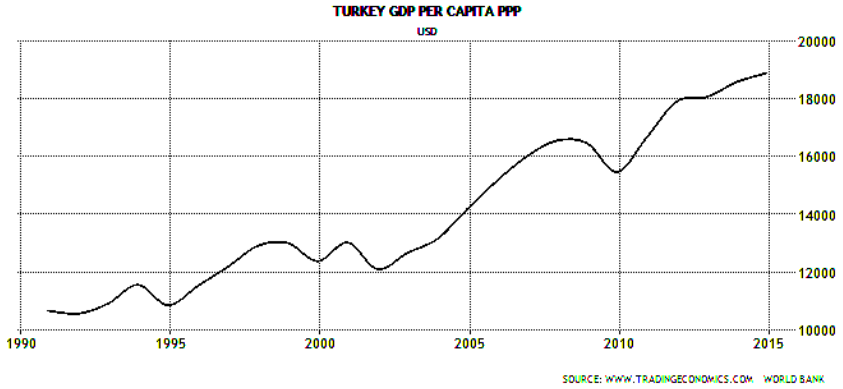
Greece: 1 case, Trikala, Farkadona municipality, Thessaly region, introduced

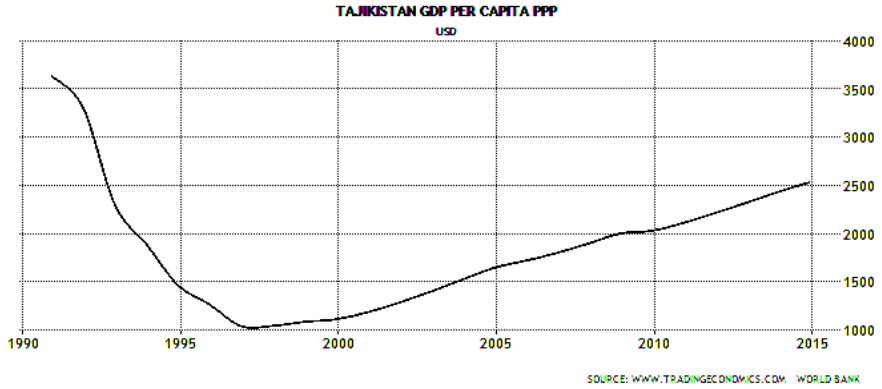
Regional Framework

Overall development



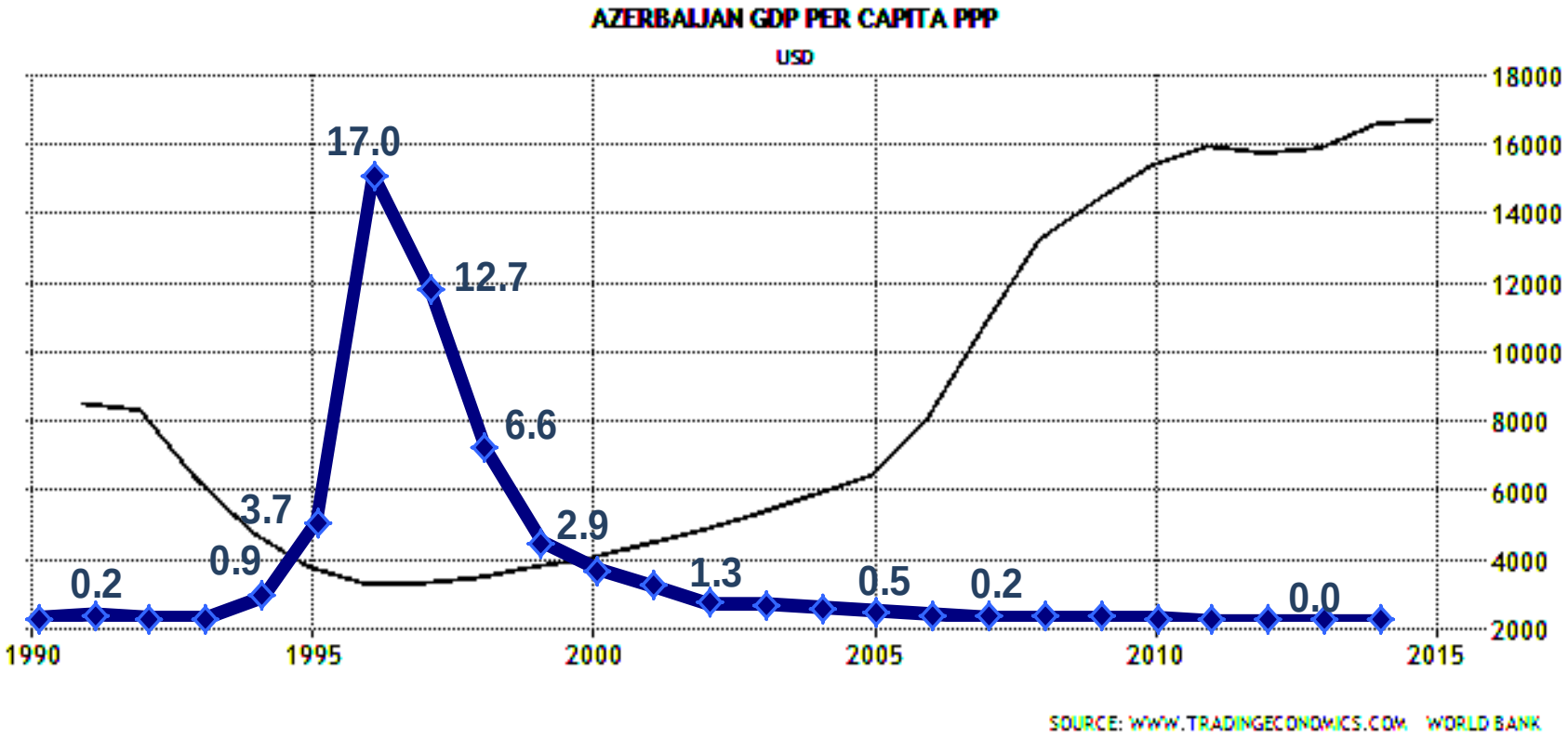






Source: http://www.tradingeconomics.com/

Azerbaijan: GDP/Malaria incidence

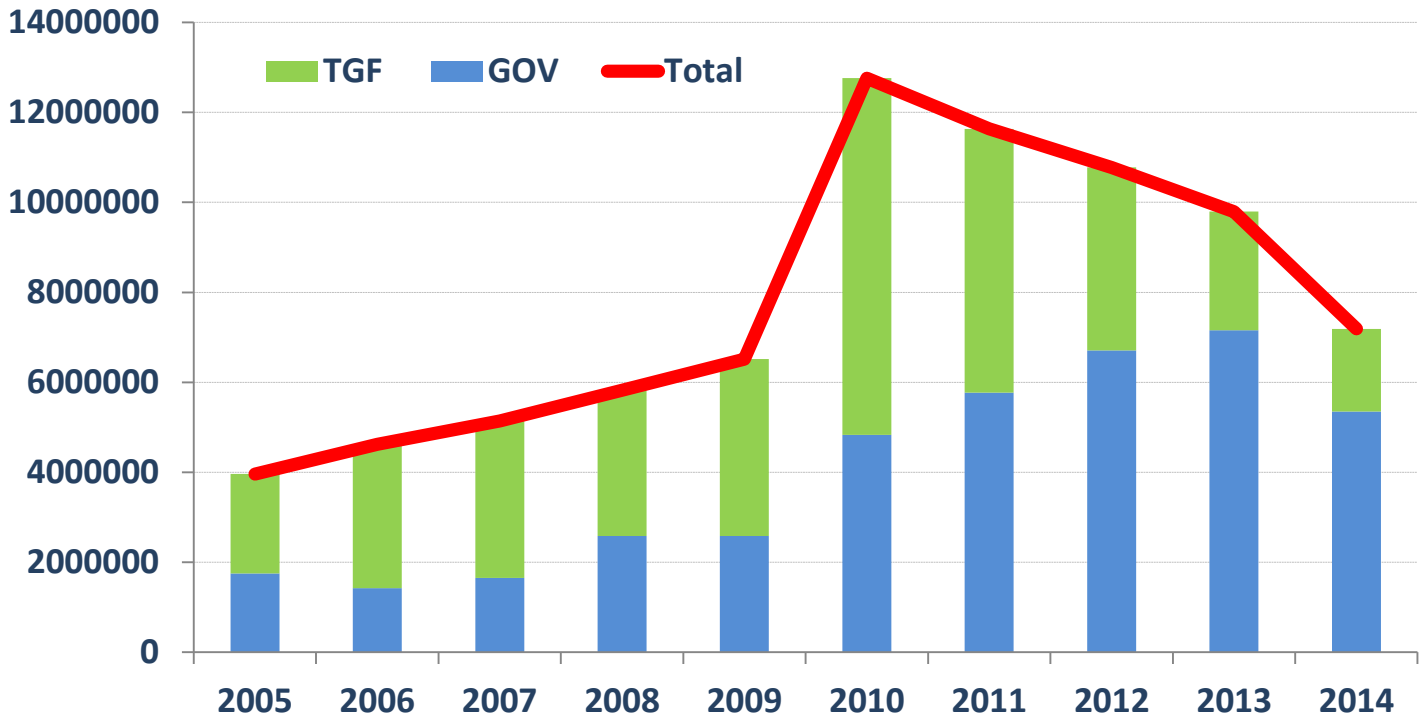


Political commitment

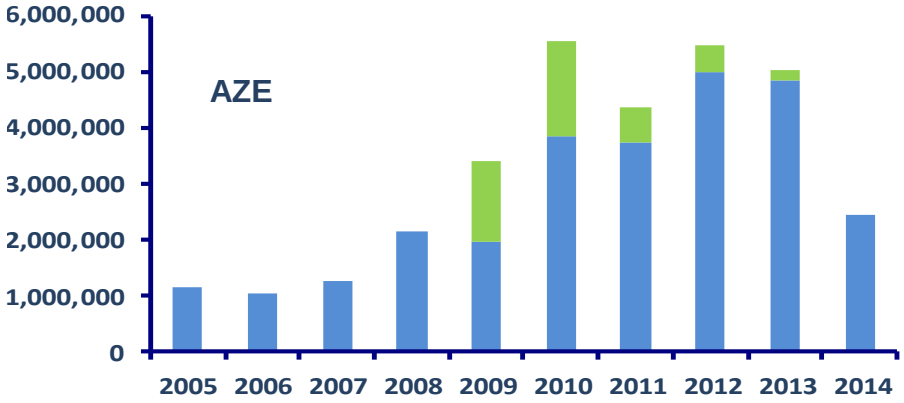
Funding

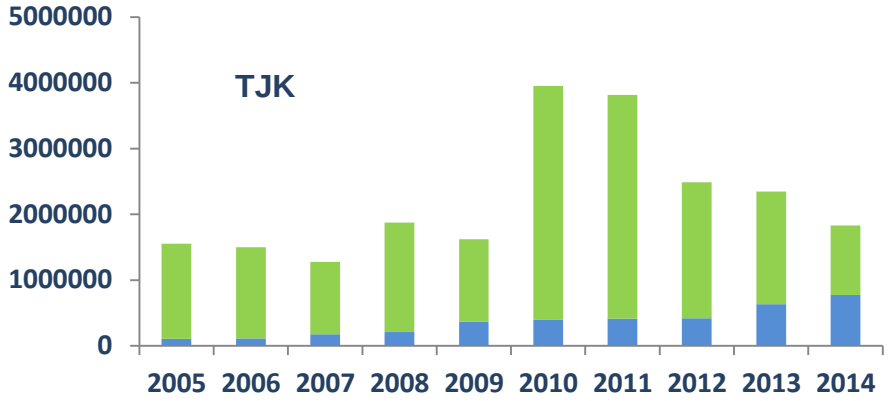
Government

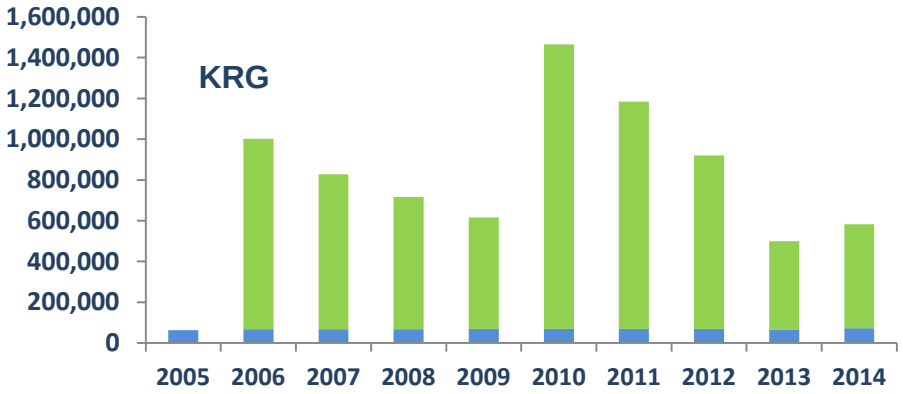
The Global Fund

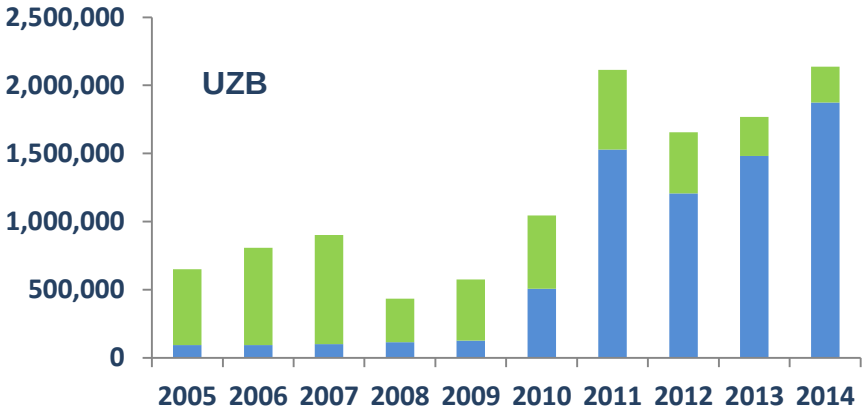


GOV vs TGF funding (2005-2014)



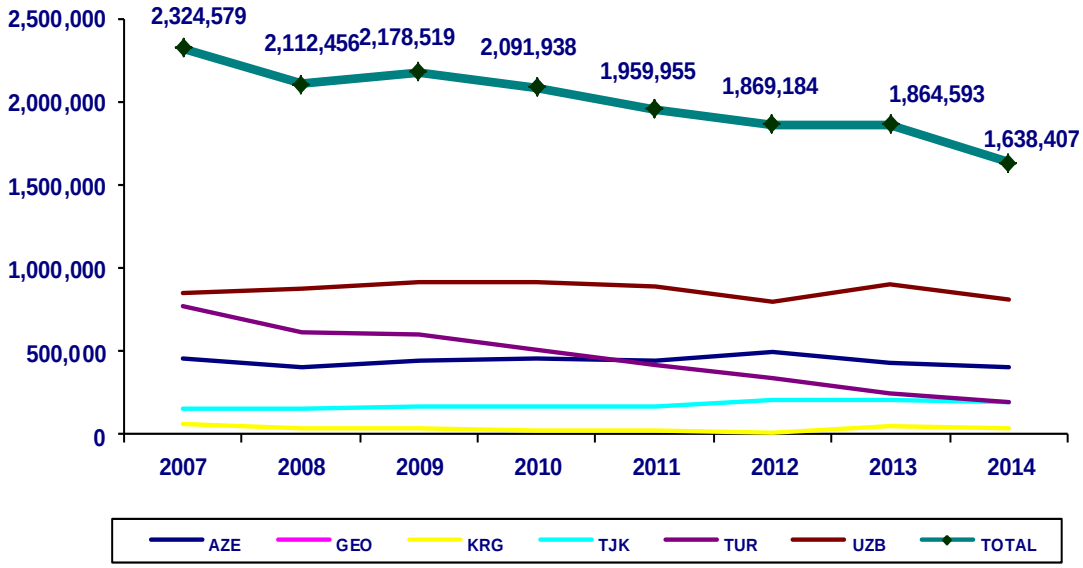




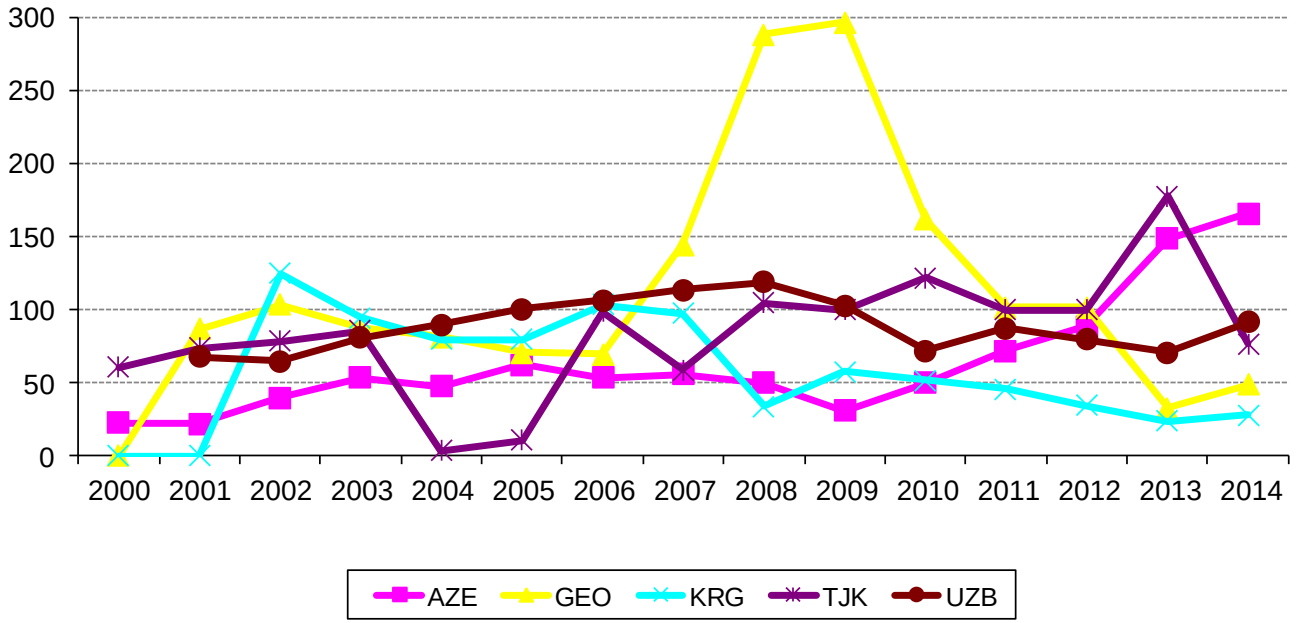


Surveillance

-Notifiable disease (urgent notification)
-ACD and PCD
-Cases are investigated and classified
-Foci are investigated and classified
-National register of cases
-Lab register

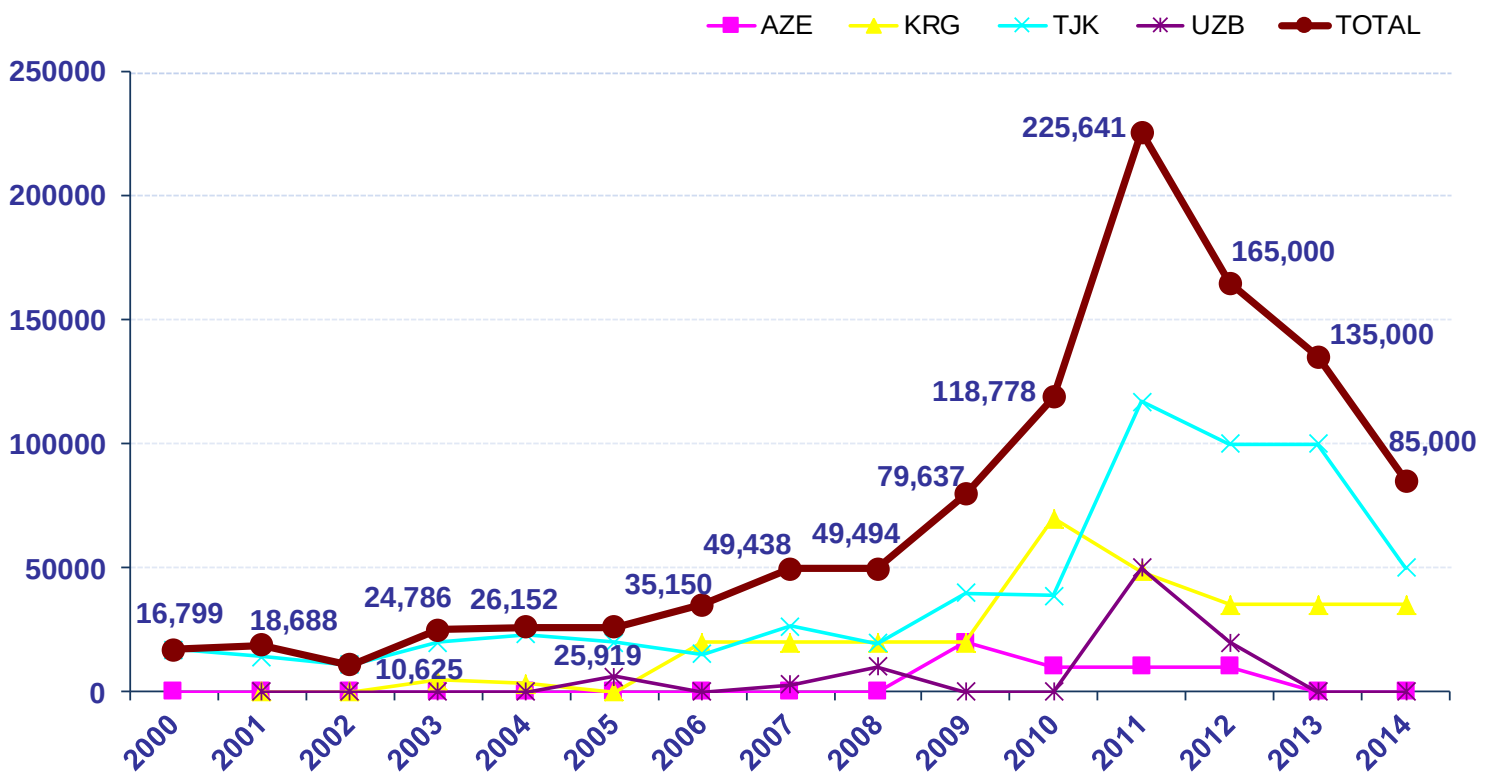


Vector control: IRS, 2000-2014



1,081,918 people protected by IRS in 2014

Vector control: ITN, 2000-2014 (1,066,107)



Cross-border collaboration: AZE-GEO

JOINT STATEMENT

on cooperation between the Ministry of Health of Azerbaijan Republic and the Ministry of Labour, Health and Social Affairs of Georgia on malaria elimination

The Tashkent Declaration, "The Move from Malaria Control to Elimination" endorsed by Azerbaijan and Georgia in 2005, puts particular emphasis on situations in which there is a risk of malaria spreading between countries. The rationale for this Joint Statement, endorsed at the meeting between Azerbaijan and Georgia on cross-border cooperation, held in Baku on 19 March 2009, is to stress the need to scale up cross-border cooperation in order to promote and facilitate joint efforts aimed at malaria elimination in Azerbaijan and Georgia.

We, the joint signatories of this statement:

- remain fully committed to the principles expressed in the Tashkent Declaration on issues related to malaria elimination and cross-border cooperation;
- agree to take all necessary steps to scale up efforts to solve common malaria-related problems in Azerbaijan and Georgia, with particular emphasis on border areas, since cross-border cooperation on malaria remains a priority public health topic for both countries;
- call upon the World Health Organization (WHO) to continue to take the lead in strategic coordination and technical guidance of malaria elimination programmes in Azerbaijan and Georgia, taking into account the positive world experience accumulated over the past years;
- call upon WHO, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and other donors to continue to support the countries in their efforts towards implementing the new national programmes with the goal of eliminating *Plasmodium vivax* malaria;
- underline the need to streamline the approaches and mechanisms used to better coordinate the action aimed at malaria elimination by all parties concerned (governmental bodies, international agencies, nongovernmental organizations and the private sector) at both inter-country and country levels.

We recommend:

- to establish operational modalities for regular exchange of information on malaria, particularly in border areas;
- to synchronize action plans for coordinated implementation of malaria elimination activities in border areas;
- to ensure early notification on any changes in epidemiological situation related to malaria in border areas of the two countries;
- to establish an joint working group, composed of national counterparts and local WHO and GFATM staff, in order to assist in planning, implementing and evaluating joint malaria elimination activities in border areas of both countries;
- to appoint focal points in each country to assist in coordination of cross-border issues related to malaria elimination;
- to coordinate mobilization of additional resources to support the countries' malaria elimination efforts;
- to take actions to create greater awareness of the successes of malaria elimination programmes.

Ministry of Health, Azerbaijan Republic

Ministry of Labour, Health and Social Affairs, Georgia

Global Fund to Fight AIDS, TB and Malaria, Azerbaijan

Global Fund to Fight AIDS, TB and Malaria, Georgia

World Health Organization Regional Office for Europe

Baku, 19 March 2009

Cross-border collaboration: KAZ-KRG-TJK-UZB

World Health Organization Europe

JOINT STATEMENT ON
CROSS-BORDER COOPERATION ON MALARIA
IN KAZAKHSTAN, KYRGYZSTAN, TAJIKISTAN AND UZBEKISTAN

The Tashkent Declaration, "The Move from Malaria Control to Elimination" endorsed by abovementioned countries in 2006 put particular emphasis on situations in which there is a risk of malaria spreading between countries. The rationale for this Joint Statement, endorsed at the Inter-country meeting between mentioned countries on cross-border cooperation, held in Bishkek, Kyrgyzstan on 1-2 November 2010 is to stress the need to establish cross-border cooperation in order to promote and facilitate joint efforts aimed at malaria elimination in Kyrgyzstan, Tajikistan and Uzbekistan and prevention of reintroduction of malaria transmission in Kazakhstan.

We, the joint signatories of this statement:

- remain fully committed to the principles expressed in the Tashkent Declaration on issues related to malaria elimination and cross-border cooperation;
- agree to take all necessary steps to solve common malaria-related issues in Kyrgyzstan, Tajikistan and Uzbekistan and prevention of reintroduction of malaria transmission in Kazakhstan, with particular emphasis on border areas;
- call upon the World Health Organization (WHO) to continue to take the lead in the strategic coordination and technical guidance of malaria elimination programmes in mentioned countries;
- call upon WHO, Global Fund and other partners to continue supporting the Ministries of Health of the countries in their efforts towards implementing the national anti-malaria programmes with the stated goals;
- underline the need to streamline the approaches and improve coordination mechanisms for malaria elimination by all parties concerned (governmental bodies, international agencies, non-governmental and community-based organizations and the private sector) at both inter-country and country levels.

We recommend that

- focal points be identified for each country to assist in the coordination of cross-border issues related to malaria elimination and prevention of reintroduction in border areas;
- an inter-country working group be established, composed of managers and national counterparts representing all levels and local WHO staff, in order to assist in planning, implementing and evaluating malaria elimination activities and prevention of reintroduction of malaria in border areas of the countries;
- operational modalities be established for regular and timely exchange of information on malaria, particularly in border areas;
- joint action plans be developed to synchronize and harmonize malaria elimination activities and prevention of reintroduction in border areas;
- information exchange be given of any unusual situations related to malaria in border areas of the countries;
- action be taken to create greater awareness of the successes of malaria elimination programmes
- and to coordinate the mobilization of additional resources to support the countries' malaria elimination efforts.

Ministry of Health, Kazakhstan

Ministry of Health, Kyrgyzstan

Ministry of Health, Tajikistan

Ministry of Health, Uzbekistan

World Health Organization, Kazakhstan

World Health Organization, Kyrgyzstan

World Health Organization, Tajikistan

World Health Organization, Uzbekistan

Bishkek, 2 November 2010

Cross-border collaboration: TKM-AFG

World Health Organization
Regional Office for the Eastern Mediterranean

JOINT STATEMENT ON CROSS-BORDER COOPERATION ON MALARIA IN TURKMENISTAN AND AFGHANISTAN

The Tashkent Declaration, "The Move from Malaria Control to Elimination" endorsed by Turkmenistan in 2005 and the Kabul Declaration "Health for All. Health by All: Communicable Diseases Recognize No Borders" endorsed by Turkmenistan and Afghanistan in 2006, put particular emphasis on situations in which there is a risk of malaria spreading between countries. The rationale for this Joint Statement, endorsed at the inter-country meeting between Turkmenistan and Afghanistan on cross-border cooperation, held in Ashgabat, Turkmenistan, 19-20 November 2009, is to stress the need to establish cross-border cooperation in order to promote and facilitate joint efforts aimed at malaria control and elimination in Afghanistan and prevention of reintroduction of malaria transmission in Turkmenistan.

We, the joint signatories of this statement:

- remain fully committed to the principles expressed in the Tashkent and Kabul Declarations on issues related to malaria control and elimination and cross-border cooperation;
- agree to take all necessary steps to solve common malaria-related issues in Turkmenistan and Afghanistan, with particular emphasis on border areas, since cross-border cooperation on malaria remains a priority public health issue for both countries;
- call upon the World Health Organization (WHO) to continue to take the lead in the strategic coordination and technical guidance of malaria control and elimination programmes in Turkmenistan and Afghanistan;
- call upon WHO, donors and other partners to continue supporting the Ministries of Health of the two countries in their efforts towards implementing the national anti-malaria programmes with the stated goals;
- underline the need to streamline the approaches and improve coordination mechanisms for malaria control and elimination by all parties concerned (governmental bodies, international agencies, non-governmental and community-based organizations and the private sector) at both inter-country and country levels.

We recommend that

- focal points be identified for each country to assist in the coordination of cross-border issues related to malaria control and elimination;
- an inter-country working group be established, composed of national counterparts representing all levels and local WHO staff, in order to assist in planning, implementing and evaluating malaria control and elimination activities in border areas of both countries;
- operational modalities be established for regular and timely exchange of information on malaria, particularly in border areas;
- joint action plans be developed to synchronize and harmonize malaria control and elimination activities in border areas;
- information exchange be given of any unusual situations related to malaria in border areas of the two countries;
- action be taken to create greater awareness of the successes of malaria control and elimination programmes and to coordinate the mobilization of additional resources to support the countries' malaria control and elimination efforts;
- the possibility of rendering assistance by Turkmenistan to Afghanistan in strengthening human resource capacities, implementing preventive activities and improving research capabilities for malaria control and elimination in border areas, be explored, in collaboration with WHO;
- in collaboration with WHO, an inter-regional meeting to follow up on progress made with the Kabul Declaration "Health for All. Health by All: Communicable Diseases Recognize No Borders" endorsed by a number of countries of the WHO European and Eastern Mediterranean Regions, and the Tashkent Declaration "The Move from Malaria Control to Elimination" endorsed by all malaria-affected countries of the WHO European Region, be organized in Ashgabat, Turkmenistan in 2010.

Ministry of Health, Turkmenistan

Ministry of Health, Afghanistan

World Health Organization, Turkmenistan

World Health Organization, Afghanistan

Ashgabat, 20 November 2009

REGIONAL OFFICE

Cross-border collaboration: TJK-AFG

EUROPE

World Health Organization
Regional Office for the Eastern Mediterranean

JOINT STATEMENT ON CROSS-BORDER COOPERATION ON MALARIA IN TAJIKISTAN AND AFGHANISTAN

The Tashkent Declaration, "The Move from Malaria Control to Elimination" endorsed by Tajikistan in 2005 and the Kabul Declaration "Health for All. Health by All: Communicable Diseases Recognize No Borders" endorsed by Tajikistan and Afghanistan in 2006, put particular emphasis on situations in which there is a risk of malaria spreading between countries. The rationale for this Joint Statement, endorsed at the Inter-country meeting between Tajikistan and Afghanistan on cross-border cooperation, held in Kurgan-Tube, Tajikistan, 11-13 October 2010 is to stress the need to establish cross-border cooperation in order to promote and facilitate joint efforts aimed at malaria control and elimination in Afghanistan and prevention of reintroduction of malaria transmission in Tajikistan.

We, the joint signatories of this statement:

- remain fully committed to the principles expressed in the Tashkent and Kabul Declarations on issues related to malaria control and elimination and cross-border cooperation;
- agree to take all necessary steps to solve common malaria-related issues in Tajikistan and Afghanistan, with particular emphasis on border areas, since cross-border cooperation on malaria remains a priority public health issue for both countries;
- call upon the World Health Organization (WHO) to continue to take the lead in the strategic coordination and technical guidance of malaria control and elimination programmes in Tajikistan and Afghanistan;
- call upon WHO, donors and other partners to continue supporting the Ministries of Health of the two countries in their efforts towards implementing the national anti-malaria programmes with the stated goals;
- underline the need to streamline the approaches and improve coordination mechanisms for malaria control and elimination by all parties concerned (governmental bodies, international agencies, non-governmental and community-based organizations and the private sector) at both inter-country and country levels.

We recommend that

- focal points be identified for each country to assist in the coordination of cross-border issues related to malaria control and elimination;
- an inter-country working group be established, composed of national counterparts representing all levels and local WHO staff, as well as partners and interested parties in order to assist in planning, implementing and evaluating malaria control and elimination activities in border areas of both countries;
- operational modalities be established for regular and timely exchange of information on malaria, particularly in border areas;
- joint action plans be developed to synchronize and harmonize malaria control and elimination activities in border areas;
- information exchange be given of any unusual situations related to malaria in border areas of the two countries;
- action be taken to create greater awareness of the successes of malaria control and elimination programmes and to coordinate the mobilization of additional resources to support the countries' malaria control and elimination efforts;
- the possibility of rendering assistance by Tajikistan to Afghanistan in strengthening human resource capacities, implementing preventive activities and improving research capabilities for malaria control and elimination in border areas, be explored, in collaboration with WHO
- support in organizing coordination meetings on malaria control and its elimination in border areas between the two countries on a regular basis;
- to develop project proposals to the Global Fund on enhancing cross border activities to control and eliminate malaria in the border areas.

Ministry of Health, Tajikistan — Ministry of Health, Afghanistan

World Health Organization, Tajikistan — World Health Organization, Afghanistan

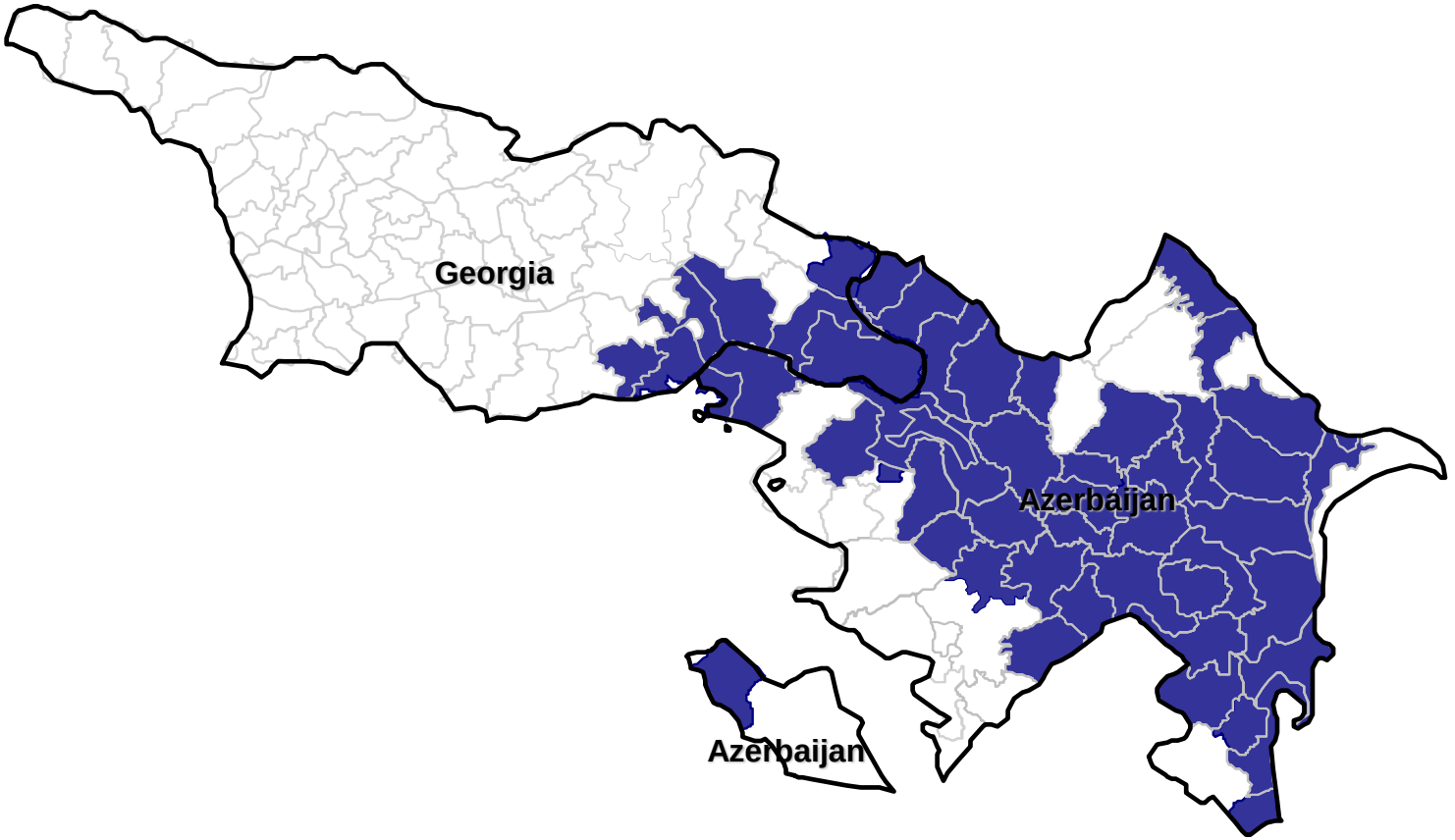
The Global Fund, Tajikistan — The Global Fund, Afghanistan

TEBLA MEZEMIR
UNDP TAJIKISTAN
GFATM PROGRAM
MANAGER.

Kurgan-Tube, 13 October 2010

REGIONAL OFFI

2004



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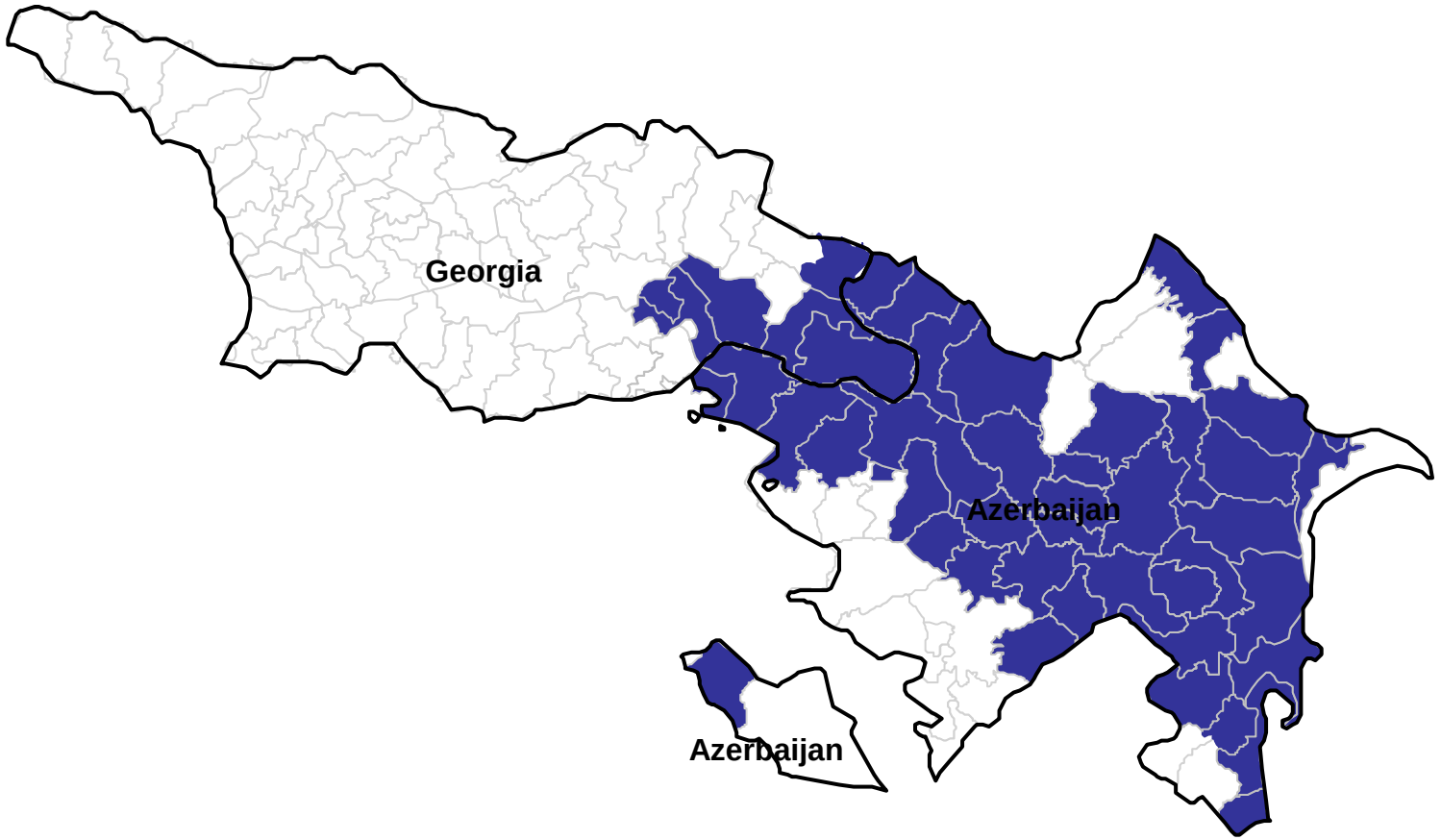

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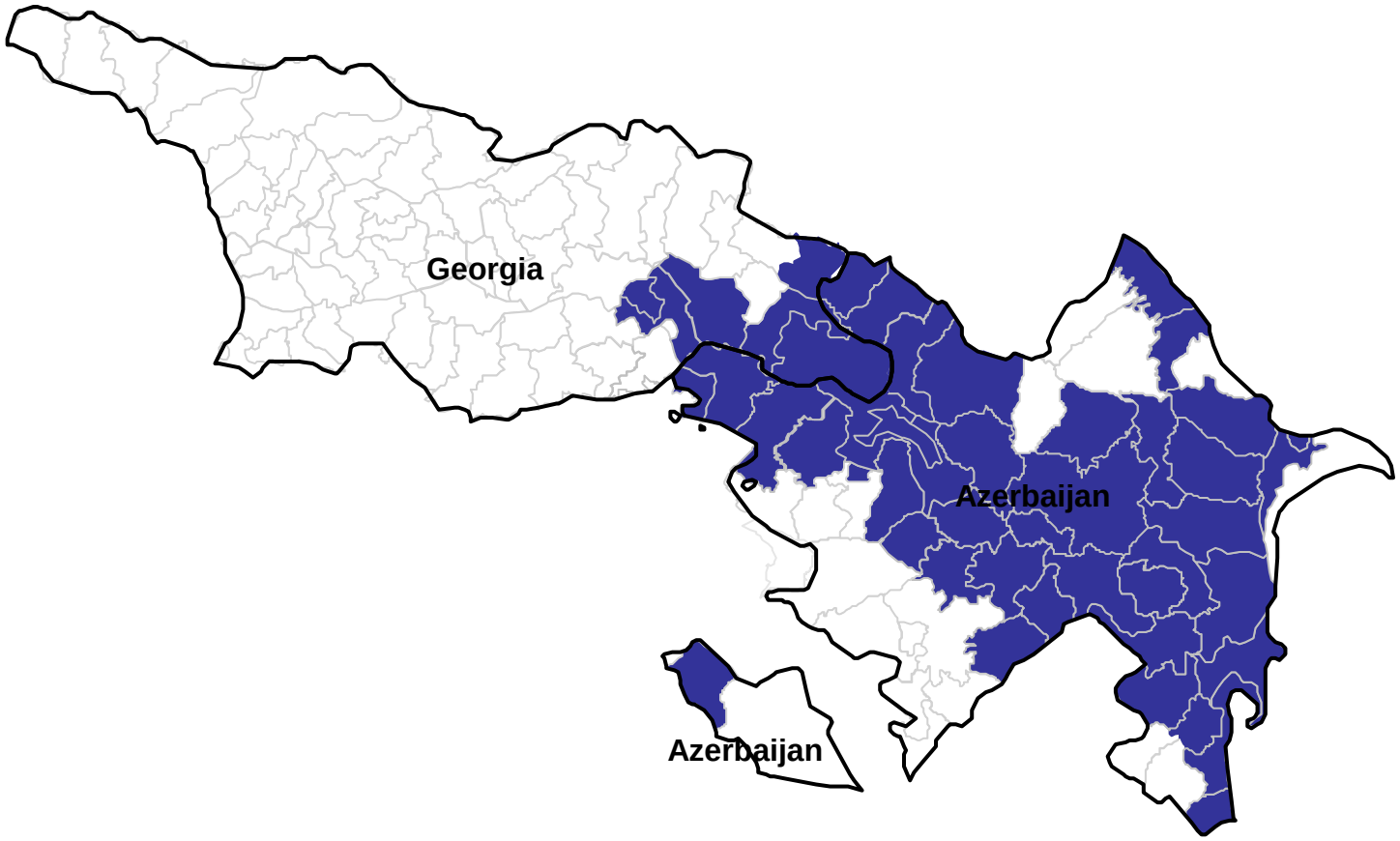

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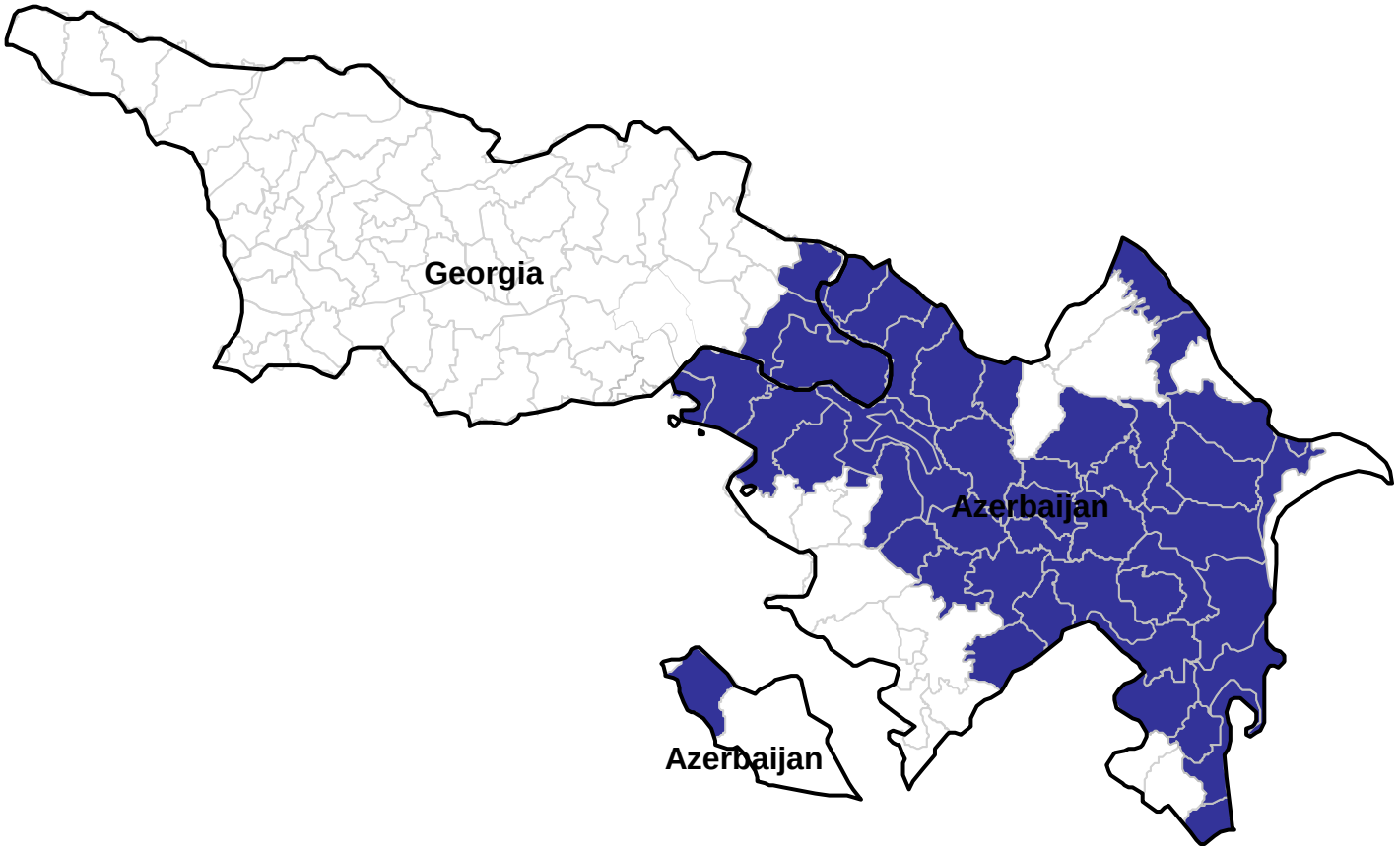

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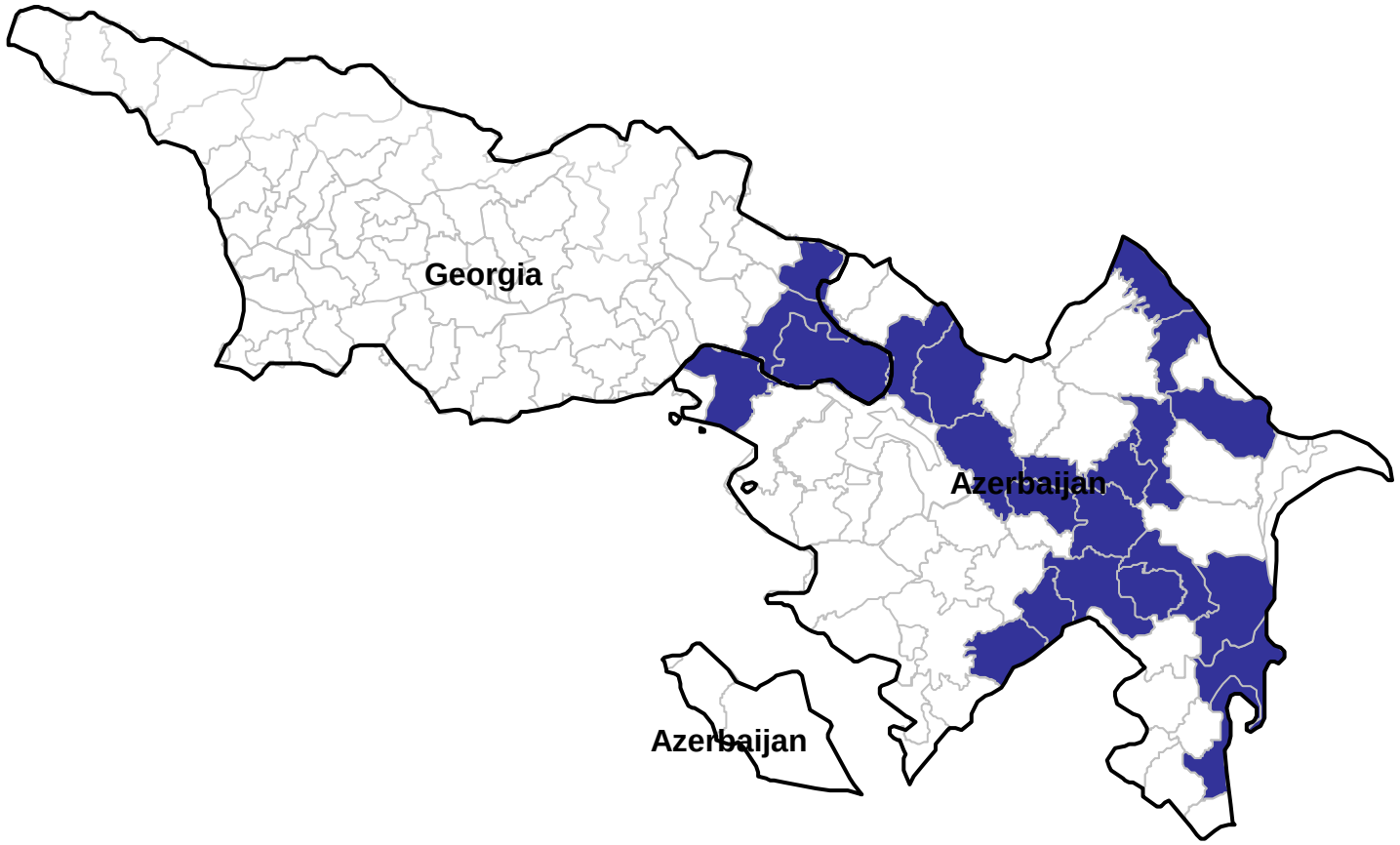

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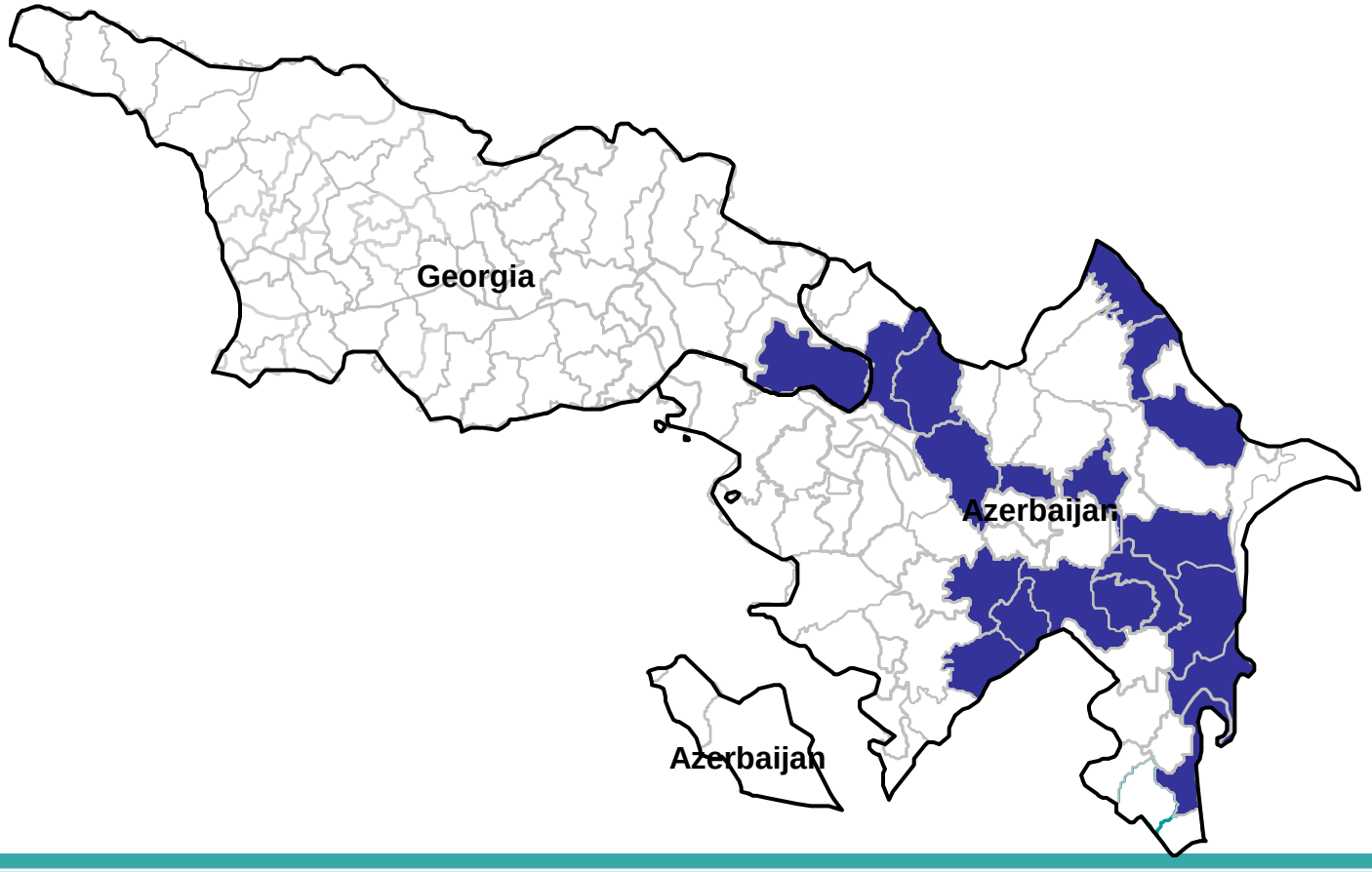

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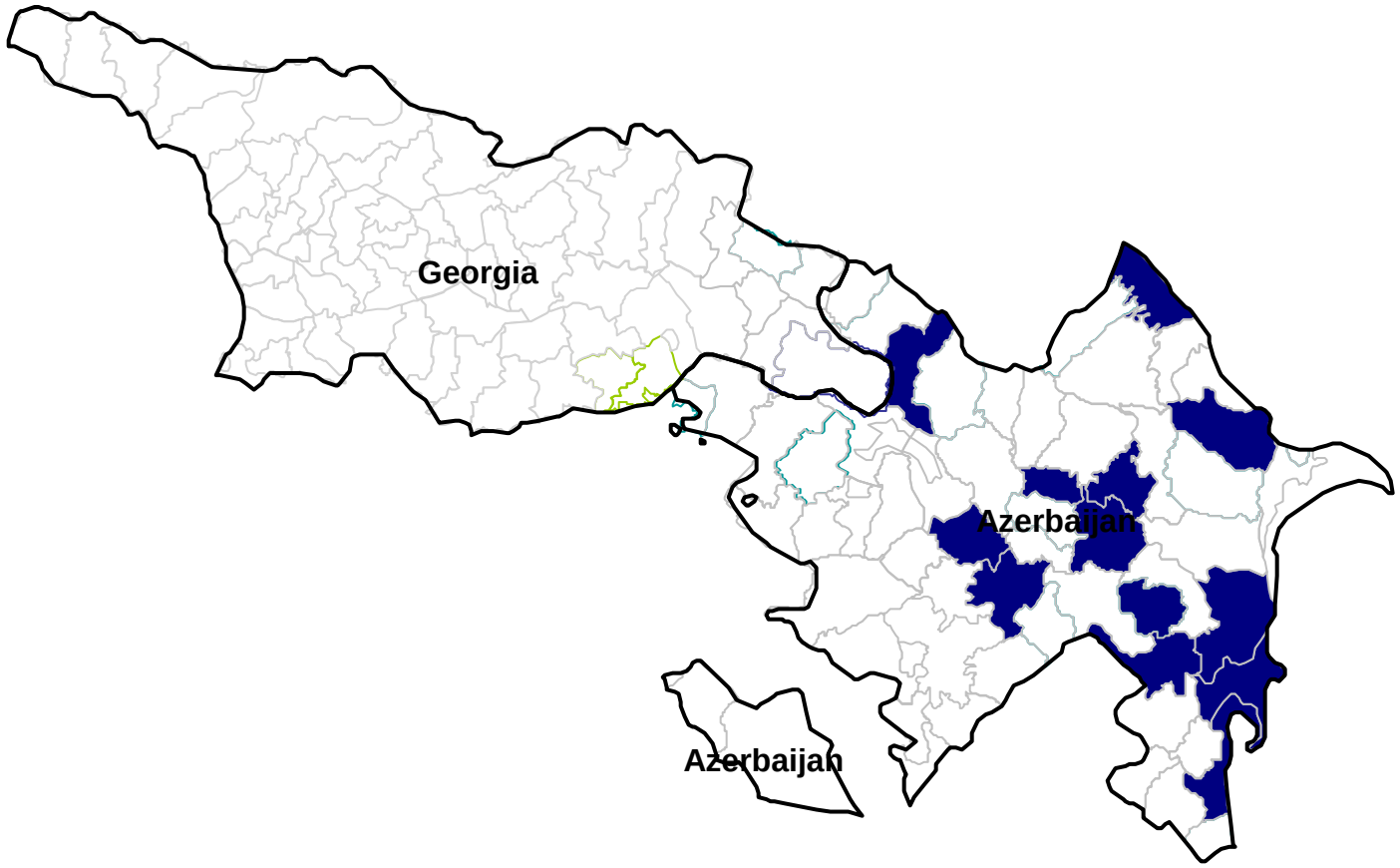
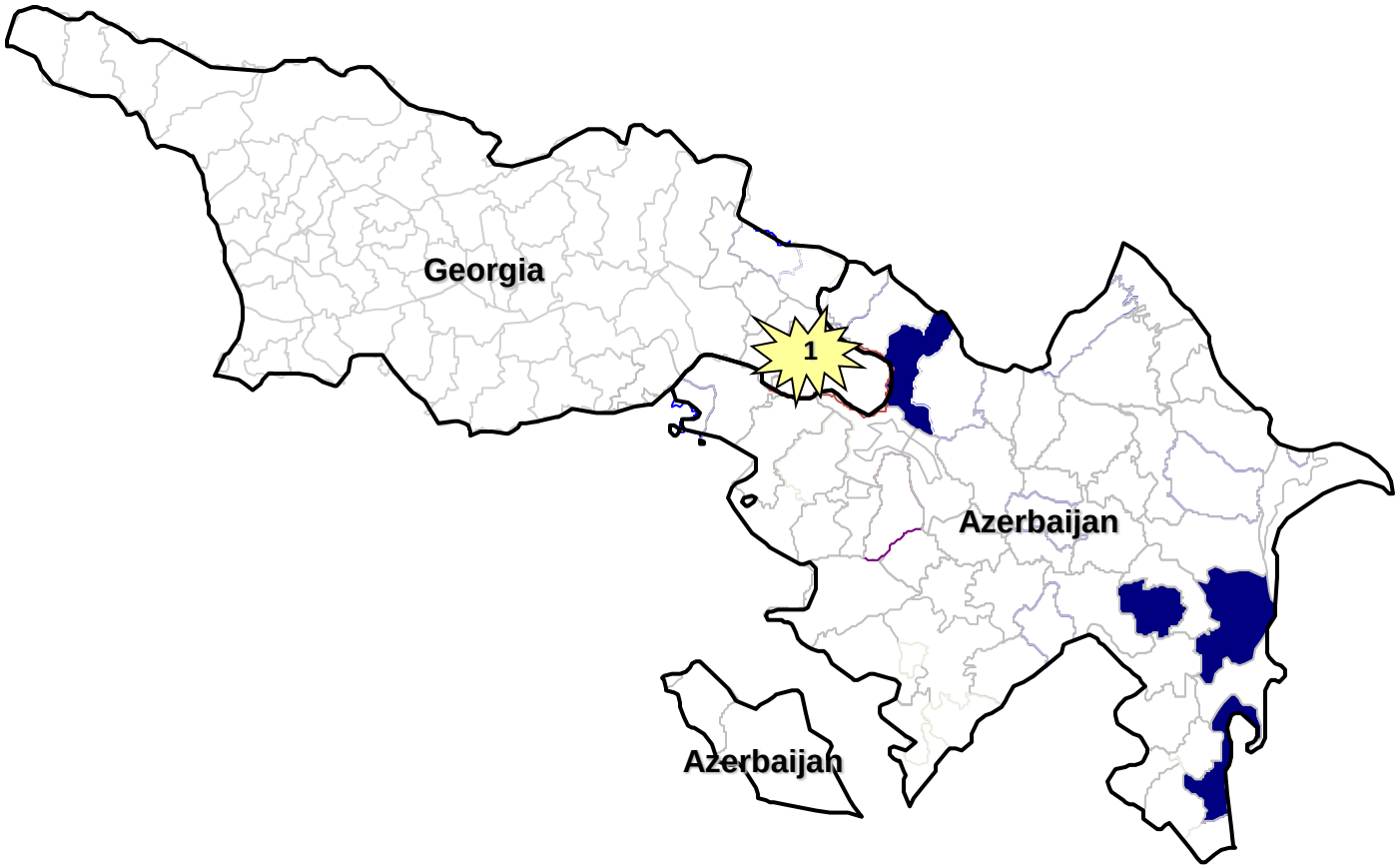


2011



2012

2013

Risk of reintroduction

-Tajikistan

Border with Afghanistan

-Turkey

Refugees

Challenges

-Political commitment

High Level Consultation on Prevention of Malaria Reintroduction in the WHO European Region, 22-23 February 2016, Ashgabat, Turkmenistan

-Funding

-Vigilance

Thank for attention

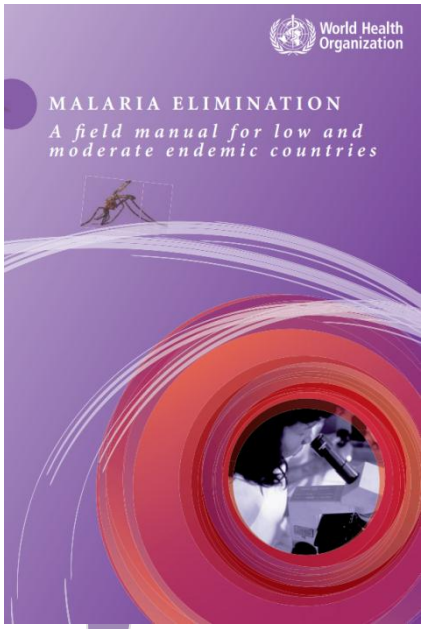
GLOBAL MALARIA PROGRAMME

World Health Organization

Guidance on malaria elimination in the context of the Global Technical Strategy for Malaria (2016-2030)

Malaria Policy Advisory Committee
Geneva, Switzerland
16-18 September 2015

Rationale for ERG on field manual for malaria elimination



- The malaria landscape has changed dramatically since 2007
  - Increased funding for malaria programme activities
  - Large-scale implementation of malaria interventions
  - Impressive reductions in malaria burden
  - Increasing number of countries eliminating or considering elimination of malaria
  - Changes in policy recommendations and available tools
  - Development of new Global Technical Strategy for Malaria 2016-2030

2015–2016

Need to update the manual to reflect these changes

WHO malaria policy changes and reviews since 2007

Policy changes since 2007

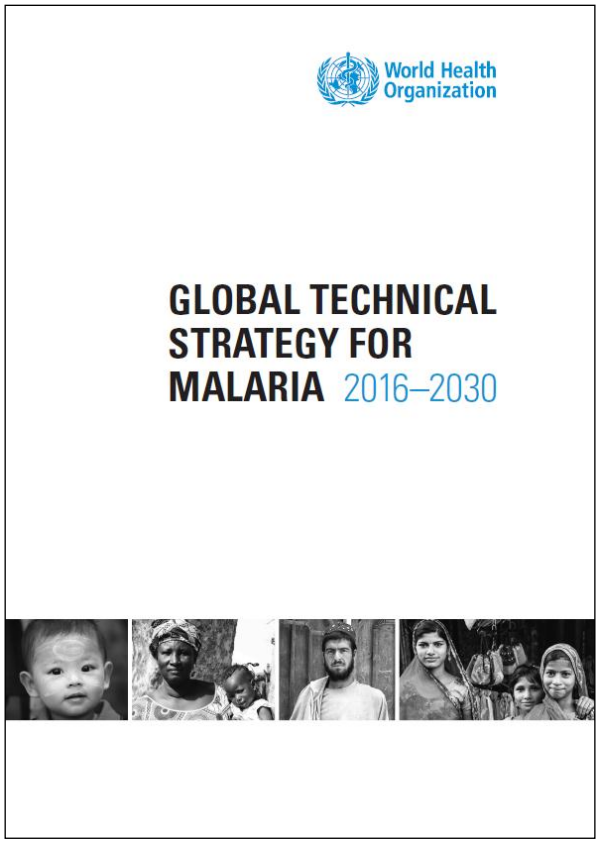
- Universal bednet coverage
- Universal testing
- Treatment with primaquine

Policies recently reviewed

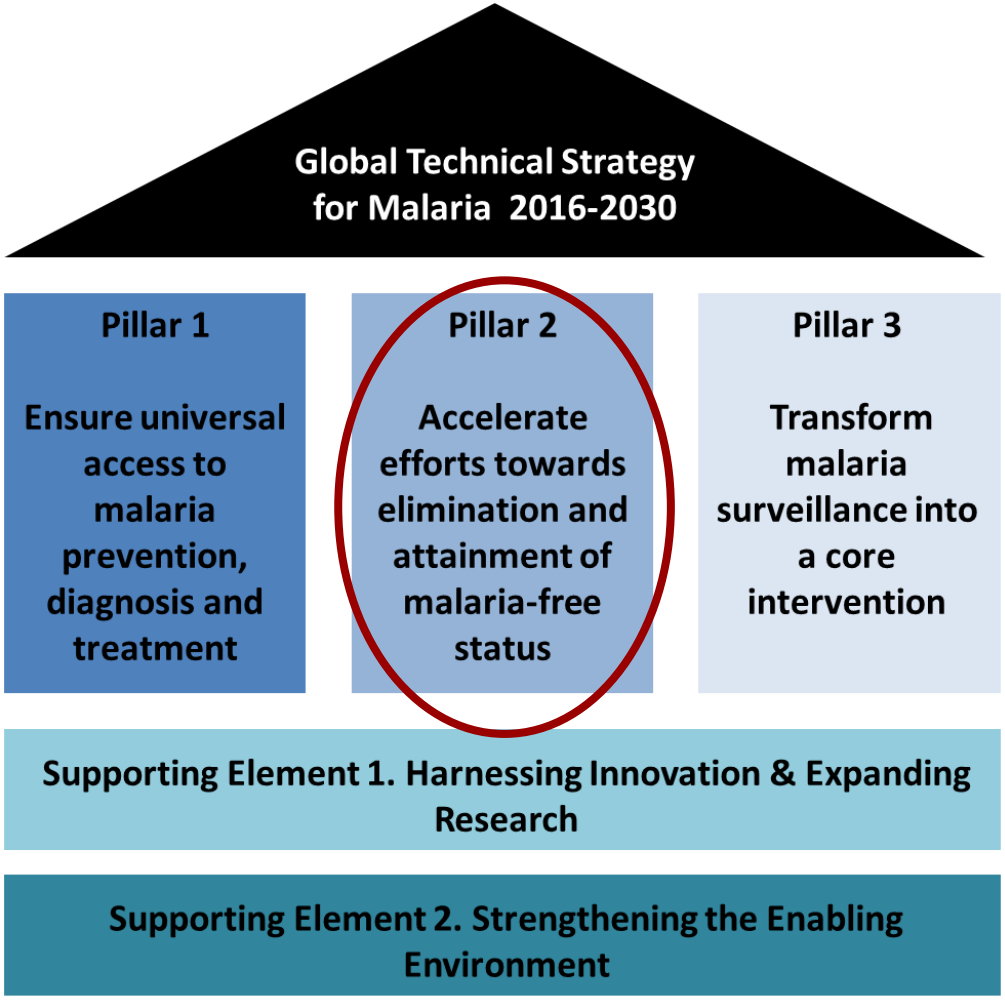
- Molecular testing methods
- Mass drug administration
- Malaria treatment guidelines
- *P. vivax* strategy

Global Technical Strategy for Malaria developed with five principles in mind

1. **All countries can accelerate** efforts towards elimination through combinations of interventions tailored to local contexts.
2. **Country ownership and leadership**, with involvement and participation of communities, are essential to accelerating progress through a multisectoral approach.
3. **Improved surveillance, monitoring and evaluation**, as well as **stratification** by malaria disease burden, are required to optimize the implementation of malaria interventions.
4. **Equity in access to services** especially for the most vulnerable and hard-to-reach populations is essential.
5. **Innovation in tools and implementation approaches** will enable countries to maximize their progression along the path to elimination.



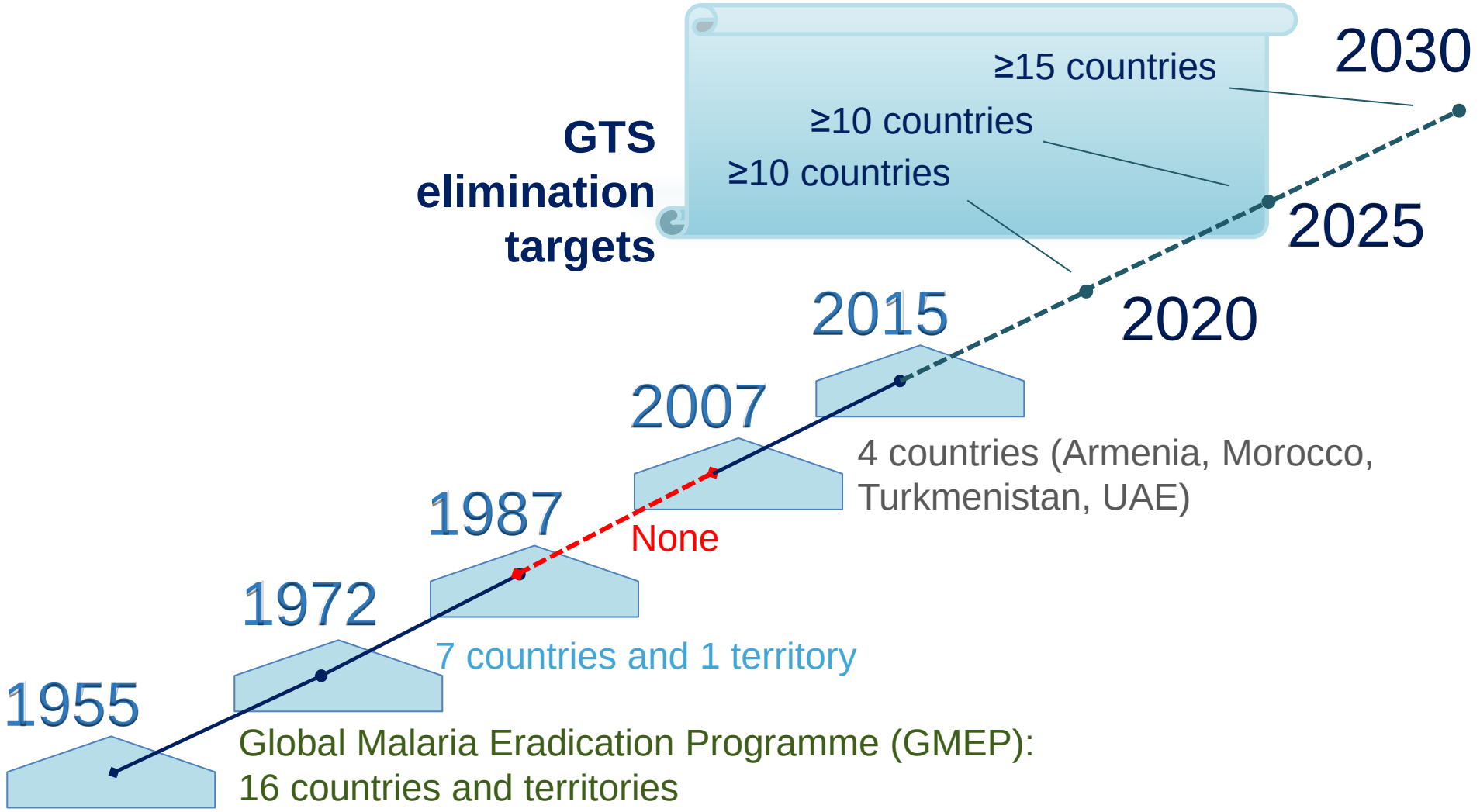
Malaria elimination reflected in GTS structure, pillars and supporting elements



Malaria elimination reflected in 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

Number of countries certified malaria-free by WHO to 2015

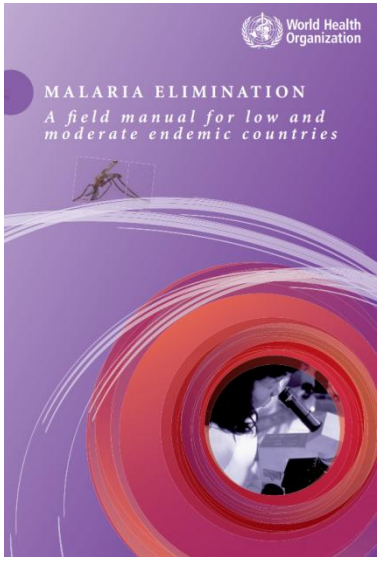


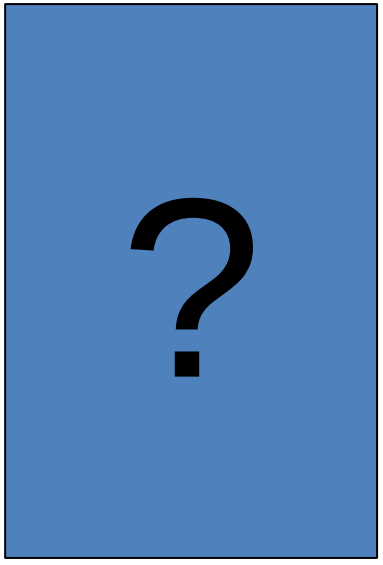
Process and timelines for the development of new guidance on malaria elimination

Evidence Review Group (ERG) objective

- Update the Malaria Elimination guidance to cover all epidemiological settings, and provide comprehensive and relevant guidance in the new malaria landscape, in line with the mandate of the Global Technical Strategy for Malaria 2016-2030.

2007 → 2016





ERG establishment and membership, June-July 2015

- Results from a wide consultative process led by the GMP Director and the malaria advisors in the Americas and Eastern Mediterranean regions, with inputs from other coordinators and advisors in HQ/WHO regions

- **13 experts outside WHO:**

  - representing the wide range of malaria control/elimination stakeholders and all malaria-endemic regions, and covering key disciplines, expertise, and experience related to elimination of malaria and other vector-borne diseases at national and sub-national levels;

  - knowledgeable of critical areas of work relevant for the development of new elimination guidance are covered: malaria certification processes and key technical and intervention areas, namely epidemiology, entomology, vector control, drug/insecticide resistance and surveillance.

ERG members

- Dr Majed Al-Zadjali, Department of malaria, MoH, Oman
- Dr Graham Brown, Nossal Institute for Global Health
- Pr Tom Burkot, James Cook University
- Dr Justin Cohen, CHAI
- Dr Mikhail Ejov, independent consultant
- Dr Gao Qi, Jiangsu Institute of Parasitic Diseases
- Dr Rossitza Mintcheva-Kurdova, independent consultant
- Dr Bruno Moonen, Bill & Melinda Gates Foundation
- Dr Frank Richards, The Carter Center
- Pr Christophe Rogier, Pasteur Institute of Madagascar
- Dr Allan Schapira, independent consultant
- Pr Robert Snow, KEMRI Wellcome Trust Research Programme
- Dr Rick Steketee, PATH-MACEPA

Process for development of new guidance (June 2015-Dec 2016)

- Deep dive into the manual
- Consensus on the gaps and suggested changes
- Outline of new guidance and each chapter
- Focal point to coordinate the process of collecting revised sections and compiling inputs

Prep. work

Experts to develop working papers, conduct in-depth search, review papers/collect historical experience. Consultant/partner to consolidate

1st ERG meeting New Delhi

July-Aug 2015

2nd ERG meeting Montreux

Dec 2015

Review of the draft guidance

- Draft guidance to be sent to all partners and stakeholders for review and input
- Discussion at regional meeting with programme managers

MPAC presentation and finalization

3rd ERG meeting Geneva

Sept 2016

- Production & publishing

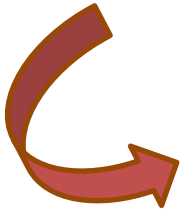
Dec 2016

Teleconferences between ERG members (as needed) bringing in additional partners as relevant depending on the topics for discussion.

Outcome of the 1st ERG meeting and work underway

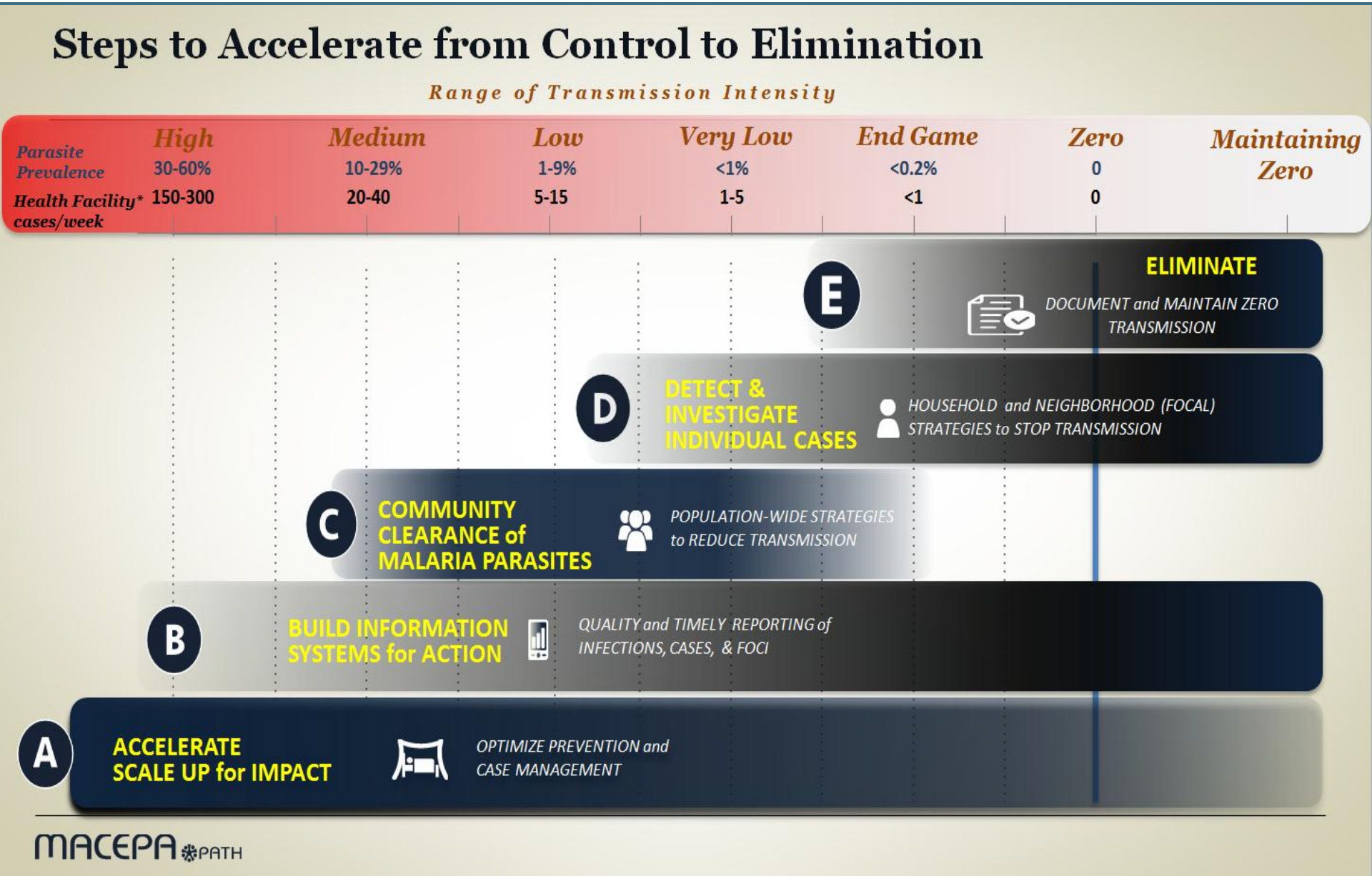
Consensus points for new guidance under development

- **New title**: “Malaria elimination: An operational manual”
- **Audience**: all, but primarily National Malaria Control Programme managers
- **Scope of guidance**: all epidemiological settings as opposed to countries nearing elimination only
- **Focus**: progression of **all** malaria-endemic countries towards elimination in accord with the GTS, moving away from the previous multi-staged / compartmented process from control to elimination.

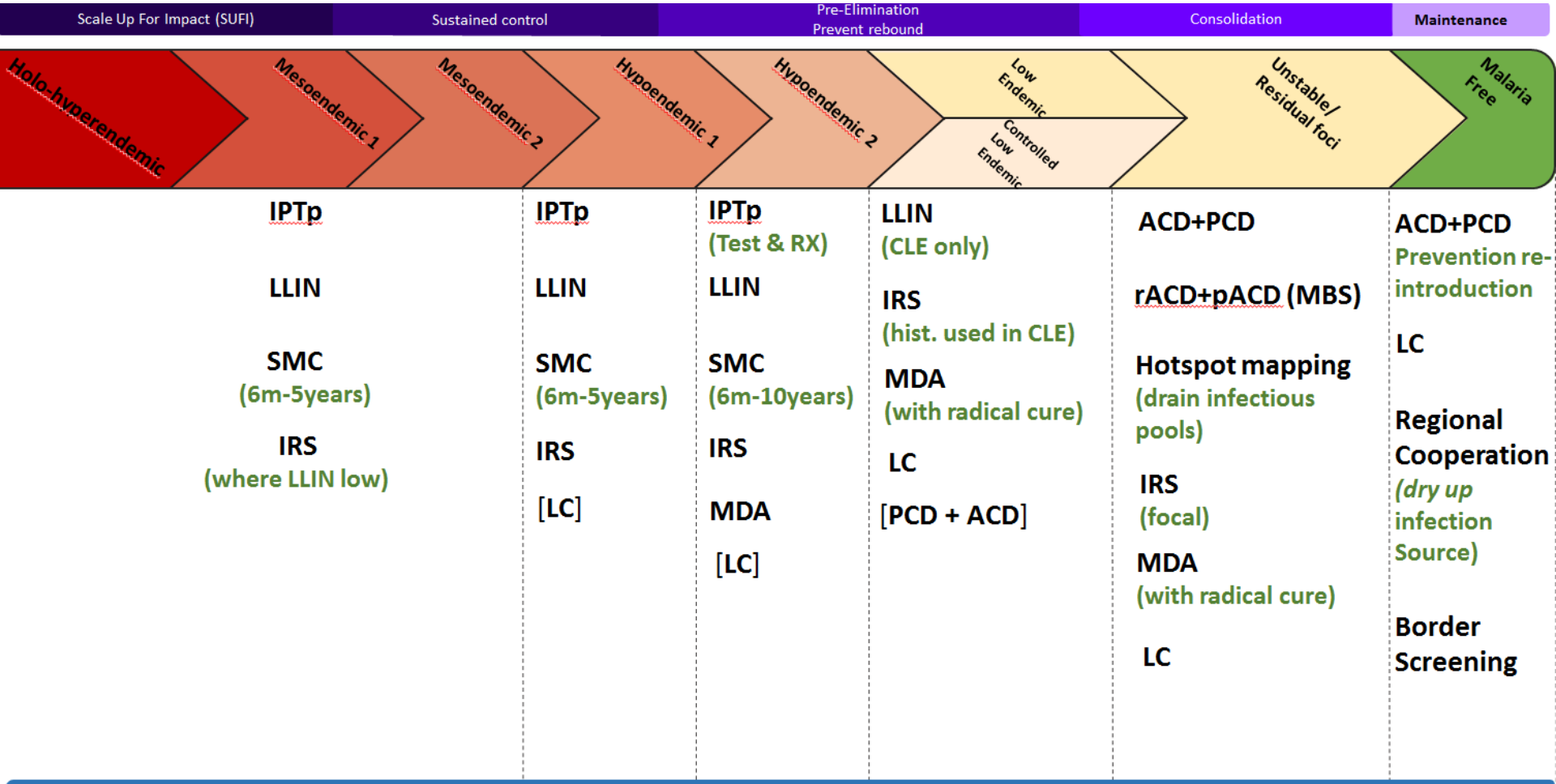


Previous Chapter 2 “Feasibility of malaria elimination” will be renamed (e.g. “Progression towards elimination”) to preclude the “*Go/No Go*” idea behind “Feasibility of…”

Steps of "progression towards malaria elimination" and link with GTS pillars and supporting element 2



Spectrum of interventions for “progression towards malaria elimination” depending on each transmission setting (R. Snow)



New content for guidance on malaria elimination

- New chapter “Innovation and research for elimination” (*GTS supporting element 1. Harnessing innovation and expanding research*).
- New section on subnational elimination of malaria, referred to as Subnational **verification** of malaria elimination (country process) on the way to the WHO-led process of national certification.
- Special situations, lessons learnt from malaria elimination: examples and or boxes will be inserted where appropriate.
- Glossary to be aligned with the malaria elimination / eradication terminology work underway and led by Andrea Bosman (WHO) and Rick Steketee (MACEPA).

Outline of new guidance – sections currently under development or review (1)

- **Introduction:** history of malaria, elimination challenges; scope; audience; current status of elimination; regional & subregional initiatives; GTS continuum; alignment with GTS, *P. vivax* strategy, AIM.
- **Principles of malaria elimination:** from GTS principles; Steps/interventions of progression towards elimination; concept of subnational elimination; focus on multisectoral, cross-cutting issues/enabling elements.
- **Progression towards elimination:** planning and management; elimination scenario planning; milestones; subnational elimination; regulations required for elimination; border malaria, cross-border collaboration and migrant populations.
- **GTS supporting element 1:** Harnessing innovation and expanding research.
- **Approaches for achieving elimination:** expand on principles and link with GTS pillars (1-2-3) and Supporting element 2 required; quality of interventions.

Outline of new guidance – sections currently under development or review (2)

- **M&E progress towards malaria elimination:** monitoring framework for elimination with indicators; present metrics to be used along the continuum; measure to evaluate the strength of surveillance system, response capacity, etc.).
- **Prevention of the re-establishment of malaria transmission:** define and highlight importance of the risk of reintroduction, re-establishment of local transmission at subnational/national level, simplify the issue of receptivity and vulnerability; need for sustained strength of surveillance and response capacity; importance of policy/legislation, annual reporting, training people even when local transmission is interrupted; resurgence).
- **Subnational verification and national certification of malaria elimination:** emphasis on the need to sustain efforts when transmission is interrupted; reporting of subnational and national milestones thru WMR; subnational verification will encourage early documentation efforts for national certification; importance of capacity to prevent outbreaks.
- **Special situations:** lessons learnt from malaria elimination.
- **Glossary aligned with malaria elimination/eradication terminology work**

WHO Malaria Elimination Certification Panel

Certification of malaria eradication - History (1)

- 1960: the World Health Assembly (1960), requested the Director-General to establish an **official register** listing areas where malaria eradication has been achieved, after inspection and verification by a **WHO evaluation team**. *resolution WHA 13.55*
- The guiding principles for WHO's certification procedures published in reports of the **WHO Expert Committees** on Malaria in **1960, 1963, 1973, 1980**.

Certification of malaria eradication – History (2)

- **1990s: certification no longer conducted.**
  - The annual updates of International Travel and Health, provide information on malaria risk areas in endemic countries, or its absence

- **2004:** certification of malaria elimination was re-initiated when the United Arab Emirates officially requested WHO to certify its achievement of malaria elimination.

Weekly epidemiological record, 18 July 2014, No. 29 , 321-336
http://www.who.int/wer

2014, 89, 321-336 No. 29

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record
Relevé épidémiologique hebdomadaire

18 JULY 2014, 89th YEAR / 18 JUILLET 2014, 89e ANNÉE
No. 29, 2014, 89, 321-336
http://www.who.int/wer

Contents

WHO procedures for certification of malaria elimination

Malaria elimination is defined as the reduction to zero of the incidence of infection caused by human malaria parasites[1]

Procédures de l'OMS pour la certification de l'élimination du paludisme

L'élimination du paludisme est définie comme la réduction à zéro, suite à des efforts délibérés, de l'incidence de l'infection causée par les

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[2] Available at http://www.who.int/malaria/publications/world_malaria_report_2012/wmr2012_full_report.pdf; accessed June 2014.

[3] Of note: sub-national validation of achievement of malaria elimination by the Ministry of Health may be an option in decentralized health systems. This process is independent of WHO.

General principles of WHO certification of malaria elimination

- Whole country
- 4 human malaria species - Plasmodium falciparum, *P*. vivax, *P*. *malariae* and *P. ovale*.
- Process managed by WHO (Global Malaria Programme + Regional Office)
- Independent expert assessment teams
- Final decision by WHO's Director-General
- Process initiated after official request from the country

Certification – Proof

The country requesting certification should provide the assessment team with proof that:

- malaria transmission has been interrupted in the country at a given time;
- good-quality surveillance systems are in place, capable of detecting any single case and responding to local transmission, if occurred;
- a programme of preventing re-establishment of transmission is in place.

Current process of certification

- **Official written request** for certification originated from the **MoH** of the Member State to the DGO, with copy to the respective WHO Country and Regional offices.
- **WHO mission**, to assess the chances of certification and if the claim is considered plausible, to prepare a plan of action for the certification procedures.
- The **country prepares the required documentation and a national report**.
- Inspection and evaluation are carried out by an **independent assessment team**, organized by WHO-GMP (review of documentation, field visits).
- The **assessment report** of the inspection team is reviewed by at least 5-10 members of the **WHO Expert Panel on Malaria**.
- The Chair of the most recent **Expert Committee** submits a recommendation to the **WHO Director-General** on whether or not to be certified.
- WHO publishes certification in the **Weekly Epidemiological Record** and announces it during the next World Health Assembly.

Proposal for updating the process of WHO Certification of Elimination

Why an update?

- Policy setting in WHO/GMP has changed.
- Malaria Policy Advisory Committee (MPAC) is the key decision-making body replacing the WHO Expert Committee.
- Global Technical Strategy for Malaria with a key pillar on malaria elimination.
- Suggestion: update certification of malaria elimination process.
- Objective: simplification and harmonization, to be within MPAC role.

Establishment of WHO Malaria Certification Elimination Panel (CEP)

Key roles

- Conduct country missions for country assessment/field observation
- Review the country documentations, validate the national certification report
- Prepare a final evaluation report for country certification with the recommendations, to be submitted to the WHO /MPAC

Elimination Certification Panel - Role and responsibilities (1)

Conduct country assessment/ evaluation missions: consider 2-3 identified members

- Review submitted country documentation and report, discuss content, via video conference, teleconference or face-to-face meetings.
- Review, assess how proposed WHO procedures and criteria implemented to document elimination of malaria transmission. Includes evaluation of the performance of the surveillance system, quality case management etc.
- Verify data and information included in county documentation and report are accurate; includes field visits for validation and evaluation, especially to the latest active malaria foci.
- Review national guidelines and plan of action to ensure strategic technical components and guidelines are up-to-date.
- Collect and review other needed information from meetings with key stakeholders, published/unpublished documents, journal publications, etc.
- Assess the capacity of the Government to maintain the malaria-free status and prevent reestablishment of malaria transmission.
- Prepare evaluation report of the country certification mission and submit to WHO secretariat.

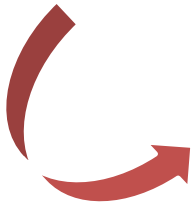
Elimination Certification Panel - Role and responsibilities (2)

- Final review and recommendation: all members of CEP review the evaluation report and agree on the recommendations on certification of malaria elimination or postponing such decisions with details on the extra evidence required to demonstrate that this has occurred.
- Report to WHO/MPAC: the key findings in the evaluation report, with the recommendations for decision-making
- Upon approval by WHO/MPAC, the summary will be forwarded to the Director-General of WHO.
- If the claim of elimination is postponed, WHO will request the country to provide any further evidence needed to certification.

Composition of the Malaria Certification Elimination Panel CEP

- Members appointed by DG, in consultation with relevant WHO/Regional Offices
- The appointment for at least 3 years, with possibility of renewal,
- The composition may include up to 8 members and formal chairperson
- Members should have knowledge and skills on elimination of malaria, with at least one of them is as entomologist

  (may cover various fields, such as tropical medicine, laboratory science, epidemiology, vector biology/control, information system, other public health specialists).
- Should provide independent opinion and have no conflict of interest
- Those going for assessment/evaluation mission should not be citizen of the applicant country, should not have provided recent support to the country in reviewing it malaria programme, not involved in developing the country certification report



Members yet to be nominated

MPAC (Sept 2013)

- Documentation of certification of elimination refers to the whole country while verification/or validation of malaria elimination can be in an area inside the country and is national responsibility.
- National verification committee can be established

Malaria Policy Advisory Committee Meeting

16–18 September 2015, Geneva, Switzerland
Background document for Session 3

Innovation to Impact – WHO change plan for strengthening innovation, quality and use of vector-control tools

August 2015, Geneva, Switzerland

1 Introduction

Vector control can play an important role in reducing the transmission of malaria and major vector-borne neglected tropical diseases (NTDs) such as dengue, chikungunya, Chagas disease, lymphatic filariasis, visceral leishmaniasis, human African trypanosomiasis and schistosomiasis. Effective vector-control strategies have been pivotal in reducing worldwide mortality and morbidity from vector-borne disease. Over the past decade, the main vector-control tools that contributed to a reduction in malaria morbidity and mortality were pesticides and pesticide products. However, the later part of the 20th century has seen an expansion of areas with insecticide resistance in malaria vectors, coupled with low investment in development of public health pesticides; hence, there is currently a dearth of effective vector-control products.

WHO has recognized the need to change current systems to support the development, evaluation and appropriate use of new tools for vector control, and to manage pesticides throughout their life-cycle, to maximize their impact on disease and reduce risks to humans and the environment. Catalytic funding support is required to drive the change to strengthen innovation, assure quality and promote low-risk and judicious use of vector-control products. WHO has therefore recently submitted a funding proposal to the Bill & Melinda Gates Foundation to seek support for such a project.

The project proposes ambitious changes to improve the systems for vector-control product evaluation and quality, strengthen normative and technical guidance, and facilitate synergies and collaboration among the WHO Member States and other partners. The system developed will help to expedite the availability of effective, safe, high-quality and innovative vector-control tools, as well as guidance for their appropriate operational use and regulation. The project will also help to create conditions for greater investment in the development of new public health pesticides and their judicious use within an overall context of integrated vector management. Considering that vector control will constitute 50–60% of all investments required to eliminate and control malaria and NTDs from now until 2030, the project will help to catalyse the reforms required to meet future technical needs. Accelerated availability of innovative high-quality vector-control products, along with improved guidance on appropriate use, will greatly reduce the transmission of vector-borne diseases.

1.1 Background

Since 1960, the WHO Pesticide Evaluation Scheme (WHOPES) has been the primary global mechanism for assessing the efficacy and safety of pesticides for use in public health and in setting quality standards. WHOPES was established by the World Health Assembly with the

WHO/HTM/GMP/MPAC/2015.14

purpose of facilitating evaluation of pesticides and pesticide products for vector control, and providing guidance and setting policies for their sound use in public health. Today, WHOPES recommendations are relied on by Member States and by international procurers of pesticides and pesticide-related products.

WHOPES provides the following range of functions and activities:

- testing and evaluation of pesticides and pesticide products for public health, with the aim of facilitating their acceptance, national registration and use by Member States;
- normative functions such as setting norms and standards for the evaluation and use of pesticides and pesticide-related products, and promoting and monitoring their judicious use in various settings;
- technical support for vector-control policies and strategies, operational guidance, monitoring global insecticide use, building institutional capacity, and disseminating valuable knowledge; and
- policy for pesticide and pesticide-related products used in a public health context.

WHOPES facilitates testing of pesticides within established product categories – long-lasting insecticide-treated nets, indoor residual spraying, larvicides, space sprays and so on – whose public health impact is already accepted.

In 2013, WHO established a Vector Control Advisory Committee (VCAG) to assess the public health value of new paradigms (i.e. innovative concepts) of vector control, and shepherd the development of tools that represent these new paradigms. VCAG and its process for new paradigms are designed to provide WHO with broad recommendations on whether certain forms of vector control can affect disease transmission. The group is structured to guide prospective innovators of new paradigms to generate required data in the best, most scientifically robust and cost-effective way possible. VCAG is a normative activity jointly managed by the WHO Global Malaria Programme (GMP) and the WHO Department of Control of NTDs.

In recent years, the stakeholder community has expressed interest in collaborating further with WHO to accelerate the availability of vector-control tools to meet contemporary and future needs.

1.2 The need for reform

Increasing insecticide resistance, rapidly expanding arboviral diseases and the impact of climate change on vector distribution threaten to thwart the global gains in control of vector-borne diseases. New tools and strategies are needed to respond to these challenges; in particular, innovative products that can safely and effectively target key transmission settings (e.g. outdoor transmission, areas of high resistance and high-risk populations) and effective use strategies. WHO recognizes the need for reforms in evaluation of innovative tools; system quality; evaluation of vector control; and timely development of normative guidance to strengthen innovation, availability, quality and best use of vector-control tools for public health.

Several key areas have been identified for improvement:

- shorten timelines to bring products to market;
- increase transparency and improve communication with stakeholders;
- streamline product-evaluation processes to comply with ongoing practice in medicines, vaccines and diagnostics (under the WHO Prequalification programme);
- include pre- and post-marketing quality assurance (QA); and

- facilitate registration, quality control (QC) and sound management of pesticides by working with national authorities.

2 The process of change and internal coordination

Over the past 6 months, WHO has been detailing its plans to improve current systems and procedures for pesticide evaluation, and to strengthen vector-control normative functions. These activities are part of a larger *Innovation to Impact Initiative* (I2I), which is supported by the Bill & Melinda Gates Foundation. The main aim of I2I is to encourage the development of innovative, effective and high-quality products for vector control. I2I is part of a larger goal to eliminate and eradicate malaria and NTDs by engaging many stakeholders in vector control, including industry, procurement agencies, regulatory bodies and WHO.

Within WHO, the senior leadership has been highly supportive of the restructuring of vector-control evaluation processes and the strengthening of normative vector control. Changes to WHOPES will be part of a broader package of collaboration between NTD, the WHO Vector Ecology and Management (VEM) unit, the GMP, the Entomology and Vector Control (EVC) unit, and the Regulation of Medicines and other Health Technologies (RHT)/Prequalification Team (PQT).[1]

2.1 Approach

Over a transition period that will end in December 2018, WHO will implement a series of reforms leading to key outcomes for which the three departments (NTD, VEM and GMP, EVC) have agreed on division of functions. The key outcomes, discussed below, are:

- driving innovation in public health vector control;
- accelerating the availability of vector-control products;
- improving the quality of vector-control products;
- increasing the appropriate use of vector-control products; and
- developing a sustainability plan.

2.1.1 Driving innovation in public health vector control

To address the great need for innovative vector-control products, WHO will work to foster a product development environment that supports innovation by:

- developing a network of test sites that are accredited for good laboratory practice/good experimental practice, and that can be used to generate quality-assured data for WHO to evaluate – this will shift data generation to manufacturers;
- reviewing the existing technical criteria for equivalency for evaluation of generic products; and
- optimizing processes for assessing new vector-control paradigms (via VCAG).

WHO oversight will involve a variety of factors, including:

- pre-submission guidance;
- prior agreement on trial site selection, to ensure that field trials are representative of product claims and geographical diversity factors (related to diverse vectors, seasonality and other entomological requirements);

1. The prequalification programme is abbreviated as PQ or RHT/PQ within text

- protocol review and agreement before trial initiation, to align with WHO guidelines and harmonize across sites;
- monitoring of agreed timelines;
- trial site inspections, where technically necessary; and
- further site capacity development to meet new or revised needs.

2.1.2 Accelerating the availability of vector-control products

The goal defined by WHO within this grant proposal is to align and integrate pesticide evaluation in RHT/PQ by the end of 2016, while maintaining strong links with other important functions such as setting norms and standards, and life-cycle pesticide management. During the transition period, product-evaluation functions will continue to be managed by WHOPES, but PQ will build internal capacity to fully take over these functions. Therefore, the current structure of WHOPES will be maintained in the interim period between the current and end states. However, reforms will be made to current evaluation processes, to improve efficiency and transparency and to accelerate the availability of vector-control products on the market, aligned with best practices within RHT/PQ. Key reforms proposed include:

- formalizing procedures for product testing and evaluation during the transition period;
- formalizing pre-submission guidance for manufacturers to align on data and testing requirements;
- implementing a "clock-stops" mechanism[2] and real-time tracking of progress on product evaluation; and
- recruiting an expanded pool of independent experts to review efficacy, safety and quality data for public health pesticide products, and to make recommendations as needed.

2.1.3 Improving the quality of vector-control products

To ensure that WHO-recommended pesticides are of high quality, the PQ will develop a pre-marketing QA system analogous to that used for medicines and similar products. This will involve factory inspections to improve the manufacturing processes and development of QA systems. NTD/GMP will initiate measures to improve post-marketing quality management through situational analyses of post-marketing QC regulatory practices in 10 priority countries (1–2 per region, including major procurers of public health pesticides and countries with poor-quality management systems). Additionally, in collaboration with PQ, an assessment of best practices in quality management for other product streams will be undertaken, looking at stringent regulatory authorities (Australia, Canada, Europe, Japan and the United States). Measures taken to strengthen post-marketing quality management will include:

- developing guidelines and training documents for regulators on post-marketing quality management; and
- conducting regional policy workshops for capacity-building in this area.

Also, as a joint activity of NTD/PQ and GMP, meetings will be held with global and national procurement agencies to encourage the development of coordinated quality tracking systems, which can then feed into PQ quality management systems once developed, which in turn may be linked with product evaluation and listing, as defined by PQ.

2. This refers to calculating exact time taken by the industry and WHO for assessment of a product, including time taken to respond to a request for particular information.

2.1.4 Increasing appropriate use of vector-control products

The following normative, technical and strategic functions will be enhanced:

- supporting insecticide resistance monitoring and management for vectors of NTDs and malaria through capacity building of control programmes and operational guidance;
- normative guidance supporting pesticide product evaluation (efficacy, safety and quality);
- normative and technical guidance support for judicious and appropriate use of product through implementation of integrated vector management and through situational targeting; and
- building national regulatory capacity for the sound management of public health pesticides, including registration, and regulatory practices, according to the *International Code of Conduct on Pesticide Management*.[3]

2.1.5 Developing a sustainability plan

A final outcome of the project will be the development of sustainable systems supporting activities from NTD/GMP (normative, technical and strategic) and RHT/PQ (evaluation) related to vector control, with reduced need for donor funding. Strong governance will ensure that the proposed activities are implemented effectively. A joint project management committee of NTD, GMP and PQ will ensure close collaboration across departments for the project, which will be especially important for developing new systems for pesticide product evaluation within WHO.

2.2 Overall impact

Through these changes, WHO aims to support the development, evaluation, QC, adoption and sound management of pesticides and their products for the control and elimination of vector-borne diseases.

Vector-control product manufacturers will benefit from faster, clearer and more transparent vector-control product-evaluation systems, including a new and independent evaluation review process, control over data generation and priority given to innovative products with stronger pre-submission guidance support to manufacturers. The aim would be rapid evaluation of completed dossiers and subsequent normative guidance on use of new paradigm products. Evaluation functions will move to RHT/PQ to be aligned with evaluation of other product streams in WHO by the end of 2016.

National regulatory authorities will benefit from a more transparent global evaluation system in support of countries and regional systems, and stronger support for national registration through more transparent global evaluation. Additionally, increased support and guidance on registration, capacity strengthening and QC will be provided.

Procurement sectors will benefit from a larger array of products and strengthened development of normative guidance for deployment of innovative tools. This is expected to include more efficient evaluation, to enable innovative tools to be available faster for procurers, as well as timely and strengthened development of normative guidance for innovative tools and new product categories.

WHO Member States will benefit from decreased incidence of vector-borne disease because of the availability of high-quality and effective products in the field, and strong normative support to monitor and manage insecticide resistance and manage pesticides over their life cycle.

3. Available at: http://who.int/whopes/resources/en/

3 Conclusions

Effective vector-control strategies have been pivotal in reducing worldwide mortality and morbidity from vector-borne diseases. Despite these gains, such diseases continue to be a leading cause of mortality and morbidity across sub-Saharan Africa, Asia and other regions. Also, the NTDs such as dengue are continuing to cause outbreaks, and have emerged as the most prevalent vector-borne diseases in several countries of South-east Asia and Latin America. New innovative tools and methodologies are needed to confront challenges such as increasing insecticide resistance across vectors; outdoor transmission; impact of global climate change; and the rising incidence of dengue, chikungunya and other arboviral diseases. WHO has initiated ambitious reforms in response to the needs of the vector-control community and within the broader context of the I2I initiative. This proposal details WHO change plans to foster a greater drive for development of innovative high-quality products, and efficient evaluation and QC systems supported by normative guidance and technical guidance, with the aim of moving towards effective evidence-based use, regulation and life-cycle management of products in the field. This investment will help to:

- develop global capacity to evaluate and efficiently manage vector-control tools; and
- strengthen health systems in:
    - monitoring the impact of interventions and environmental changes; and
    - developing guidance for entomological surveillance during the post-elimination phase of all vector-borne diseases.

GLOBAL MALARIA PROGRAMME

World Health Organization

Innovation to Impact – WHO change plan on evaluation of pesticides

Malaria Policy Advisory Committee
Geneva, Switzerland
16-18 September 2015

Raman Velayudhan and Abraham Mnzava

WHO leadership is strongly committed to vector control reform

WHO has initiated ambitious reforms in response to needs of vector control community

- WHO **recognizes the need for reforms** regarding evaluation of innovative tools, improving quality in the system, standardized vector control evaluation and timely development of normative guidance, etc.
- To support the development, evaluation, quality control, adoption, and sound management of pesticides, **an initial change plan was presented at last Stakeholder Convening** in Feb and June 2015.
- Since then, **WHO has been detailing its plans to reform** evaluation systems and procedures, and to strengthen vector control normative functions
- Plan shown today is the **result of joint work across several WHO teams** relevant to vector control (NTD and GMP) and prequalification (PQ/HSI)

WHO leadership clearly expressed full support of this change

Quotes from selected members of WHO leadership

"A global health agenda that gives higher priority to vector control could save many lives and avert much suffering."

"I fully support this WHO vector control change and am looking forward to see significant progress by the end of 2016 and celebrate success in 2017."

Margaret Chan,
Director-General WHO

"I2I is a really important vector control reform, in line with WHO reforms for drugs, vaccines and diagnostics."

Marie-Paule Kieny,
Assistant Director-General for Health Systems and Innovation

Background : WHO PESTICIDE EVALUATION SCHEME (WHOPES)

WHOPES provides the following range of functions and activities:

1. **testing and evaluation of pesticides and pesticide products for public health, with the aim of facilitating their acceptance, national registration and use by Member States;**

2. **normative functions such as setting norms and standards for the evaluation and use of pesticides and pesticide-related products, and promoting and monitoring their judicious use in various settings;**

3. **technical support for vector-control policies and strategies, operational guidance, monitoring global insecticide use, building institutional capacity, and disseminating valuable knowledge; and**
4. **policy for pesticide and pesticide-related products used in a public health context.**

Key areas for improvement

Several key areas have been identified for improvement:

- **shorten timelines to bring products to market;**
- **increase transparency and improve communication with stakeholders;**
- **streamline product-evaluation processes to comply with ongoing practice in medicines, vaccines and diagnostics (under the WHO Prequalification programme);**
- **include pre- and post-marketing quality assurance (QA); and**
- **facilitate registration, quality control (QC) and sound management of pesticides by working with national authorities.**

WHO reform aims to deliver 4 primary outcomes

1. **Stimulate development of more innovative products**
   Increased drive for innovation in development of vector control products for public health

2. **Accelerate availability of vector control products**
   Improved efficiency and transparency of WHO vector control evaluation process

3. **Improve quality of vector control products**
   Enhanced quality management by WHO for vector control products across the system

4. **Increased appropriate use of innovative vector control interventions**
   Strengthened normative guidance functions

Target system will ensure effective, safe, high quality and innovative vector control tools

WHO will reinforce several areas of vector control and build additional capabilities to achieve these outcomes

1 Stimulate development of more innovative products	2 Accelerate availability of vector control products	3 Improve quality of vector control products	4 Increased appropriate use of innovative vector control interventions
A Trial data generated by manufacturers	Provided specific systematic pre-submission guidance	E Standards, team and process in place to conduct pre-marketing manufacturing site inspections	Facilitated insecticide resistance monitoring and management
Established network of sufficient GLP sites	D Reduced time required for dossier evaluation to < 100 days		F Enhanced evidence-based normative guidance available
B Reviewed technical criteria for equivalents	Increased transparency to allow tracking of evaluation progress	Standards, team and process in place to conduct post-marketing QA and manage complaints from procurers and countries	Assisted countries in implementing IVM strategies
Optimized evaluation of public health value of new paradigms	Pesticide evaluation system harmonized to WHO-PQ		Strengthened countries in pesticide life cycle management, including effective registration processes and insecticide resistance management
C Revised review committee procedures and composition to maintain independence			

X *Details on following slides*

Note: Does not reflect all proposed changes

Context for shifting data generation to manufacturers

WHO has agreed to move the generation and ownership[1] of testing data to manufacturers

As a result, WHO together with IVCC will help build an infrastructure of GLP sites

- That would guarantee high quality data and provide confidence in testing quality

Building this infrastructure will take time, so WHO has developed a transition plan

- To start shifting data generation to manufacturers with stringent WHO oversight during the testing
- And to allow GLP sites to be used as soon as they become available

1. Ownership will not reside with WHO anymore, it will be a manufacturer/testing site discussion

World Health Organization

Rationale and approach of reviewing equivalency

Rationale:

Need to review criteria of equivalency in vector control product evaluation

WHO to organize technical consultation with a broad range of experts and the goal to review and align on technical criteria for equivalency for vector control tools

Approach for reviewing equivalency:

Determine reason for issue

- At last I2I convening, all stakeholders recognized that this is a technical issue that can be solved by technical experts
- WHO has started to collect the technical issues that manufacturers see in the current criteria of evaluation process

Organize technical consultation

- WHO will hold expert consultation to review technical criteria for equivalency
- Criteria is different for each type of health product and is an area where expertise from other health fields can also be leveraged (e.g., from drugs, vaccines, diagnostics)

Review criteria

- Equivalency determined according to agreed upon criteria
- Technical criteria for equivalency revised if/as necessary

World Health Organization

New evaluation process, operating model and set of experts

Rationale:

Need for improved and evaluation process to accelerate high quality product availability

WHO to revise review committee composition for broader expertise, evaluation model to ensure independent recommendations and reviewing frequency to enable faster evaluation process

Process for changing evaluation process:

	Current state	Target state
Review frequency	▪ Review 1x/year	▪ Assessment of dossier completeness within 30 days ▪ Review of product dossier within 100 days of complete dossier submitted
Evaluation model	▪ All recommendation decisions taken by one main review committee	▪ Presentation of all testing results to full committee ▪ Recommendation decisions made by core members not affiliated with testing or development of products under evaluation
Review experts	▪ Mostly entomologists, one statistician, QC expert, and epidemiologist	▪ Number of review experts will expand ▪ Breadth of expertise will increase to include (more) statisticians, epidemiologists, regulatory, and product development experts

World Health Organization

Pre-/post-marketing quality control

Rationale:

Need for improved quality of vector control products in the field

WHO to establish QA criteria for manufacturing facilities, conduct site inspections and establish regular post-marketing quality testing to assure quality standards are met by all recommended products

Approach for establishing pre-/post-marketing quality control

Establish standards and team	Establish process	Execute QA
▪ Establish criteria, baselines and formalized procedures for quality management, for both pre- and post-marketing quality control ▪ Build and train a quality assurance team at the WHO	▪ Update product evaluation process to include manufacturing inspections ▪ Provide assistance to manufacturing site for QA compliance	▪ Complete manufacturing site inspections for all products under evaluation (***pre-marketing***) ▪ Conduct quality testing for recommended vector control products on the market (***post-marketing***)

World Health Organization

Change reform to strengthen six areas of normative functions

Expected outcomes	Description
I Facilitated insecticide resistance management in NTDs/malaria vectors	▪ Develop global policy on insecticide resistance management ▪ Build capacity to support **monitoring and managing insecticide resistance**
II Enhanced evidence-based normative guidance available	▪ Develop/update testing guidelines, specifications and risk models for evaluation of VC ▪ Enable timely development of **normative guidance** (< 6 mos) for new product & categories ▪ Standardize and enhance required entomological procedures and practices
III Assisted member countries in implementing IVM strategies	▪ Develop and publish policies, recommendations and topical guidance for countries ▪ Develop operational guidelines for **non-pesticide vector control tools** and their evaluation
IV Optimized situational targeting of vector control products in countries	▪ Develop LLIN **durability standards** for quality control (e.g., expert review of intra-lab tests) ▪ Develop guidance on best targeting of vector control interventions
V Strengthened countries in registration processes for vector control products	▪ Increase **registration process efficiency** at country level by providing technical and normative support to countries & regional networks in pesticide registration (trainings and tool kits)
VI Strengthened countries in regulation of pesticides lifecycle management	▪ Develop and update guidelines and support countries on life-cycle management of pesticides ▪ Set up routine **monitoring of insecticide use** by member states

Overall impact

- **WHO** aims to support the development, evaluation, QC, adoption and sound management of pesticides and their products for the control and elimination of vector-borne diseases.
- **Vector-control product manufacturers** will benefit from faster, clearer and more transparent vector-control product-evaluation systems, including a new independent evaluation review process.
- **National regulatory authorities** will benefit from a more transparent global evaluation system in support of countries and regional systems, and stronger support for national registration through more transparent global evaluation.
- **Procurement sectors** will benefit from a larger array of products and strengthened development of normative guidance for deployment of innovative tools.
- **WHO Member States** will benefit from decreased incidence of vector-borne disease because of the availability of high-quality and effective products in the field, and strong normative support to monitor and manage insecticide resistance and manage pesticides over their life cycle.