MANUAL FOR STRATIFYING MALARIA RISK AND THE ELIMINATION OF FOCI

Region of the Americas

PAHO Pan American Health Organization World Health Organization Americas

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SUMMARY

This manual operationalizes the principles and concepts contained in the Global Technical Strategy for Malaria 2016-2030 *(1)* and in *A Framework for malaria elimination (2)* with the objective of guiding the countries of the Americas in how to implement actions to achieve elimination of this disease and prevent the reestablishment of transmission. The document outlines the following elements to guide the stratification and approach to malaria foci:

- The first step in actions to combat malaria is to stratify a territory according to the risk of transmission in order to plan and prioritize interventions and populations. This manual presents a methodology for country stratification consistent with the interventions and with the goal of elimination.

- For all strata, the basic intervention for elimination or for preventing the reestablishment of the disease consists of a sequence of actions that are triggered by the detection of each case, and includes **diagnosis, treatment, investigation, and response** (DTI-R). This strategy emphasizes the importance of communities having access to diagnosis and treatment in the shortest time possible and seeks to operationalize the concept of surveillance as an intervention promoted by the World Health Organization (WHO) in its Global Technical Strategy.

- In strata where there is transmission, and in those that are receptive and have a high risk of importation of the parasite, in addition to early detection and treatment, localities and foci should be prioritized for indoor residual spraying (IRS) or mosquito nets. Such interventions should be part of national strategies for integrated vector management and insecticide resistance prevention.

- Elimination of transmission at the national level involves consolidating transmission-free territories by transforming active foci into eliminated foci through systematic DTI-R and vector control. Thus, identifying, characterizing, and addressing malaria foci must be a central element in adapting the control strategy toward eliminating malaria in the countries.

- The identification and characterization of malaria foci involves micro-analysis at the local level. Thus, in this manual, the term **microstratification** is used to refer to the identification and characterization of malaria foci or clusters of localities (micro-areas) that share the same transmission dynamics and are epidemiologically linked by the movement of people. The term **microplanning** is used to refer to the organization of DTI-R interventions in such operational areas. It is mainly about identifying needs and solutions to organize the local network in order to achieve early detection and prompt access to diagnosis and treatment.

- The organization of DTI-R and vector control in malaria foci requires a national strategy to ensure technical and operational support in the field, as well as the necessary regulatory framework for eliminating malaria. This strategy should cover logistical and operational aspects, such as timely management of medications and intra- and intersectoral coordination, as well as more structural elements, such as the development of human resources, an effective platform for actions by community agents, the development of primary health care, and epidemiological surveillance in malarious areas.

INTRODUCTION

Background and objective of the manual

All malaria-endemic countries in the Americas have taken on the challenge of eliminating the disease, and they are taking actions to direct their health programs and strategies toward that goal. In line with the principles of the Global Technical Strategy for Malaria 2016-2030 *(1)*, in 2016 Member States adopted the Plan of Action for Malaria Elimination 2016-2020 through Resolution CD55.R7 *(3)*, which urges countries to review plans and implement strategies to eliminate and prevent the reestablishment of transmission.

Since 2010, the changes recommended by WHO, aimed at transforming control programs toward effective elimination, have been promoted at the regional level. The new Framework for malaria elimination, published by WHO in 2017, presents additional elements that should be included in national programs. This manual provides guidance on how to translate these elements into core malaria intervention efforts. It attempts to bring a change in malaria operations, emphasizing the need to address the focus and organization of operations at the most local level. The document begins with the need to identify and define an operational environment (focus or micro-area) where a specific programmatic intervention (DTI-R) is being implemented. Although standardized at the national level, the DTI-R must be guided by an understanding of the dynamics of transmission at the local level.

This document does not attempt to cover all issues related to managing malaria elimination programs. Nor is it a compendium or guide to malaria surveillance. WHO has developed materials to guide malaria elimination, which are referenced in this document and which this manual attempts to help implement, namely: WHO's *A framework for malaria elimination (2)* and the WHO *Malaria surveillance, monitoring and evaluation: a reference manual (4)*.

Target audience

The present manual is intended for technicians involved in malaria efforts, from countries and institutions that support them in planning, organizing, and supervising actions at the national, provincial, and local levels. This material seeks to guide countries in developing their own technical-strategic instruments to guide malaria operations, in accordance with each country's regulatory framework.

Structure of the manual

The manual is organized into four chapters and a section of annexes with additional details on the main interventions. The content of the chapters is as follows:

- **Chapter 1:** Refers to the conceptual framework, which introduces a series of basic principles and concepts that provide the basis for stratification and foci management.
- **Chapter 2:** Describes the stratification of malaria risk in a country: background to stratification, changes to address the context of disease elimination, and prioritization of interventions.
- **Chapter 3:** Concerns microstratification and micro-planning, and the methodology for carrying these out. The chapter describes the identification and characterization of foci or micro-areas, and the planning of intervention in micro-areas, aimed at ensuring an appropriate strategy for diagnosis, treatment, investigation, and response (DTI-R) at the

local level. Elements to help guide vector control, according to the described stratification approach, are also presented.

- **Chapter 4:** Describes the coordination of actions to eliminate transmission in the foci and prevent the reestablishment of transmission. Guidance is included on local malaria management models, and on monitoring and evaluation.

The document's annexes include details on malaria interventions, including, but not limited to, concepts for classifying malaria foci; case investigation; passive, reactive, and proactive detection; and DTI-R strategy. In addition, some examples are given to guide reactive case detection and an example of a format for microstratification and supervision in foci, as well as suggested indicators for malaria programs.

1.

CONCEPTUAL FRAMEWORK

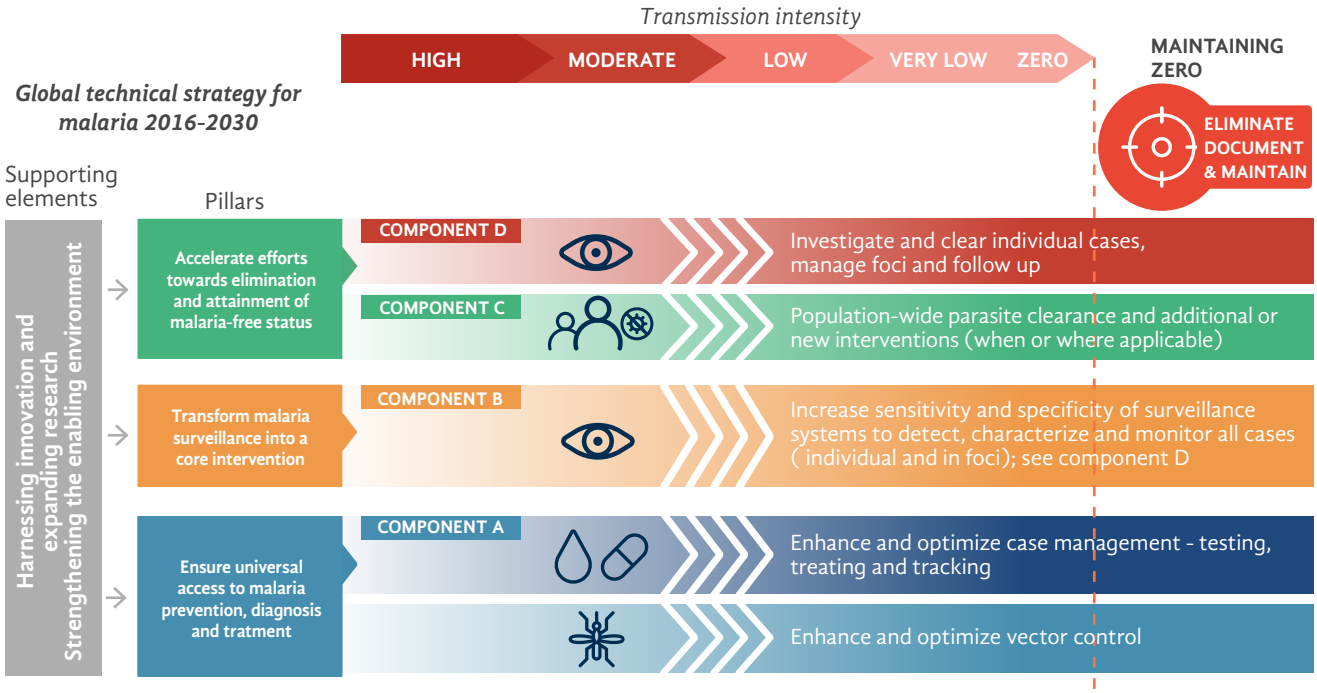
1. CONCEPTUAL FRAMEWORK

1.1. Elimination as a continuous process

The new Framework for malaria elimination *(2)* highlights malaria interventions along the entire scale of transmission intensity, from high to very low, with an emphasis on planning the next steps. The terms "control, consolidation, pre-elimination, and elimination" are no longer used.

The principles and strategies being proposed are applicable to **all** countries where malaria is endemic and where there are efforts to prevent reestablishment of transmission. Each country will plan activities according to the intensity of transmission and the stratification of malaria risk. Thus, a national program will provide a differentiated approach to different areas, based on the risk of malaria transmission (Figure 1).

Figure 1. Intensity of interventions, based on disease burden



Source: World Health Organization, A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/bitstream/handle/10665/254761/9789241511988eng.pdf;jsessionid=D3B2A3B858B0352AC46856A98231BD9D?sequence=1

1.2. Diagnosis, treatment, investigation, and response strategy

WHO recommends that countries have standardized operating procedures at the national level that set out the times required for the sequenced tasks of detection, case investigation, and foci investigation *(4)*. For this reason, PAHO is promoting the DTI-R strategy to assist countries in establishing systematic detection and response activities, with programmatic implementation and monitoring, taking as a reference WHO's T3 (diagnosis, treatment, and surveillance) initiative *(5)*, the 1-3-7 Surveillance Strategy for malaria developed in China *(6)* (consisting of notification

on the day of diagnosis, investigation of the case within the first three days, and response to the outbreak within the first seven days to prevent further transmission), and the WHO *Malaria surveillance, monitoring and evaluation: a reference manual (4)*.

The sequence of actions that initiates with case detection should be systematic and applicable in the shortest possible time by the local team. The objective of this sequence of actions is to help interrupt the chain of malaria transmission through early detection and response, thus constituting the **basis of the elimination effort**. DTI-R emphasizes the importance of timely response, and the need for additional activities to rapidly detect new cases in the community. Actions do not end after a case is diagnosed and treated; rather, efforts to detect other possible cases related to each identified case continue, through diagnosing, treating, and detecting additional cases. This cascade of surveillance-led actions is considered a key element in operationalizing the concept of surveillance as an intervention. The process of diagnosis, treatment, investigation, and timely response is applicable to different strata in all countries. However, the form and intensity of its implementation will depend on each situation.

The DTI-R strategy has four components (see Figure 2 and Annex A):

1. **Diagnosis:** Every suspected case of malaria should be diagnosed by microscopy or rapid diagnostic tests (RDT) within the first 48 hours from onset of symptoms.

2. **Treatment:** All confirmed cases should receive appropriate treatment according to national protocols, beginning on the day of diagnosis.

3. **Investigation:** Each case should be investigated and classified, in order to determine the appropriate response actions, within three days from diagnosis.

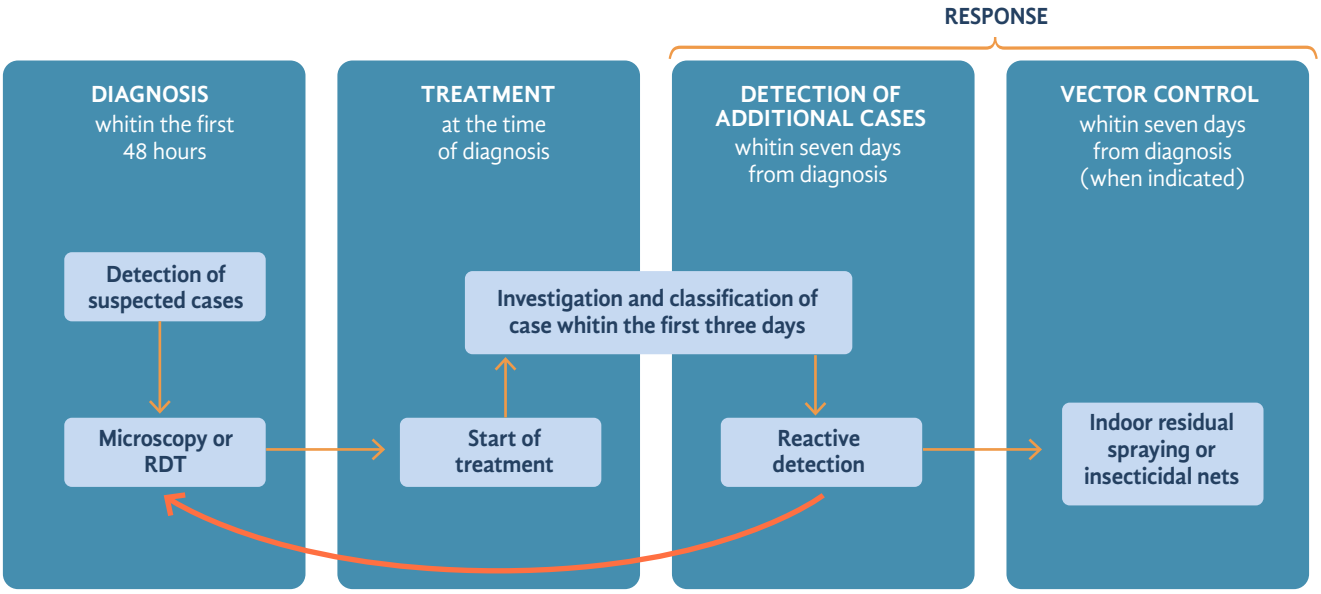
4. **Response:** Each case or cluster of cases should trigger basic actions, involving the timely detection and treatment of other cases (reactive detection[1]), within the first seven days from diagnosis. Reactive vector control activities, in addition to proactive or routine ones, especially long-lasting insecticidal nets (LLIN) and indoor residual spraying (IRS), are part of the integrated response to a malaria foci, where appropriate. [2]

These components must be clearly established at the local level of care. To implement DTI-R on a large scale, diagnosis, treatment, investigation, and response actions must be translated into concrete activities in the field, which in turn must be fully understood by all health personnel responsible for diagnosing and treating cases. The communication component is therefore an essential part of the strategy.

1 Reactive case detection is mentioned in *A framework for malaria elimination and in WHO's Malaria surveillance, monitoring, and evaluation: a reference manual*. Case detection among contacts is a common intervention in the control of infectious disease outbreaks. However, it is important to note that no studies have evaluated the effectiveness of reactive (or proactive) detection in interrupting malaria transmission.

2 While vector control actions are included as a key element in responding to detection of transmission in an area, they are not, themselves, the primary form of intervention; this consists, rather, of systematic actions for use of insecticidal nets (LLIN) or indoor residual spraying (IRS), planned proactively according to risk stratification.

Figure 2. Diagram of DTI-R strategy



RDT: rapid diagnostic tests

Source: The authors

1.3. Vector control

The Global Technical Strategy for Malaria 2016-2030 establishes that malaria control programs must provide universal access to malaria prevention, diagnosis, and treatment (pillar 1). The Global Technical Strategy establishes effective vector control as a major component. The main vector control intervention applicable to all malaria-risk populations in most epidemiological and ecological settings consists of: (1) the installation of WHO-prequalified LLIN; and (2) IRS with a WHO-prequalified product. In certain settings and circumstances, complementary interventions such as larval source management may be used in addition to one of the two main interventions. This Manual distinguishes two types of vector control actions in the context of malaria elimination: (1) routine actions planned proactively according to risk stratification, with the aim of achieving high local coverage with one of the two main interventions, which should be the main focus in vector control; and (2) targeted reactive case response actions, which are part of the DTI-R "response" and constitute only one additional element in the malaria vector control strategy, with potentially greater importance where efforts are centered on preventing reestablishment of transmission.

1.4. Principles for addressing foci

1. **Stratification according to malaria risk** helps identify and classify areas with active transmission and those with the greatest potential for malaria, in order to plan and prioritize interventions.

2. Malaria transmission in a given area is reduced by **eliminating it in each focus** (active foci are transformed into residual foci and then eliminated). Thus, reduction of transmission in the country involves consolidating malaria-free territories by eliminating foci. If the intervention

is not designed to eliminate transmission in the foci, transmission in the territory will not be reduced. Once transmission has been eliminated, the objective is to prevent its reestablishment.

3. **Heterogeneity in transmission and focalized pockets of transmission** is a characteristic of malaria epidemiology in areas of low and moderate transmission. Within a municipality or district, malaria transmission occurs in a heterogeneous manner depending on receptivity, human activity *(2, 7)*, and the quality of the health system.

4. To **reduce transmission** in municipalities, the model should be based on a lower level of management (at the focus or micro-area). Adjustments to the intervention should be based on more refined and ongoing analysis and management at the micro level. This element is part of the concept of "surveillance as intervention."

5. Transmission at each focus is eliminated through **early detection and treatment** of the human reservoir, and with sustained vector control actions, with high coverage and quality (especially LLIN and IRS).

6. The rate of incidence or annual parasite index (API) does not determine the strategy. There is only one strategy: to **diagnose and treat in the shortest possible time**, regardless of the API. What may change is the intensity of detection activities (reactive detection, case investigation), but not based on the API, but rather according to the absolute number of cases at the local level.

7. **Time is a key factor** in having an impact on the chain of transmission. The elimination of malaria requires a surveillance system that can detect and respond to individual cases quickly. WHO promotes early diagnosis and treatment within the first 24 to 48 hours after the onset of symptoms *(8, 9)*. The new surveillance manual sets the goal of notifying each case within 24 hours of diagnosis, conducting the case investigation within three days after diagnosis, and conducting the foci investigation and response within seven days of case notification *(4)*.

8. The **suspicion and diagnosis of malaria cases is a major bottleneck** in most countries in the Americas. Without diagnosis, there is no treatment, no case investigation, no data to stratify, and no response.

9. **Diagnostic operations should focus primarily on passive detection**. The objective of active detection is not to fill in the gaps of passive detection. In terms of malaria surveillance, what is most important is to maintain a high level of malaria suspicion and quality diagnosis at health facilities, especially in vulnerable areas; the point is not to replace this with active case detection or sentinel sites for individuals with fever.

10. **Inducing diagnostic demand** should be seen as a programmatic action linked to improving passive detection for timely diagnosis.

11. **Intervention in a malaria case does not end with treatment**. There must be additional efforts to detect more cases (reactive case detection around cases or clusters of cases), along with vector control to contain transmission.

1.5. Concepts of malaria biology essential to organizing operations

To understand the timing and importance of detection, treatment, case investigation, and response coordination, it is necessary to understand basic concepts of malaria biology and epidemiology. Some of these concepts are presented below.

The extrinsic incubation period, also called sporogony, refers to the cycle of the parasite in the mosquito during which the infecting sporozoites are formed. This period has a minimum duration of eight days and an average of 9-10 days, and can extend to as much as 16 days, depending on the temperature. The intrinsic incubation period extends from the inoculation of the sporozoites until the onset of symptoms. This period includes the hepatic and erythrocyte phase. It has a minimum duration of seven days, most frequently lasting between 9 and 17 days. In the case of *Plasmodium vivax*, due to the presence of hypnozoites (latent intrahepatocyte forms), it is possible to have late incubation periods and relapses at 3 and 18 months (very rarely, up to five years later [see Annex A]) *(10)*. Knowing these incubation periods is important in identifying the cases' origin of infection (Table 1).

The time for appearance of gametocytes in the blood is shorter in *P. vivax* than in *P. falciparum*: *P. falciparum* gametocytes appear 7 to 15 days after the onset of symptoms, whereas *P. vivax* gametocytes appear and can infect mosquitoes even before the onset of fever. Therefore, while early diagnosis and treatment are important to lessen the severity of malaria, they are also important to prevent more people from becoming infected. Unlike *P. vivax*, chloroquine and artemisinin derivatives have little activity on mature *P. falciparum* gametocytes; thus, if a dose of primaquine with a gametocidal effect is not included, they can remain in the blood for several weeks and continue to be transmissible.

Table 1. Duration of critical intervals for the two main species that cause malaria in humans

	Duration	
Interval	***P. falciparum***	***P. vivax***
Sporogony (extrinsic incubation period)	9 to 10 days at 28 °C	8 to 10 days to 28 °C
Incubation in nonimmune (intrinsic incubation period, from sporozoite inoculation to the first clinical manifestation): • Short (without hypnozoites) • Long (caused by hypnozoites)	• 7-30 days • Not applicable	• 10-30 days • 3 to 18 months (on very rare occasions, up to five years)
Time between the appearance of asexual parasites and the mature gametocytes	7 to 15 days	0 days - immediate
Latency period (from first attack to relapse; in some strains – those which have late incubation periods – also refers to the period from inoculation of sporozoites to first attack)	Not applicable	3 to 18 months (on very rare occasions, up to 5 years)
Time to effective elimination in the blood of gametocytes with schizontocidal drug treatment (without gametocidal)	3 to 6 weeks	< 1 day
Typical duration of untreated infection (if no death)	1-2 years (1 year or less in approximately 80% of cases)	1 to 2 years (on very rare occasions, up to 5 years)

Sources: [1] World Health Organization. Malaria surveillance, monitoring, and evaluation: a reference manual. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf.

[2] Gilles H, Warrel D. Bruce-Chwatt's essential malariology. 3rd ed. Florida: CRC Press: 2010.

[3] Ngwa C, Rosa T de A, Pradel G. Current topics in malaria. London: INTECH; 2016. Available at: https://www.intechopen.com/books/current-topics-in-malaria/the-biology-of-malaria-gametocytes.

[4] Pampana E. Mexico City: Centro Regional de Ayuda Técnica, Agencia Para El Desarrollo Internacional: 1996.

In order to eliminate malaria in the Americas, special attention must be given to the problems of controlling *P. vivax* malaria *(11)*. Table 2 presents the main distinguishing characteristics of *P. vivax* malaria and the respective implications for malaria epidemiology and actions. Relapses due to the presence of hypnozoites in the liver can contribute significantly to the morbidity and maintenance of transmission *(11),* and can become major determinants of residual malaria in the final stages of elimination. The main obstacles to a radical cure of *P. vivax* infections relate to 1) the risk of hemolysis due to deficiency of the enzyme glucose 6-phosphate dehydrogenase (G6PD); 2) the efficacy of primaquine at the current doses in use (3.5 mg/kg total dose) in areas with possible circulation of tropical strains (South America); 3) case management in persons over 70 kg *(9)*; and 4) poor adherence to 7- or 14-day treatments. Addressing these challenges with national policies that translate into better strategies in case of malaria outbreaks is a major element in the elimination of malaria in the Region *(1)*.

Table 2. Characteristics of *P. vivax*

Characteristics	Consequences
P. vivax sporogony occurs at lower temperatures than *P. falciparum*	*P. vivax* has a wider geographic distribution and a longer transmission season
The sporogony of *P. vivax* has a shorter duration	Interventions aimed at reducing the longevity of the vector may be less effective for *P. vivax*
Some important transmission vectors in certain areas where *P. vivax* is endemic bite early in the day and feed and rest outdoors	Conventional preventive measures (LLIN and IRS) may provide less protection
P. vivax has a latent phase of hypnozoites that can cause multiple relapses after a primary infection, but is undetectable with current diagnostic methods	Malaria cases without additional infectious mosquito bites
	Increases potential transmission RO (reproductive number)
	May be a potential source of reintroduction without an imported case
P. vivax mostly infects reticulocytes (young red blood cells) in the bone marrow	Repeated destruction of young erythrocytes causes chronic anemia
	Complicates the culture of asexual parasites in the laboratory, making it difficult to discover new tools
	Blood phase infections often have low parasitemia
	Traditional microscopy and RDT may not detect all infections and thus underestimate the prevalence of malaria
P. vivax gametocytes appear early, even before the onset of symptoms	Increased risk of subsequent infection

LLIN: Long-lasting insecticidal nets; IRS: indoor residual spraying; RDT: rapid diagnostic tests.

Source: World Health Organization. Control and elimination of *plasmodium vivax* malaria: a technical brief. Geneva: WHO; 2015.

2.

MALARIA RISK STRATIFICATION

2. MALARIA RISK STRATIFICATION

WHO defines malaria risk stratification as "classification of the geographic areas or localities according to factors that determine receptivity and vulnerability to malaria transmission" *(12)*. Similarly, WHO defines malaria stratification as "classification of geographic areas or localities according to epidemiological, ecological, social, and economic determinants for the purpose of guiding malaria interventions" *(12)*.

Stratification, then, consists of a tool to assist in decision-making, and is the first step in planning malaria interventions. Stratification makes it possible to direct resources and actions to areas with the highest disease burden and, at the same time, guide actions to prevent the reestablishment of transmission in areas where transmission has been successfully interrupted. Stratification is a dynamic process that involves the periodic analysis of information and should lead to the establishment of differences in the intervention for each stratum.

2.1. Receptivity and vulnerability

Receptivity is defined as the ability of the ecosystem to allow malaria transmission *(2)*. Vulnerability refers to the risk of importing the parasite *(2)*, an expression used later in this document. When both receptivity and the risk of importation of the parasite into an area are equal to zero, there is no risk of reestablishing transmission.

The level of receptivity should be evaluated and mapped based on available entomological information, which allows identification of the most receptive areas. Historical data or other evidence of malaria transmission can be used as a proxy in areas where current entomological information is not available. The risk of importation of the parasite should be assessed and mapped based on the establishment of surveillance that identifies populations at risk of importing cases and areas at greatest risk of receiving imported cases. In certain contexts, the risk of transporting the infected mosquito to other areas should also be considered.

>Factors that affect malaria receptivity

Climate changes, such as variations in rainfall and temperature, ecological changes, such as urbanization and economic development, changes in land use, modification of crop acreage, deforestation, dams, and drainage, among other factors, can affect the distribution and densities of Anopheles mosquitoes in one way or another.

>Factors affecting the risk of importing the parasite into the Region of the Americas

Socio-demographic and socioeconomic changes involving population mobility from endemic areas pose a risk of importing the parasite. Areas at risk of importing the parasite in the Region are, for example, those that receive tourism, or migration of populations from endemic areas to work in certain risky activities such as gold mining, rice, chestnut, banana, or oil palm plantations, and the harvesting of sea jellyfish. The illegal status of some activities introduces additional barriers and difficulties in identifying the population and the demand and supply of services. These factors are compounded by the population's lack of knowledge about the risk of malaria, people's behavior with respect to seeking health services, and insufficient capacity of health services to detect and manage the disease.

2.2. History of stratification

All countries in the Americas use or have used the incidence of malaria or the annual parasite index (API) for stratification of high-, medium-, and low-risk areas,[3] and for reporting to WHO in a standardized way. Analysis of the API and its trends has guided the identification of priority areas for work – for example, those areas with higher APIs or where the API was not decreasing despite interventions. With the same approach, since 2013, several Central American countries have used the API of the last three years to identify strata 1, 2, and 3,[4] in the framework of the regional initiative for the Elimination of Malaria in Mesoamerica and the Island of Hispaniola (EMMIE). The stratification of municipalities in these strata, based on the API, was carried out as an intermediate step before moving on to establish strata at lower levels such as localities, and even foci.

In the current epidemiological context, the API has limited utility for stratification of municipalities or larger administrative units for the following reasons:

- In countries where transmission has been interrupted in many areas or where the number of cases is very low, the value of the API provides very little guidance for stratification. Moreover, this index does not make it possible to identify areas that, though without malaria, have a high potential for the disease (receptive areas and at risk of importing the parasite); thus, the identification of these areas is essential for preventing the reestablishment of transmission.
- Nor is the API useful in contexts with many cases, since the absolute number of cases per locality (or health unit)5 or the positivity index, and not the municipal risk, are the elements that guide the intensity and coverage of surveillance actions, which in turn are what make the difference in operations between strata. In addition, the heterogeneity and localization of malaria within municipalities limit the interpretation of a risk measure at that level.

2.3. Stratification along the scale of malaria transmission intensity

According to the new Framework for malaria elimination, malaria programs should select strategies that are appropriate for each situation along the malaria intensity scale (coexistence of very low and high transmission situations). It is in this context that the WHO advises that stratification should be carried out according to the intensity of transmission (number of cases), the risk of importing the parasite, and receptivity *(2)*, applicable to a country's entire territory. Stratification therefore includes, but is not limited to, foci.

The proposed strata are as follows:

- **Stratum 1.** Non-receptive.
- **Stratum 2.** Receptive, with no autochthonous cases and no risk of importing the parasite. It includes eliminated foci, without imported cases or without immigration from endemic territories.
- **Stratum 3.** Receptive, without autochthonous cases and with risk of importing the parasite. Includes eliminated outbreaks, with imported cases or with immigration from endemic territories.
- **Stratum 4.** Receptive, with autochthonous cases. Includes active and residual foci.

3 High risk: API ≥ 10; medium risk: API 10-1; low risk: API < 1. Some countries use different criteria than those cited here, while others use "Very high risk" as a fourth level.

4 Stratum 1: 0 indigenous cases in the last three years; stratum 2: API ≤ 1 in the last three years; stratum 3: API > 1 in the last three years.

5 The number of cases at the local level, and not the API, is the criterion that determines when an investigation and response strategy is necessary, triggered by each case detected (strata with three or fewer cases per investigation team per week), versus an action oriented more by the identification and analysis of clusters of cases (strata with higher transmission).

In countries where numerous areas show stable transmission, stratum 4 will need to be broken down according to the level of endemicity (based on the number of local cases[6]). This distinction is necessary in order to differentiate areas with transmission, but with a very low number of cases, which require more intensive surveillance, than areas where the intensity of transmission means that a specific response to each case is not yet relevant. A country with high transmission could establish, for example, a 4-A stratum, which would include areas with three or fewer cases per week per surveillance unit, and a 4-B stratum, with more than three cases per week per surveillance unit, thus differentiating between areas in which all cases should be investigated, and areas where an investigation of each case is not necessary. Annex A provides an example of guidelines for establishing the units that should carry out case investigation in a country based on the transmission. The information required for stratification includes:

1. Information on autochthonous cases of malaria in recent years by place of origin (at the locality level), which allows identification of historical and current areas of malaria.[7] Data from the last four years will make it possible to differentiate the localities that should be classified in stratum 4 (active and residual foci) or in stratum 3 (eliminated foci).

2. Information on risk of the parasite being imported: imported cases, by locality and local knowledge of population movement from endemic territories. The analysis of population movements from endemic countries, and between localities within the concerned territory, is essential for guiding local surveillance strategy aimed at transforming active foci into eliminated foci, and in order to consolidate malaria-free territories.

3. Information on receptivity. In many countries, entomological data are quite limited. In these situations, a proxy indicator of receptivity might consist of the number of autochthonous cases over the last 10 years, since localities with malaria transmission also are often the most receptive locations. Areas with similar ecology to those in which transmission has occurred may also be considered as a factor.

4. List of georeferenced geographic units[8] where the stratification will be conducted.

When the exercise is carried out at the national level, especially in geographically large countries, the initial stratification is often at the administrative unit level two (ADM2) (municipality, district). Ideally, ADM2 stratification is the result of a refined effort to stratify localities or sectors within municipalities. In a country with many cases and several foci with active transmission, this exercise can begin by identifying and characterizing the foci, to be designated as stratum 4 (microstratification, see Chapter 3), then differentiating those foci with the greatest endemicity (number of cases per week) from foci with more sporadic transmission. Once the stratum with recent transmission has been defined, the exercise will continue with identifying areas corresponding to strata 3, 2 and 1. At a more local level, however, stratification should always be conducted according to localities or population clusters (with the exception of areas that are highly homogeneous in their non-receptive or receptive and non-vulnerable status).[9]

6 The number of cases per investigation team, and the dispersion of cases, is what will determine differences in the basic surveillance operation (case investigation and reactive case detection) *(3)*.

7 Since most cases of malaria in the Americas are caused by *P. vivax*, it should be noted that in contexts where relapses are a major contributor to the disease burden and where there is major population movement, it may be difficult to define the site of infection. Relapses do not always occur at the sites of transmission. This needs to be considered, for example, in seasonal work situations, where people spend much of the year in areas of transmission but reside in other areas.

8 The list of georeferenced geographic units can often be obtained from statistics bureaus in the countries, if unavailable in the health system.

9 Once classified in a stratum, a comment should be placed to justify the reason for the decision. Since the stratification must be updated every year, these comments will provide a reminder of the rationale for the current classification and will allow updates based on any changeS.

The analytical exercise of classifying localities should involve local staff familiar with the terrain and the mobility of the population. This stage should include personnel experts in epidemiology, entomology, and computer science, including a team that oversees the case databases, has access to receptivity information, and can assist in preparing the maps.

For example, a locality with transmission in the last year would be in stratum 4 (this locality would be part of an active focus or would constitute an active focus by itself); a locality that had transmission two years ago (inactive residual focus) would also be in stratum 4; a locality with no cases for more than three years (eliminated focus), but considered vulnerable due to the arrival of imported cases or movement of the population from endemic areas (for example, a banana area that receives workers from malaria-endemic countries), would be in stratum 3; a locality in which malaria vectors are present (based on entomological data or historical malaria data), with no history of imported cases or population movement from malaria-endemic areas, would be classified as stratum 2; finally, a locality that is not receptive (with no vectors) according to entomological surveillance, because it does not have the conditions for vectors to live (altitude and temperature) or because it is not a historical malaria area, would be considered to be stratum 1.

Stratification, therefore, is a local exercise to analyze the degree of endemicity and the risk conditions in geographic areas. This is a dynamic process that relies on the quality of case surveillance and the ability to establish systematic processes to monitor receptivity and the risk of parasite importation.

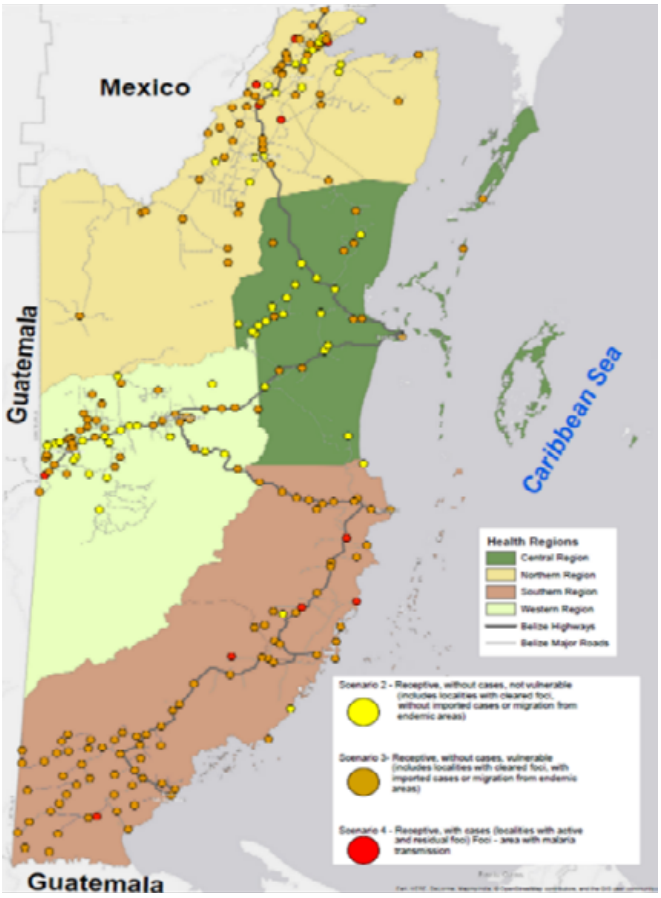
Once the country has been stratified, interventions will be planned based on this stratification. For example, if there is a high risk of importing the parasite into a receiving area, consideration should be given to maintaining passive surveillance, along with active case detection and measures to protect populations with LLIN or IRS to prevent reestablishment of transmission. In areas with low risk of the parasite being imported and with no receptivity, timely diagnosis based on passive case detection, accompanied by investigation and response, may be sufficient. In active transmission settings, the at-risk population should be protected with LLIN or IRS. The number of cases (cases per week per investigation team) determines the need for, and feasibility of, individual investigation and response, and therefore determines differences in the operations to be conducted. Examples of stratification exercises are shown in Figure 3 and in Tables 3 and 4, with the maps produced and the generic DTI-R interventions appropriate for each stratum.

Table 3. Example of stratification in Costa Rica (database)

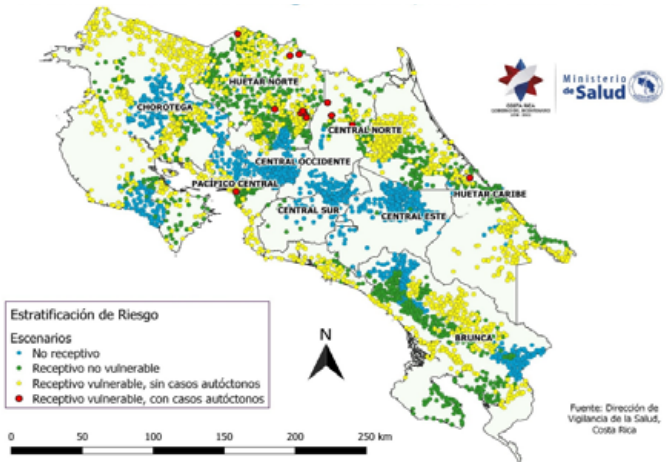
Province	Canton	District	Locality	Coordinate X	Coordinate Y	Stratum	Comment
Alajuela	San Carlos	Buena Vista	Buena Vista	-84.4598	10,276	1	Located at 875 meters above sea level, and is not considered a malaria area
Alajuela	Guatuso	San Rafael	Aguas Negras	-84.8379	10.68261	2	Presents favorable conditions for presence of the vector (altitude less than 600 meters); however, there have been no cases recently and there is low migratory flow
Alajuela	Los Chiles	El Amparo	Alto Los Reyes	-84.6271	10.85105	3	High migration flow and pineapple crops
Alajuela	San Carlos	Pocosol	Llano Verde	84.382	10.8853	4	Reforestation, livestock, transient population, bedroom community, and active focus

Figure 3. Example of stratification: maps of Belize, Costa Rica, and Dominican Republic

Belize



Costa Rica



Dominican Republic

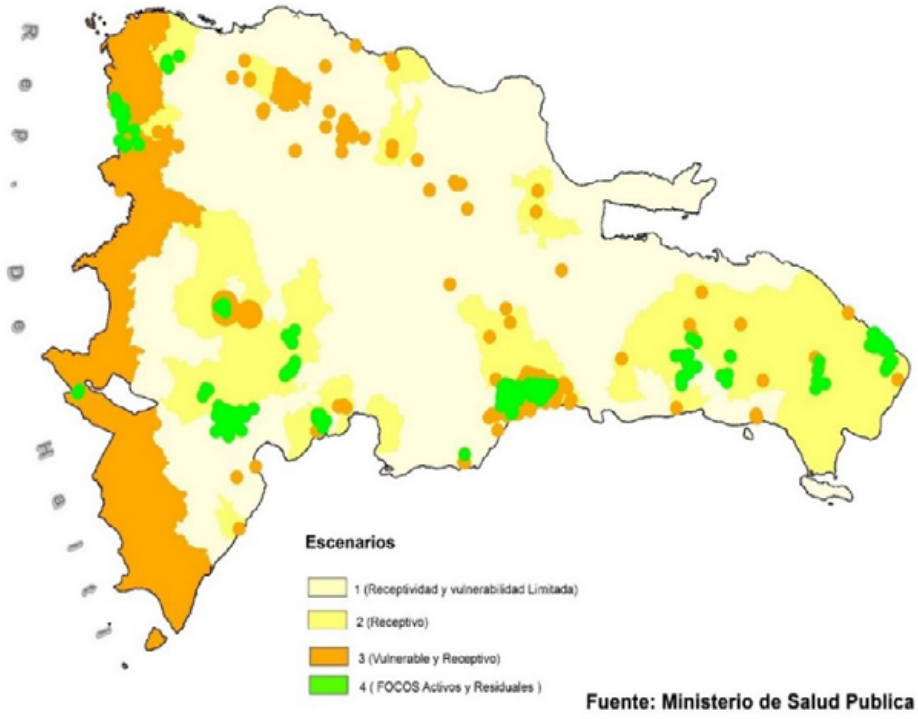


Table 4. Generic activities of specific malaria interventions, by stratum

Component	Stratum 1 (non-receptive)	Stratum 2 (receptive, no risk of parasite importation)	Stratum 3 (receptive, with risk of parasite importation)	Stratum 4 (4-A and 4-B local transmission: active and residual foci)
Routine vector control	NA	NA	Routine vector control (in prioritized localities or based on increased receptivity or vulnerability)	Routine vector control with high coverage of the at-risk population (LLIN or IRS)
Passive detection	Passive detection with diagnosis available in reference health units of local networks	Passive detection with diagnosis available in reference health units of local networks	Passive detection with diagnosis available at local levels and in transit and migration areas	Passive detection with diagnosis available at local levels and according to the dynamics of transmission
	NA	NA	**Information, education, and communication (IEC) to stimulate demand**	Information, education, and communication (IEC) to induce demand
	Training of health personnel	Training of the health personnel	Training of health personnel	Training of health personnel
Proactive detection	NA	NA	• Proactive case detection (mobile and migrant population) • Fixed scheduled actions (for example, one per month) or specific actions based on changes in vulnerability	☐ Proactive case detection ☐ Periodicity: for example, one or two per month
Timely reading of slides	Reading slides in less than 48h	Reading slides in less than 48h	Reading slides in less than 48h	Reading slides in less than 24h
Quality assurance of diagnosis	Direct control, indirect control, training and supervision	Direct control, indirect control, training and supervision	Direct control, indirect control, training and supervision	Direct control, indirect control, training and supervision
Location of cases	NA	NA	NA	☐ Georeferencing of localities with cases ☐ Mapping of important focus characteristics

Treatment and follow-up of cases	Treatment available in reference health units of local networks	Treatment available in reference health units of local networks	Treatment available at local levels and in transit and migration areas	Treatment available at all diagnostic points
	Early treatment (starting 24 hours from diagnosis)	Early treatment (starting 24 hours from diagnosis)	Early treatment (starting 24 hours from diagnosis)	Early treatment **(in the first 48 to 72 hours from onset of symptom**s)
	Follow-up on all cases	Follow-up on all cases	Follow-up on all cases	Follow-up on all cases **(if there are many cases, adherence to treatment should be based on appropriate guidance and partial supervision)**
Investigation of all cases and foci, and response	Investigation of all cases	Investigation of all cases	Investigation of all cases	Investigation of all cases and foci or **micro-areas** (if there are many cases, only differentiate between local or imported case at diagnostic point (without going to the locality to finalize the case investigation)
	Reactive case detection	Reactive case detection	Reactive case detection	Reactive case detection (when there is an index case or cluster of cases)
	NA	Entomological surveillance when a case is detected (foci investigation)	Entomological surveillance when a case is detected (foci investigation)	Entomological surveillance (foci investigation) to guide vector control when needed
	NA	Vector control (LLIN or IRS) in response to a case **(if vectors are found**)	Vector control (LLIN or IRS) in response to a case **(if vectors are found**)	Vector control (LLIN or RRI) in response to a case, in situations of few cases and in localities not covered by vector control
Routine entomological surveillance	NA	NA	Entomological surveillance at sentinel sites	Entomological surveillance at sentinel sites
Malaria risk surveillance	NA	Monitoring the influx of people from endemic areas and factors influencing receptivity (irrigation, deforestation, etc.)	Monitoring the influx of endemic area people and of factors that influence the receptivity (irrigation, deforestation, etc.)	Monitoring the influx of endemic area people and of factors that affect receptivity (irrigation, deforestation, etc.)
Information systems and data analysis	Mandatory notification of confirmed cases, record of diagnoses made, and weekly analysis	Mandatory notification of confirmed cases, record of diagnoses made, and weekly analysis	Mandatory notification of confirmed cases, record of diagnoses made, and weekly analysis	Mandatory notification of confirmed cases, record of diagnoses made, and weekly analysis

DTI-R: diagnosis, treatment, investigation, and response; IEC: information, education, and communication; NA: not applicable; LLIN: lasting insecticidal nets; IRS: indoor residual spraying; RDT: rapid diagnostic tests.

2.4. Prioritization

Prioritization is an important element in planning malaria interventions and is part of the stratification exercise. It involves identifying populations or geographic areas (foci, municipalities) that require greater attention and actions, in order to achieve cost-effective resource management and greater epidemiological impact. Once geographic units have been classified into strata, it is necessary to prioritize certain units according to their epidemiological importance in a given stratum.

Several criteria can be used in prioritization, including: malarial burden, parasitic species, certain geographic contexts that signal increased risk to public health, and areas with greater potential for malaria. The following are considerations that national malaria programs should take into account in establishing priorities:

1. Settings in which malaria transmission is concentrated in a limited number of municipalities and within individual municipalities; and when the malaria burden is concentrated in pockets or clusters of localities. These municipalities and clusters often export malaria cases to other areas of the country with active transmission, or to malaria-free territories where transmission has the potential to be reestablished. Municipalities with the greatest concentration of malaria burden in specific countries should receive the greatest attention, bringing to bear the necessary technical capacity, resources, and political attention. Prioritization of municipalities (or corresponding ADM2 unit depending on the country), based on the number of cases in the most recent year, or the average number of cases in recent years (taking into account year-to-year variation), should be the first step in prioritization.

2. During the stratification exercise, the use of a Pareto chart,[10] with the cumulative percentage of cases in the country or in a given region, can be useful in identifying localities, foci, or municipalities with the highest burden. This exercise can help prioritize stratum 4 localities with the highest burden, at the country level and within each municipality (ADM2 level).

3. Elimination of *P. falciparum* malaria is a priority, given the potential emergence of treatment resistance and higher mortality than for other Plasmodium species. Thus, elimination of *P. falciparum* can be an intermediate goal in national malaria elimination. Ensuring territories free of *P. falciparum* malaria transmission in various contexts can be another key factor in prioritization.

4. The prevalence of *P. falciparum* malaria over *P. vivax* is, in many cases, a sign of poor diagnostic and treatment efforts. This can therefore serve as a criterion for prioritization, identifying areas where organized action can have major impact.

5. The presence of urban malaria transmission has also been used by countries as another criterion for prioritizing actions. In general, urban malaria foci have the highest disease burden. Urban transmission represents a stratum in which one can expect to reduce the times for diagnosis and treatment, and for implementation of measures such as the supervision of *P. vivax* treatments and vector control operations (including larval control, when indicated). The risk of exporting malaria to rural localities is also a factor to consider in giving priority to such urban malaria foci.

6. In many contexts, preventing the reestablishment of transmission can also be a major element in prioritizing actions. In countries with active transmission, maintaining the interruption of

10 The Pareto chart is a graph that organizes data in bars in descending order, thus showing the Pareto principle, or 80-20 principle, to prioritize problems.

transmission in territories with a history of malaria can be as important as reducing transmission in active foci. In establishing priorities, the balance between emphasizing municipalities with higher burdens versus municipalities at high risk of malaria reintroduction is dictated by each particular situation. The risk of importing malaria from municipalities with transmission highlights the importance of paying special attention to areas that are continuing to generate cases of malaria within the country.

7. Areas that are not experiencing malaria transmission, but that are receptive and at risk of importing the parasite (stratum 3) from countries with active transmission, should also be prioritized based on the risk of importing the parasite. On the other hand, in some contexts, certain stratum 1 areas will be especially important, given the high uptake of imported cases, situations where it is important to ensure adequate diagnosis, clinical management, and investigation in order to identify potential areas of transmission.

8. Although the API is not the main factor for stratification in the current context of elimination efforts, it can be a useful variable, together with the Pareto chart, in prioritizing localities within the stratum with active transmission (stratum 4). In this regard, the API at the locality or focus level may be useful for identifying localities which, while not a priority in terms of their contribution to the disease burden, are important because of the risk that malaria poses to the population. An approach that assigns special importance to the number of cases, as a criterion for more effectively impacting the disease burden, deserves serious consideration.

3.

MICROSTRATIFICATION AND MICROPLANNING

3. MICROSTRATIFICATION AND MICROPLANNING

Microstratification is an element of local epidemiological analysis directed at organizing malaria interventions by targeting transmission sites. It involves the identification and characterization of foci or micro-areas and is especially relevant in areas with active or recent transmission (stratum 4).

Some countries in the region have used the terms focus and micro-area interchangeably. For simplicity, this manual equates micro-areas with foci. It should, however, be clarified that the two concepts are different. The concept of a "focus" is based on vectoral transmission. The concept of a micro-area is based on the link between localities, movements of people, and other variables that provide guidance on how to organize access to diagnosis and treatment.

For the purposes of this manual, a micro-area is a set of localities or malaria foci that are close together and that share the eco-epidemiological conditions and dynamics of malaria transmission. It may therefore include several foci that are related to each other by virtue of population mobility (for example, three separate banana farms, where workers move from one farm to another), or it may be a focus (such as a gold mine where transmission occurs) and the location where miners usually rest. In microstratification, the epidemiological concept of focus is taken into account, but the concept of micro-areas is used to define a geographic area where operations can be planned and coordinated.

Once the microstratification has been carried out, the response can then be planned. Thus, the actions to eliminate malaria from foci include two components: microstratification and microplanning (Table 5).

Table 5. Components for eliminating transmission in foci

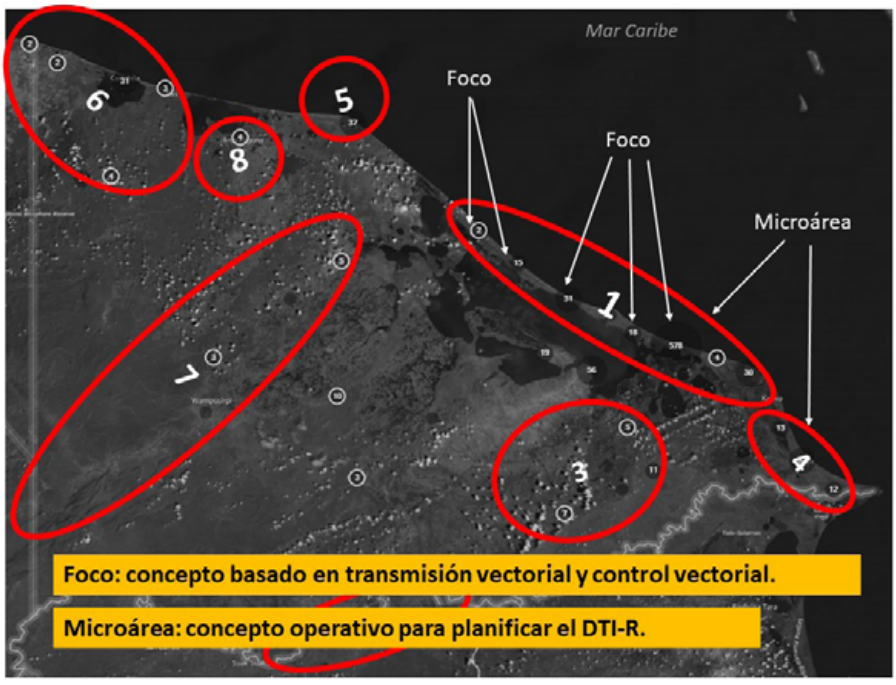
Component	Elements	Objective
1. Microstratification of malaria in the municipality	• Identification of the foci • Analysis of the transmission dynamics in the foci • Characterization of the care micro-networks (gaps, barriers, and needs) • Formulating hypothesis on the transmission, its maintenance, the social dynamics that determine it, and, thereby, the keys for impacting it	Generate the necessary inputs to organize diagnosis, treatment, investigation (micro-networks), and response
2. Microplanning: organization of actions for diagnosis, treatment, investigation, and response	• Emphasis on organizing passive detection. • Direct, guide, and stimulate demand. • Connect the various actors in the micro-network. • Optimize active detection. • Optimize measures for vector control of adult mosquitos. • Dynamic exercise with weekly cycles to analyze and reorganize actions. • Local supervision model.	Implement a local model for surveillance and management that diagnoses cases in less than 48 hours, treating on the day of diagnosis, and investigating and responding appropriately.

3.1. Microstratification: identification and characterization of malaria foci

Microstratification is an exercise in micro-epidemiology that characterizes the social aspects and health services to be taken into account in organizing detection, diagnosis, investigation, and response actions in the focus (Figures 4 and 5). The five steps of microstratification, which will be explained in detail in section 3.1.3, are as follows:

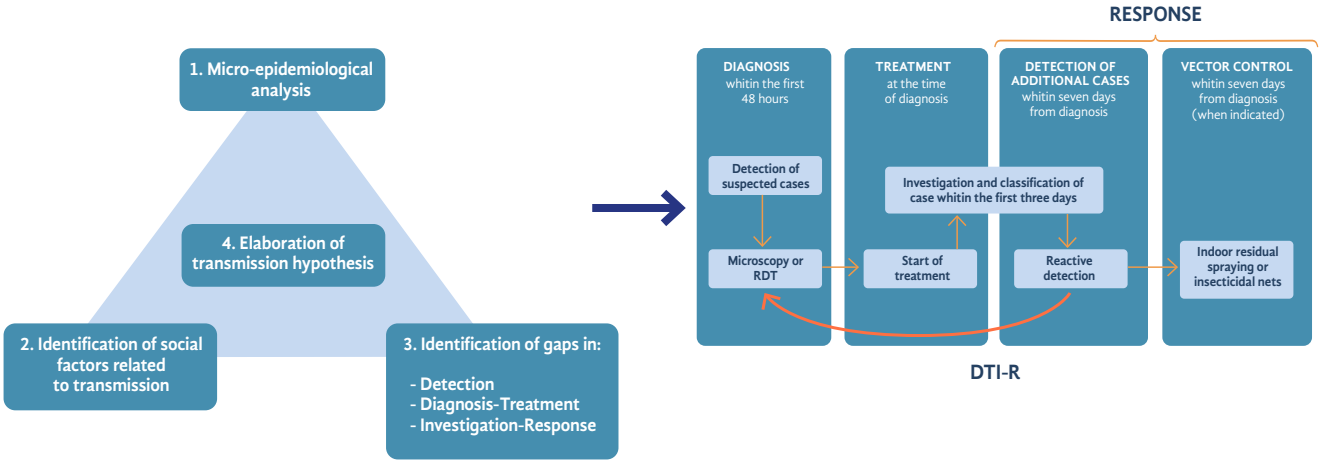
1. Identify the distribution of cases in the territory by identifying the localities and clusters of localities with transmission.
2. Understand the factors in the populations that affect or may affect malaria transmission: relation between transmission in one community and transmission in another, distances and routes of movement, and factors that determine transmission (for example, whether this involves the arrival of imported cases, or, rather, is related to a very isolated community in which transmission is being maintained; whether transmission is the result of economic activity, or is perpetuated by relapses of *P. vivax*).
3. Group the different localities into micro-areas based on the factors deemed to be important for transmission: (a) they are close to each other, within the same radius of the vector (less than 3 km); (b) they share the same transmission dynamics; (c) there is extensive contact between the populations; or (d) they share the same health care network.
4. Characterize the micro-areas in terms of the organization of DTI-R. In other words, analyze the network; the number of microscopes and whether they are properly located; whether rapid diagnostic tests are available; determine what gaps exist; consider delays between taking and reading slides, and beginning treatment; identify the barriers or causes of existing gaps, and vector control coverage, etc.
5. Establish a hypothesis that explains the persistence of transmission, the social dynamics that determine it, and the keys for impacting it.

Figure 4. Delimitation of foci and micro-areas



DTI-R: diagnosis, treatment, investigation, and response

Figure 5. Characterization of micro-areas and foci: triangulation of local information to develop transmission hypotheses and organize the DTI-R strategy



3.1.1. Principles to guide microstratification

1. Begin with the available information (even if it is not of optimal quality). Do not postpone the exercise because the information is not complete. Proper handling and analysis of existing information is the first step. Careful review of existing information at the local level is also important to demonstrate to health personnel the importance of data, while promoting a culture of analyzing data, along with the necessary diligence for action. Microstratification should demonstrate the need for better and more specific data, in order to understand the dynamics of transmission and organize the response or microplan. Obtaining more and better data should be a continuation of the initial microstratification exercise.
2. The locality or community constitutes the minimum level of analysis. All data should be aggregated and analyzed at this level. When the number of cases is very small, they should be located on the map.
3. Absolute certainty is not always possible. Differentiating transmission dynamics, especially in highly endemic areas, can be difficult. Therefore, the best available evidence should be used, and the analysis should be refined, confirmed, and adjusted (if necessary) during site visits.
4. There may be doubts about the boundaries of a micro-area or concerning which stratum to designate for a given locality. In such situations, it is useful to consider the resulting differences in the response or microplan. When there are no such differences, it is best to consider a single micro-area.

To facilitate the organization of the health care network and surveillance processes, and to avoid a fragmented response, it may be useful to consider, in addition to the epidemiological elements, the micro-area that is to be covered by the local health team. When a malaria foci or micro-area occurs in different health areas or municipalities, coordination between them will be essential to ensure that the foci is properly characterized and that an appropriate response follows.

3.1.2. Recommended information for conducting microstratification and microplanning

- Cases by locality of diagnosis and place of residence, or origin of infection, disaggregated by species and epidemiological week (or month). Additional desirable information includes: onset of symptoms of cases, localities where the sample was taken, method of diagnosis (RDT vs. microscopy), age, sex, and type of surveillance.
- Number of suspected cases by type of surveillance and locality
- Map indicating all of the localities in the municipality
- Location of diagnostic posts (microscopy and RDT)
- Map indicating accessibility to the nearest localities with diagnostic posts
- Information on the use of health services (barriers to access, care routes, use of services patterns, and other alternatives for the population)
- Available information on the presence of vectors, and of major permanent or semi-permanent breeding sites (information from neighboring municipalities may also be useful)
- Information on vector control activities conducted, and their coverage in the municipality or locality in the last three years
- Other contextual information on factors affecting transmission in the area (mining, agriculture, other legal or illegal productive activities, unrecognized border crossing sites, presence of ethnic groups and reserves, etc.)
- Information on population movements between localities, access routes, community meeting points, and other social dynamics that may play a major role in transmission

3.1.3. Methodology

The information recommended for use in microstratification is obtained from: (a) a review of the data at health directorates and health units; (b) interviews with health workers at health units, volunteer health promoters and community health workers, patients, and community neighbors; and (c) visits to key localities to understand the main variables related to transmission dynamics, barriers to accessing services, living conditions, and population dynamics.

This process may include two stages (Table 6): (1) analysis of the situation in the health area, municipality, or nation in the case of small countries, with the objective of identifying the main foci and operational gaps; and (2) analysis of each focus or micro-area, with the objective of organizing the operation at the corresponding level (microplan).

>Analysis of the health area, municipality, or nation (in the case of small countries):

1. Analyze the epidemiological situation in the municipality[11]

Once the area to be analyzed (e.g., a municipality or a district) has been defined, maps or sketches should be used to identify localities with malaria transmission or at risk of transmission. In urban areas, neighborhoods or sectors should be differentiated, and in rural areas, population clusters should be differentiated with as much disaggregation as possible. Table 6 details the type of information needed for the analysis. The number of malaria cases by locality of origin of infection or place of residence is the most important information in this first step. While information from the previous and current year is the most relevant in identifying localities at risk of transmission, it is essential to analyze information from previous years as well. The analysis of trends, changes over time or seasonal behavior of malaria is also useful, as well as the analysis of those sectors of possible epidemiological silence. At the end of the analysis, it will also be important to differentiate those localities with continuous transmission from localities with sporadic transmission and key clusters in the spread of transmission that should be the focus of the most important activities to interrupt transmission. In summary, this first step of the exercise is to understand the spread of transmission in the micro-stratified area.

2. Understand the key aspects of transmission dynamics in the municipality or corresponding area

The basic analysis of malaria dispersion should be complemented with contextual elements that help to explain the transmission dynamics and therefore the key elements of the response. These may include the mobility of people, access routes, distances between localities, commercial or cultural relations between localities, the flow of workers and economic activities in general. Aspects to consider in rural areas include the flow of students between urban and rural areas determined by the school cycle or population movements due to economic activities. Road and river maps and above all the knowledge of local staff is essential to guide the exercise at this point. Analysis of nominal databases or case investigation reports (in low-case contexts) will be useful to identify likely sites of infection or important elements of the dynamics such as the involvement of age groups and occupations particularly affected. Entomological information on recognized anopheline breeding sites can complement epidemiological and human mobility data when identifying localities with a major role in the export and spread of transmission.

At this point the analysis should help to identify elements such as the relationship of transmission between localities, the relationship of transmission with imported malaria and occupational activities versus household transmission, as well as cultural and social aspects affecting transmission. These elements should allow the construction of initial hypotheses that explain the behavior of malaria and its distribution and provide the main clues to define or delimit foci or micro-areas. Both the hypotheses and the delimitation of foci should, however, be complemented by an analysis of the health structure and the existing gaps in malaria care.

3. Characterization of the network structure and malaria actions in the municipality, region or corresponding area

The dynamics of malaria transmission are largely conditioned by the coverage and quality of interventions. Lack of medicines, closure of diagnostic points, and barriers to access services are among the main explanations for changes in transmission. The micro-stratification exercise is therefore only complete when analyzing the structure, functioning and failures of the local malaria care model. This analysis will allow the identification of actions and changes needed and will be the basis for the elaboration of the micro-plan. The desk analysis at the municipality or district

11 It is in line with standard operations to begin the analysis at the municipal level. However, special attention should be paid to foci that are on the border between municipalities. It is important to identify and work with these, in coordination with the neighboring municipality or municipalities, in order to respond appropriately and interrupt transmission.

level should start with the identification of the structure of the network of RDT and microscopy diagnostic posts (health units and volunteer collaborators) and their location using maps and sketches to be superimposed on the above analysis of the dispersion of the transition. At this point it is fundamental to understand the gaps in case detection, therefore the number of suspected cases and positivity per detection point is fundamental, as well as the coverage, periodicity and productivity of the active search. Understanding barriers to access due to geographical factors, cultural aspects, direct costs, problems with schedules or flow of care between health units is a key part of this analysis. At the municipal level it is essential to triangulate the data analysis with interviews with district health staff, and at the local level it is especially useful to conduct interviews with local health staff, volunteers, patients and community leaders. It is also part of the micro-stratification exercise to analyze the structure of the team responsible for the malaria response in the area, the sectorization of the territory for both malaria care and service provision in general, and how the local team is organized for supervision, investigation, active search and vector control.

4. Define the micro-areas or sectors according to where the operation will be organized in the municipality

The joint analysis of components 1, 2 and 3 should make it possible to establish hypotheses about the transmission dynamics and to propose improvements to the local response model, including the sectorization of the territory by limiting the micro-areas or foci.

>Analysis at the level of micro-areas (foci) or localities:

Once the micro-areas have been identified, fieldwork should be carried out to continue the refined analysis at the locality level, prioritizing those with the highest transmission. The objective is to identify key elements to explain transmission dynamics, identify clusters of cases, detect problems in early access to diagnosis and treatment and other deficiencies in control actions, in order to plan the necessary improvements, mainly to reduce the time between case detection, treatment, investigation and response. Analysis at the local level should be understood as a continuous analytical exercise fully linked to the supervision and routine of the designated operational teams. Among the actions to be carried out in the field to collect information, the following are highlighted:

- Observation of the community to learn about the type of housing, living conditions and the main points identified as breeding sites.
- Interview with community agents to learn about their work dynamics and the difficulties they face.
- Interview with health personnel from health units in the micro-area to learn about the limitations in diagnosis and treatment.
- Interviews with cases or relatives of cases and other members of the community to identify risk factors for transmission, barriers and behavior in seeking and accessing health services.

Table 6. Analysis to conduct the microstratification

Component		Information	Activities
1. Analysis of the epidemiological situation in the selected area (municipality, region)		• Cases of malaria, by localities • Dispersion of transmission • Localities with ongoing transmission • Localities with sporadic transmission • Key localities in the spread of transmission • Distribution of cases in the locality • Sector with clusters of cases, hot spots • Key sectors in the locality for the transmission dynamics	• Review of case records • Analysis of maps and available sketches • Interview with the health team in charge • Available entomological information • Visit to sectors with the highest number of cases, sectors identified as hot spots • Interview cases or relatives of cases in sectors with the highest number of cases (origin of cases, access to diagnosis) • Interview with community agents (review of records, instruments, transmission dynamics, time between onset of symptoms, diagnosis, treatment and investigation) • Reactive case detection, active case detection (criteria) • Visit to main points identified as anopheline breeding sites
2. Analysis of transmission dynamics and formulation of transmission hypotheses		• Malaria transmission in the localities • Relation between transmission in one locality and transmission in another • Relation between transmission in one focus and transmission in others • Relation between transmission and imported malaria • Relation between transmission through occupational activities and through household transmission • Economic activities and other aspects of social and cultural dynamics related to transmission • Relationship of cases to the location of breeding sites	
		• Formulation of a hypothesis on transmission dynamics and initial identification of micro-areas	
3. Analysis of the malaria operation and of the network	Diagnosis	• Location of microscopy stations • Location of rapid test sites • Number of microscopists and volunteer workers • Access to diagnostic posts in each locality • Operational model of the diagnostic process • Location of volunteer workers, their distribution, roles, supervision strategy, and access to locations • Cultural aspects that may limit access to and opportunity for diagnosis • Time between onset of symptoms and diagnosis	• Interviews with the health team • Analysis of maps or sketches with location of posts • Analysis of distances and care routes • Review of laboratory records • Review of treatment records if available • Review of available medicines • Inventory records. • Review of investigation and response records if available • Interview with community agent. • Review of community agent records • Interview with patients, family and other community members
	Treatment	• Time between diagnosis and start of treatment • Availability of medications • Prescription and dispensing conditions • Measures to ensure adherence • Management of supply inventories • Cultural aspects that can limit the timeliness and quality of treatment	
	Investigation and response	• Reactive case detection: coverage and timeliness • Coverage by vector control interventions • Cultural or other aspects that limit access to and use of vector control interventions	
4. Identification of micro-areas		• Identification of foci, localities that constitute a focus • Analysis of alternatives for delineating foci	• Analysis of data obtained in components 1, 2, and 3

Expected results	• Classification of localities according to transmission (active, residual, etc.) • Delineation of malaria foci (or micro-areas) • Identification of key social and ecological aspects of transmission • Transmission hypotheses to guide improvements in DTI-R strategy • Identification of gaps in the DTI-R strategy • Identification of network strengthening needs (location of diagnostic posts, improvements in detection processes and routes, and in DTI-R)

Note: Refers to knowledge of treatment protocols, guidance to patients when prescribing medications (for example, the importance of primaquine adherence), calculation of doses by weight, and delivery of medications in appropriate containers, etc. DTI-R: diagnosis, treatment, investigation, and response.

3.2. Microplanning

Once the micro-areas have been defined and characterized, the next step is to plan or reorganize the network and the local model for implementing the DTI-R. Microplanning consists of designing the DTI-R network based on transmission dynamics, access, service structure, and existing actors, taking into account the gaps identified in characterizing the micro-areas (Table 5).

The microplan should be **brief and concise** (e.g., one page) and, rather than being an operational plan, should set forth the model for the network structure and operation needed to implement the DTI-R in the micro-area. With the exception of situations in countries with very few active foci, the idea is not to promote the development of an operational plan for each malaria focus, but rather to have a functional elimination-operation model in each focus, as well as actions to implement it. In order to make the microplan effective, the activities, costs, and tasks of the different actors should be included in the respective malaria operational plans for the corresponding administrative levels (municipality, state, region).

The microplan should establish the localities where diagnosis, through passive or active detection, are to be conducted (for example, health posts with microscopy or RDT, community agents with RDT, or agents who take samples where RDT is not available); the routes and processes involving sample collection and slide-reading posts should be defined. The criteria for planning where to locate the diagnostic points and slide collection circuits should be tailored to ensure that diagnosis is carried out according to established times in all locations:

- Parasitological diagnosis in the first 48 hours after the onset of symptoms
- Treatment should begin on the day of diagnosis
- Investigation with reactive case detection, when indicated, should be carried out within the first three days from diagnosis of the index case

Microplanning should also establish the processes and define who will be responsible for the following actions to support the DTI-R strategy in the micro-area: oversight of medications and supplies for diagnosis; quality control of diagnosis; information flows and analysis; and supervision of detection and diagnosis points.

With respect to the vector control component, it is expected that the microplanning exercise will help determine whether planned interventions with LLIN, IRS, or larval control should target the localities within the micro-area, and what main actions are required for implementation. Understanding that the organization of vector control often requires a higher level of management, it is expected that the planning of these actions, as well as the related entomological surveillance

actions, are part of the respective vector control operational plans of the level responsible for the operations (at the municipal, district, departmental, or regional level). These preventive and planned actions constitute the main component of vector control in efforts to eliminate foci, and should be differentiated from the vector control actions of the DTI-R response component, which are targeted containment measures, relevant in contexts of prevention of the reestablishment of transmission.

4.

MANAGEMENT OF MALARIA ELIMINATION ACTIONS FOCUSED ON ELIMINATING TRANSMISSION WITHIN FOCI

4. MANAGEMENT OF MALARIA ELIMINATION ACTIONS FOCUSED ON ELIMINATING TRANSMISSION WITHIN FOCI

The model for managing malaria at the focus or micro-area level requires ongoing operational coordination, supervision, and support for local teams. This section deals with the set of actions aimed at coordinating efforts to implement the local model as it has been defined in the microplan. These actions, referred to here as "focus management," are essentially actions of coordination, supervision, support, and monitoring of DTI-R operations.

4.1. Coordination of the local DTI-R network within the focus (microplan)

The starting point is the organization of DTI-R actions in the micro-areas; this requires a clear definition of the roles and functions of the various actors involved, along with effective coordination between them. In most countries of the Americas, malaria surveillance and control efforts involve teams from malaria or vector-borne disease (VBD) programs, epidemiological surveillance agencies, and health services. At the micro level, the roles of each team member and community stakeholder must be established at the municipality or district level, and a team must be formed to coordinate actions in each micro-area. Guidelines are presented below to guide actions in the various components.

>Organization of passive detection

Passive case detection should be the main element in the local malaria elimination model. Health services should incorporate passive detection efforts, even in contexts in which the malaria and vector program remains involved in the detection and diagnosis of malaria cases.

The first step in effective passive detection is to have a clear definition of a suspect case, which can vary depending on transmission and on the health personnel involved (volunteer worker, nurse, or physician) (Table 7). **The patient's care circuit should be well defined, with diagnosis accessible to all communities; health personnel should be on the outlook for the disease and provide appropriate guidance to the population.** In areas where transmission has been interrupted, it is common for health personnel to become less alert to possible cases of malaria; ongoing training is therefore a major factor in preventing transmission from being reestablished, as well as in preventing complications and death in imported cases.

Table 7. Examples of definitions of suspected malaria cases in different settings

Context	Definition of a suspected case
Transmission (> 3 cases per investigation unit per week)	• Any case of fever (current or recent) • Anemia, headache, splenomegaly, or general malaise with no other established cause
Transmission (< 3 cases per health unit per week)	• Fever with no apparent focus
Local transmission Interrupted (with no autochthonous cases)	• Fever or history of fever, with no defined etiology, and with one of the following elements of epidemiological background: ○ Travel to an area with active malaria transmission in the past year (extended to three years for areas at risk of P. vivax) ○ Personal history of having suffered from the disease in the last three years ○ Residing in or having traveled to receptive areas of a country • Person who present anemia, hepatomegaly, splenomegaly, or both, of unknown cause (with or without fever) and history of travel to areas with malaria transmission • Recipients of blood donations or transplants who present fever with no known etiology during the three months subsequent to receiving blood donations or transplants
Volunteer or community collaborator in any epidemiological setting	• Any case of fever (current or recent) • Headache, malaise

>Organizing diagnosis

In order to ensure timely diagnosis, it is first necessary to define the diagnostic posts, according to the transmission dynamics in the foci. For example, in areas with a low level of receptivity and without risk of importing the parasite, where transmission has been eliminated, the availability of diagnostic posts in municipal or district headquarters may be sufficient. In areas with transmission, diagnostic posts should be available in communities according to transmission distribution, population dynamics, and access.

Malaria programs can organize the diagnostic network based on microscopy and the use of rapid diagnostic tests (RDT), seeking to bring diagnosis closer to less accessible areas. At sites with microscopy, RDT can also be useful at times when microscopists are not working (at night and on weekends). At the local level, nationally established microscopy quality control procedures (direct control, indirect control, and supervision) should be implemented. The circuits for preparing, collecting, reading, and communicating the results of slides must be well defined to avoid fixation of the red blood cells (erythrocytes) in the thick smear and delays in the start of treatment.

>Actions to direct, guide, and stimulate demand

Improvements in diagnostic services must be complemented with efforts to secure care in health services. In situations with numerous cases, as well as when there are none, inducing demand for early diagnosis must be a central part of the intervention. People who have symptoms of malaria but do not seek out health services can have a major role as a reservoir for the parasite *(13)*. Self-medication and malaria complications are also significant issues for these populations. Hence the importance of complementing improvements in diagnostic supply with well targeted actions to encourage demand.

Actions to induce demand should be aligned with measures that address diagnostic supply barriers. Often, demand-side stimulus actions in areas with malaria are limited to generic

messages about the importance of early diagnosis. Such situations call for a different approach, with concrete messages and communication strategies that provide guidance on locally organized care routes, and that outline the solutions that have been devised to address existing barriers.[12]

In non-endemic areas, it is also important for malaria programs and surveillance systems to develop information, education, and communication actions on malaria and on what to do when travelers to endemic areas develop symptoms.

>Organizing treatment and case follow-up

In the same way that, at the focus level, it is necessary to define the diagnostic posts based on the distribution and intensity of transmission, the distribution of medications should be organized in a similar way. A general principle is that where there is diagnosis, there must also be treatment. In foci with active transmission, treatment should be available in all diagnostic points that are detecting cases. In areas without transmission, it is necessary to identify health units in each network that are equipped with antimalarials and a reference model that allows treatment to be started in the shortest time possible. Observed treatment and follow-up of cases should be conducted according to each specific situation. In settings with few cases, where failure to properly treat even one case could affect transmission, observed treatment should be the rule. In situations where there are numerous cases, it is equally desirable for all cases to be properly treated, but efforts to provide supervised treatment should not supplant case detection, in terms of time and resources. In such situations, other ways of ensuring adherence to treatment should be considered, such as improvements in packaging, graphic instructions, partial monitoring, and the use of telephone messages. Case follow-up is important to ensure that the infection has been cured. At a minimum, all cases of malaria should be tracked and a microscopy test performed, for follow-up at the end of treatment and on day 28 or 42 (depending on the combination used for *P. falciparum* malaria). In countries with very few cases, WHO suggests, when possible, follow-up on days 0, 3, 7, 14, 21, 28, 35, and 42 (and monthly for up to three months in the case of *P. vivax* or *P. ovale*, extendable to one year depending on the context), thus integrating drug efficacy surveillance into routine surveillance systems (while also constituting a component of case management aimed at ensuring cure). In the event of treatment failure, a switch to the second line of treatment is recommended.

>Organizing case and focus investigation

For each focus, it should be determined who is responsible for conducting the case investigation and focus investigation, as well as reactive case detection (RCD).

Case investigation should be initiated within the first three days following the diagnosis, in order to provide for a timely response. Personnel at the local level should conduct the investigation, using a standardized investigation form, which higher-level staff will then review, confirming case classification and establishing any necessary additional actions. This is particularly important in the phases leading up to elimination. Case investigation records are also critical in preparing the malaria-free country process.

Case investigation is conducted in all strata. In a stratum 4 with high, stable transmission, this begins and ends at the time of detection (in both the health unit and the community), and the quality of the interview and the recording of key variables related to the place of residence or possible place of infection, as well as the dates when symptoms and diagnosis occurred, is of particular importance. Weekly analysis of data can lead to the identification of clusters of

12 Examples of possible messages: "Malaria testing is available for free in health centers A, B, and C from 9 a.m. to 3 p.m. Volunteers can get free malaria testing in their communities at any time. Don't let your work schedule stop you from getting cured. Fever and feeling bad? Look for your free malaria diagnosis at any health unit."

cases based on place of residence or possible place of infection and should trigger a community investigation through RCD. In these contexts, community investigation can be useful to stimulate demand for care, and identify gaps in passive detection. Organized and systematic identification of clusters of cases may be one of the needed changes in current operations in strata with active transmission. As the number of cases decreases (three or fewer cases per week per investigation team), it becomes more feasible and important to visit the community, as part of more detailed case investigation, while at the same time conducting RCD for each case. In this context the case investigation begins at the time of detection and ends in the community, with an attempt to understand transmission dynamics. Countries that are nearing elimination need a committee of experts to review all investigation forms to provide official confirmation of the classification of each case; if implemented in a timely fashion, this should strengthen surveillance and response actions, and facilitate the process of certifying elimination.

When a potential new active focus is identified, focus investigation and case investigation often occur simultaneously. A local epidemiologist, malaria technicians, and, ideally, an entomologist, are responsible for conducting outbreak investigations. The main objective is to determine whether vector transmission has occurred. A focus investigation involves identifying and delineating the affected locations, determining the population at risk, vector species present, breeding sites, and risk factors contributing to transmission. When a case appears in an already investigated and classified focus, there is no need to repeat the investigation, since the status will be updated periodically, for example, at six-month intervals. However, in the event of an outbreak in a known focus, or if a species of parasite different from the current one is identified, the investigation needs to be updated in order to detect any new factors responsible for transmission.

>Organizing active detection

Annex A includes a detailed definition of the concepts of passive, proactive, and reactive detection.

Proactive case detection is aimed, above all, at special and mobile populations that have difficulties in accessing health services. This detection (generally of individuals with fever) should be systematically planned in stratum 4, in areas with active or residual foci, as well as in stratum 3, where there are vulnerable and receptive areas.

Reactive case detection is part of the response to a case or cluster of cases. It involves an additional case-detection effort once a case has been identified, since cases tend to appear near other cases. In addition to detecting more cases and thus helping shrink the reservoir, RCD can identify needed improvements in diagnostic services (improving passive search), raise awareness of the importance of consulting health services if symptoms occur (stimulating demand), emphasize the need to use insecticidal nets, and determine whether the population has nets and whether their homes have been sprayed. RCD is also considered during the focus investigation, in order to identify the at-risk population and the extent of transmission.

How RCD is organized varies according to disease burden and receptivity. Examining the area around a case helps to identify the layout or proximity of houses, whether vectors are present, and possible breeding sites. During the investigation of a focus, in situations where there are very few cases or little risk of reintroduction, this examination of the area should guide subsequent entomological investigations. If vectors are found, the investigation team should delineate the area at risk of continued transmission. This delineated area determines the area in which vector control and reactive detection can be applied. Annex C includes several examples to assist countries in these detection efforts, based on the stratum and disease burden.

>Local model of DTI-R monitoring

The process of monitoring DTI-R at the local level must be well organized and systematized, according to the level involved. The main supervision actions consist of overseeing detection and diagnosis posts and other health units in the network, to include the following aspects:

- Ensure adequate passive detection, suspected cases of malaria, and application of fever algorithms where malaria is part of the differential diagnosis (community agents and health units)
- Use of RDT by community agents and health units
- Preparing and sending slides, and handling related information
- Prescribing treatment, counseling, patient follow-up, and treatment monitoring
- Availability of microscopy supplies, and channeling slides to the laboratory
- Management of antimalarials, inventories, and other supplies such as RDT
- Information management (collection, entry, and analysis)
- Conducting reactive detection and instituting measures to respond to cases or clusters of cases that have been detected, requiring additional detection actions

Volunteer workers and other community agents should be subject to continuous supervision. Limitations in transportation can hinder such supervision; health workers should therefore seek creative solutions and coordinate with other programs to implement them.

The frequency of monitoring depends on the context and operational challenges. Overall supervision of actions in the focus should be conducted at least once a month. The management team should have a tool or checklists that allow for the systematic supervision and recording of the operation's status. A supervision form for detection and diagnostic posts serves as the main instrument in DTI-R supervision. Annex D provides suggestions for the contents of such a tool, to be adapted according to the context.

Quality control of the microscopic diagnosis requires specialized supervision of microscopists and laboratory staff, as a supplement to performance evaluations (direct control) and slide cross-check (indirect control). Such actions should be coordinated by the appropriate level of the laboratory network. More simplified actions regarding preparation of slides, staining, availability of supplies, and sending slides for quality control should be part of the routine supervision cited in the previous points.

Decisions resulting from supervision: Supervision should help guide improvements and indicate tasks to be carried out by staff at the point of care, as well as by the supervisor. This chiefly involves corrections to procedures, training, provision of inputs, improvements in care procedures, and changes in strategy (intensification of passive vs. active detection). A distinction should be made between decisions that are to be made in the field at the time of supervision, and other decisions made when monitoring implementation of the local strategy (based on supervision reports and other information). Some of these decisions are described in 4.4 as information analysis.

4.2 Management of medications and supplies

Ensuring an adequate supply of antimalarials for treatment points is one of the ongoing challenges facing malaria programs, and one of the main problems in local management.

Based on historical behavior, decisions should be made about where and how many treatments should be available for uncomplicated cases and for severe malaria to ensure timely treatment. The continuous supply of antimalarials at points of care is a priority task for which systematic monitoring should be developed and responsibilities of the local team should be established.

4.3 Coordination with other levels and actors

A key aspect of organizing DTI-R operations is the need for multi-stakeholder management, beyond those directly involved in the malaria response. At the intra-sectoral level, this involves interaction with the entities responsible for providing first-level services and basic care, which play a major role in improving passive case detection. Equally important are the bodies responsible for health-promotion strategies, community participation, epidemiological surveillance, and supply management (for diagnosis and treatment). Management of these public health processes are directed to a great extent from a higher level within the system, which has little interaction with the focus-level team, which is why it is so important to have a coordinating level ensuring these actions.

Coordination with other actors also includes ongoing dialogue and coordination with local officials and leaders (mayors, indigenous authorities, community leaders, and other local government authorities), aimed at promoting community participation and overcoming cultural and social barriers to the implementation of DTI-R actions. This also involves dialogue with the private sector, and with productive sectors that could play a leading role in improving supply and in addressing barriers to passive detection and joint active-surveillance efforts.

4.4. Planning and coordination of vector control measures

Unlike the DTI-R processes described above—where it is expected that a local team (at the focus or micro-area level) will conduct periodic supervision and analysis, and ongoing reorganization of the basic operation—, responsibility for vector control operations usually lies with a higher level of management (municipality, district, region, department). During microstratification and microplanning, the local team should provide the necessary information so that vector control planning by the relevant level includes the focus, and it should establish the appropriate coordination for implementing LLIN and IRS, as well as entomological actions, if necessary.

With regard to vector control measures, there are two types of actions: (1) proactive actions, planned on the basis of stratification and microstratification; and (2) reactive actions triggered by the detection of a case or cluster of cases in an area with very low or no transmission –part of the "response" component of DTI-R.

- In terms of planned vector control actions, as a general rule, the entire population living in active and residual foci (stratum 4) should be systematically protected with LLIN or IRS (planned operations), depending on which of these interventions is best suited to the local conditions. In countries with large areas with active transmission, however, this requires a prioritization exercise. On the other hand, the decision to maintain vector control in stratum 3 (receptive and at risk of importation) will depend on the degree of receptivity and vulnerability. Thus, in an area that is highly receptive (due to the presence of a very aggressive vector such

as *An. darlingi*) and highly vulnerable (importation of parasites from endemic areas), focused and selective coverage must be maintained, using vector control interventions to optimize the use of available resources. Strata 1 and 2 will not require the use of vector control. The main focus should be on highlighting the importance of vector control as a preventive measure, one that is properly planned and not limited to response measures.

- In the context of investigation and response to a case of malaria, if the case appears within a known active or residual foci, the population should already be protected by vector control activities *(14)*. In such a situation, the case investigation should provide key information (date of last house spraying, whether insecticidal nets are being used) on the need for additional actions. If the case appears in a receptive area not protected by LLIN or IRS, the home where the case has been identified, along with the surrounding area, should be sprayed or protected with LLIN, as part of the response, within the first seven days following diagnosis. As mentioned earlier, reconnaissance of the area around a case will help identify houses and mosquito breeding sites, and, together with entomological screening, help determine the need for vector control actions.

Detailed information on malaria vector control planning and entomology is provided in WHO reference documents *(4, 14)* and in PAHO operational documents.[13]

4.5. Data management and analysis

Data analysis provides the intelligence for a malaria operation and it is a function of the local team. The operation must be analyzed at the level of foci, micro-areas, or other types of operational sectorization established by the model.

Data analysis at the micro level should be conducted weekly, so that changes in transmission can be detected in time for an appropriate response to be made (Table 8). Provided that malaria staff and epidemiologists are available, they should try to hold at least one monthly meeting to jointly update the malaria situation. Micro-area health staff (health unit personnel and volunteer workers) should develop analytical skills to guide their actions.

Frontline staff involved in detecting and reporting cases should also be primary users of the information. Whatever the local management model, one person should take on the permanent role of coordinating information processes for the focus involved, including overseeing regular weekly analyses, providing detection points with feedback, and periodic reporting at the appropriate levels.

>Minimum data to be generated and consolidated for management of a focus:

- Number of new cases, by place of residence, probable place of infection, place of diagnosis, and type of notification unit (volunteer worker, health post, etc.).
- Number of samples examined, and positivity rate by locality14 and by diagnostic post (microscopy or RDT).
- Number of samples examined, and positivity rate according to active versus passive case detection, in order to guide decisions about where diagnostic coverage needs to be increased.
- Cases per species.

13 For more information, see: Malaria [Internet]. Washington D.C.: PAHO. Available at: https://www.paho.org/en/topics/malaria.

14 Locality can refer to a village, community, neighborhood, district, or other population grouping, such as land parcels or lots.

- Time between onset of symptoms, diagnosis, treatment, investigation, and response.
- Patient follow-up, including percentage of patients with supervised treatment.
- Cases by age and special groups (e.g., pregnant women).
- Percentage of cases investigated; local cases versus imported cases.
- Inventory of localities, expansion of the micro-area.
- Coverage of vector control interventions by locality.

Analyses should include the following:

- Analysis of the malaria care points that are reporting.
- An analysis of suspected cases by parasite species, and by passive and active case detection, as well as by locality and diagnostic post. This analysis will help to determine whether adequate surveillance is being conducted, and by whom (the malaria team conducting active case detection, or the health services carrying out passive case detection), in order to take appropriate action to improve the operation, if necessary. Analysis of demand, barriers to access, and reasons for low demand for care should be a major analytical element.
- An analysis of confirmed cases by place of residence and diagnosis. Such analysis allows for the identification of localities with cases, and for early detection of malaria foci, new cluster of case, and any decrease in the number of cases, which helps verify the effectiveness of existing efforts. This analysis should be completed with a more detailed study of diagnosis and response times.
- The diagnostic positivity rate, based on an analysis of cases examined, and the positivity rate for cases at diagnostic posts or localities, helps determine the need to intensify detection activities and reorient passive versus active case detection efforts.
- Analysis of diagnosis and response times. Systematic analysis of the times between symptom onset and diagnostic testing, between testing and results, between results and treatment, and between results and reactive case detection can help identify weaknesses in the health system and help reorganize for more rapid interventions.
- Follow-up of patients after they receive treatment is critical in ensuring that cases are cured, and to raise awareness of problems related to the effectiveness of treatment.
- The distribution of cases by age and vulnerable groups makes it possible to identify risk and make changes in the detection strategy (active case detection, passive case detection, location of diagnostic posts, schedules for testing).
- Maintaining updated information on localities or communities that are part of the focus or micro-area; thus, if there is an expansion in cases, this helps to define the geographic boundaries and areas requiring intervention.

Decisions made on the basis of the information analyzed include:

- The need to increase the number of diagnostic posts (expansion of the diagnosis and treatment network).
- Relocation of diagnostic posts.
- Changes in the hours that diagnostic posts are open to the public.
- Workload distribution at the diagnostic posts.
- The need to increase detection of suspected malaria cases at detection points.
- The need to conduct actions directed at promoting and stimulating demand among the population, or to eliminate barriers to management of febrile patients.
- Make any necessary adjustments between passive and active case detection efforts.
- The need for training or other actions to increase diagnostic capacity.
- The need for more human resources to help with case investigation and treatment supervision.
- The need to increase support for community health worker networks and available services in order to increase supply of community services.
- The need to improve data recording and information processes.
- Review of prioritization of localities targeted for vector control, and adjustments in coverage of LLIN and IRS.
- The need for actions involving LLIN use and maintenance, and acceptance of IRS.

Table 8 presents examples of the use of information for decision-making in reorganizing operations in foci or micro-areas.

Table 8. Examples of data analysis in micro-areas to improve malaria detection and diagnosis

Information	Findings	Decisions
• Number of new cases, by place of residence, probable place of infection, and place of diagnosis. • Number of persons examined, and positivity rates according to neighborhoods and by diagnostic post (microscopy or RDT) within the sector. • Number of persons examined, and positivity rates as ACD versus PCD. • Cases by species (detection of cases of P. falciparum in settings with no transmission). • Parasitic monitoring of patients. • Diagnosis and response times.	Identification of case clusters or groups of households with cases	• Increase the demand for services for febrile individuals. • Relocate microscopy or RDT posts. • Review of RCD actions.
	Low number of febrile individuals who come in based on passive demand (unit, volunteer workers, and others)	Communication to address demand from febrile individuals.
	High positivity by PCD	• Increased demand for services by febrile individuals. • ACD actions.
	Low number of tested by reactive case detection with respect to new cases	Intensify RCD
	New cases in epidemiologically silent sectors	• ACD actions. • RCD actions.
	Cases of *P. falciparum* after weeks with no cases	Intensified RCD actions.
	Adherence failures	Improvements in prescribing and adherence strategies
	Therapeutic failures	Use of second-line treatment
	Detection of pregnant women with malaria	Ensure follow-up of mother and newborn.

ACD: active case detection; PCD: passive case detection; RCD: reactive case detection; RDT: rapid diagnostic test.

4.6. The DTI-R management cycle

The organization of anti-malarial actions at the focus level (DTI-R) is a dynamic effort, requiring adjustments to accommodate changes in transmission. Thus, microstratification and microplanning are not one-time actions, but are rather part of a management cycle. Based on an initial analysis of the situation, a package of activities is proposed to enable the DTI-R to effectively reduce and interrupt transmission. This intervention should be monitored through systematic data analysis, in order to determine the response. The greater the understanding of how malaria transmission behaves, the more effective the planned DTI-R actions will be. Analysis at the focus level should be continuous; periodically, for example every six months, the situation in the micro-areas should be updated to ensure that the response plan remains appropriate.

4.7. Local malaria management models and focus management teams

The organization of malaria actions at the local level and in each focus of transmission is the essence of the elimination strategy. The organization of this local model differs from country to country and within countries, and depends on the following factors, among others: (1) the type of health system; (2) how the malaria program is integrated in the health services network; (3) the structure of the area's basic health team; (4) the structure of the malaria program; (5) the size of the territory and (6) the level of malaria transmission.

Accordingly, there will be situations in which (due to the limited structure of the local team) coordination of foci operations is overseen entirely by a higher-level team or by malaria-program officials; or situations in which there are strong local teams that integrate their actions with those of the network of health units they oversee. In general, the simpler the local team is, the greater the need for support and supervision in managing the malaria foci. The following examples outline various situations to illustrate differences in local management:

- Malaria-endemic areas, where the local team responsible for implementing DTI-R in the focus area is integrated by basic health units, with health posts that have only auxiliary staff, health promoters, or volunteers; or where the health units, despite having permanent or temporary professional staff, are limited in their capacity for extramural actions. In such situations, it is essential to have a support team with one or more people, depending on the size of the area, each with specific tasks and logistic capacity for mobilization and field supervision of the diagnostic posts.
- Situations in which the malaria focus is in an area with a health micro-network led by a permanent professional team, with comprehensive public health surveillance functions, and designated personnel to oversee logistics for extramural actions. In such cases, the team must oversee coordination of the local operation and most of the actions. Ideally, there is a support team, represented in the field by an official who facilitates coordination with the higher level (municipality or region).
- In situations where there is a vertical program structure, field inspectors, duly deployed based on the distribution of the foci, can assume the tasks of field supervision, with assistance from the operational bases, in the areas of management, training, handling of supplies, and information. Depending on the local model, these malaria program officials may either be part of the local team or members of the higher-level support team.
- The model may also consist of a multidisciplinary team (local team or vector program team) responsible for coordinating various foci within its territory, with officials responsible for conducting field supervision in specific sectors (foci).

- In all cases, the model involves having a multidisciplinary team at the administrative health level for each focus (municipality or region); this team provides technical and administrative support for implementing the microplan, and for coordinating with higher-level (regional or national) management.

Within all of these models, it is important to have in place a team responsible for coordinating malaria operations in each focus.

4.8. Supporting elements for eliminating malaria foci

There are programmatic and strategic developments at the national level that enable the necessary operational changes to transform active foci into eliminated ones in a way that is locally sustainable. The basic elimination operation (DTI-R) triggered by each case, along with the corresponding vector control actions, requires a supporting regulatory framework and public health structure. This requires developing and strengthening primary health care networks and epidemiological surveillance. The national malaria elimination strategy or plan must create the necessary platform for moving from control to elimination, and develop a management model which, to be sustainable, requires increasing interaction with other stakeholders. While these components are beyond the scope of this manual, they are cited here in order to emphasize the connection between the local malaria operation, as described here, and national processes.

These essential components for management of a national malaria program are as follows:

- A policy and regulatory framework that ensures universal access to malaria diagnosis, treatment, and surveillance through the health services.
- Management mechanisms to coordinate with service networks and primary health care systems
- Development of a laboratory network and quality assurance system for microscopy and RDT
- Information systems and analysis at various levels
- Policies for procurement, distribution, use, and surveillance of antimalarial drugs
- Policies for the development and promotion of human resources in health, in areas where malaria is prevalent
- Development of an entomological surveillance network
- Policies for financing, procurement, distribution, and management of interventions with LLIN, insecticides, and IRS
- A management platform, and relationship frameworks, for intra- and inter-sectoral management of malaria

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MONITORING AND EVALUATION

5. MONITORING AND EVALUATION

At the local level, malaria interventions should be guided by changes in transmission dynamics, indicators of detection efforts, and other findings in malaria surveillance, such as the identification of new cluster of cases. The local model should be adjusted accordingly. The WHO Malaria surveillance, monitoring and evaluation: a reference manual *(4)* sets forth indicators and guidance for monitoring and evaluating malaria programs (Annex E). The transformation of active malaria foci into residual non-active foci, and finally into cleared foci, along with the consolidation of malaria-free subnational territories, is the ultimate objective of this manual, and should be the main objective of the evaluation, based on available indicators and information.

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14. World Health Organization. Guidelines for malaria vector control. Geneva: WHO; 2019. Available at: https://apps.who.int/iris/handle/10665/310862

GLOSSARY

Malaria risk stratification. The World Health Organization defines malaria risk stratification as the classification of the geographic areas or localities according to factors that determine receptivity and vulnerability to malaria transmission.[15]

Malaria stratification. Classification of geographic areas or localities according to epidemiological, ecological, social, and economic determinants for the purpose of guiding malaria interventions.[1]
Diagnosis, treatment, investigation, and response (DTI-R) strategy. Basic action for the elimination of malaria, triggered by the detection of a case or a cluster of cases, which prioritizes access to diagnosis, early treatment and the importance of an additional detection effort. The DTI-R seeks to operationalize in the Americas the concept of surveillance as an intervention promoted by the WHO in the Global Technical Strategy against Malaria.

Malaria focus. WHO defines malaria focus as "A defined circumscribed area situated in a currently or formerly area that contains the epidemiological and ecological factors necessary for malaria transmission."[16] Foci are classified as active, residual non-active, and cleared (see Annex A).

Focus investigation. This means identifying the main features of a location (focus), including the population at risk, the burden of disease, the distribution of vectors responsible for malaria transmission and the underlying conditions that support it.[17] In this manual, reference is made to the "identification and characterization of foci" and to "microstratification" as actions similar to the investigation of foci; and in order to simplify and facilitate operationalization, the three terms have been considered equal. It is clarified, however, that the concepts have certain different connotations. The focus investigation is designed especially for situations of low transmission, reintroduction, or transmission concentrated in very few locations, and generally includes actions to establish the existence of vector transmission. The other two terms, widely used in this manual, apply to situations of greater dispersion of transmission and the need to organize and monitor the operation of malaria (especially the diagnosis and treatment network) at a very local level, in sectors or operative units (micro-areas) that may include one or more foci.

Micro-area. Group of foci or clusters of localities that share the same transmission dynamics and are epidemiologically interconnected among them, mainly due to the movement of the population. The sectorization of the local health services and the logistics of operations are important elements in this exercise. Addressing these foci in a holistic approach is a key element towards the objective of transforming the active focus into cleared ones.

Microstratification. This manual defines microstratification as the identification and characterization of foci or micro-areas in order to plan a response. This is an exercise of analysis at the local level with triangulation of information from different sources to organize malaria elimination actions at the local level.

15 World Health Organization. Malaria terminology. Geneva: WHO; 2016. Updated March 2018. Available at: https://www.paho.org/en/documents/who-malaria-terminology-2016-updated-2018.

16 World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/bitstream/handle/10665/254761/9789241511988-eng.pdf.

17 World Health Organization. Malaria surveillance, monitoring, and evaluation: a reference manual. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf.

Microplanning. This manual defines micro-planning as the local exercise of organizing the DTI-R in a focus or micro-area. More than an activity plan, it involves establishing the structure, roles, and care routes of the local network (the points of care and community actors necessary to ensure DTI-R actions in the required times. Microplanning establishes the response to microstratification.

ANNEXES

ANNEX A. ADDITIONAL NOTES ON FOCI INVESTIGATION, CASE INVESTIGATION AND DTI-R

Malaria focus

A malaria focus is a "defined and circumscribed zone situated in an area that is or has been malarious and in which the necessary epidemiological and ecological factors are present for the transmission of malaria."[1] A focus includes all components needed for the life cycle of an infection or parasite without influence from external factors. It takes into account the larval habitat, feeding, and resting sites of the vector, and places frequented by people in the course of their activities, especially at night. For the purpose of malaria surveillance, the term focus refers to a defined area in which transmission persists during the final phases of elimination.[2]

This document uses the concept of focus, from an operational perspective, to delimit an area or a set of urban or rural localities (micro-areas) that must be addressed jointly due to their geographic proximity and because they share the same transmission dynamics. The approach promoted in this manual gives special importance to access to detection and diagnosis as catalysts in the chain of elimination actions. For this reason, to delimit a micro-area, much more importance has been given to understanding the population dynamics, the social links between localities, and other elements that determine the organization of the diagnostic and surveillance network, than to the entomological factors so vital to the concept of malaria foci described above. It should, however, be clarified that, for the purposes of investigating and management of new foci, or for planning specific vector control interventions, including larval control, the original concept should be used.

The aim of characterizing and delimiting a malaria focus is to launch interventions designed to interrupt transmission or prevent the reestablishment of transmission. In the event of a new foci, the local team should begin an investigation within seven days of diagnosis of a malaria case. During this foci investigation, data are collected on the population at highest risk (determined, among other factors, by active case detection and routine data), presence of the vectors responsible for transmission, and other factors or conditions that determine the dynamics of transmission.

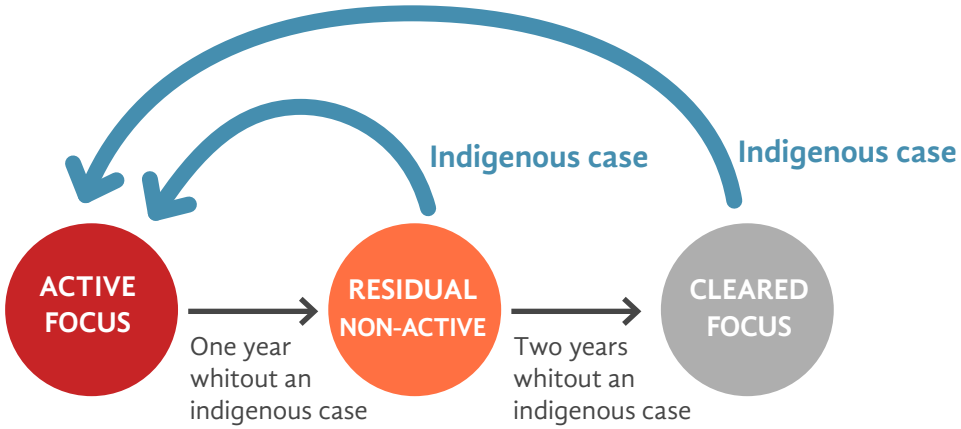
The new framework for malaria elimination simplifies the former classification of seven foci, and instead proposes three types of foci (see Figure A1):

- **Active:** indigenous cases detected during the current calendar year.
- **Residual non-active:** the last indigenous case was detected in the previous calendar year or up to three years before.
- **Cleared:** no indigenous cases for three or more years.

1 World Health Organization. Malaria terminology. Geneva: WHO; 2016. Updated March 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/208815/WHO_HTM_GMP_2016.6_eng.pdf?sequence=1.

2 World Health Organization. Malaria surveillance, monitoring, and evaluation: a reference manual. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf.

Figure A1. Classification of malaria foci



Two considerations should be taken into account when conducting the focus investigation:

a. In localities with ongoing local malaria transmission, i.e., in active foci, the aim of the investigation is to guide the planning of routine malaria elimination activities. The investigation of foci in these localities is not intended to prove that there is transmission in the foci, but to characterize the foci in order to organize DTI-R (diagnosis-treatment-investigation-response) and vector control in the affected localities in the foci.

b. In localities where there is no local malaria transmission, i.e., in residual non-active or cleared foci, the objective in this case is to determine whether vector transmission is present, to know the risk factors and to determine the response. Therefore, in these situations the entomological component is particularly important.

The Malaria Elimination Framework[3] states that a single autochthonous case in an area where the epidemiological and ecological factors necessary for malaria transmission are present constitutes an active focus. As transmission declines, the occurrence of a single autochthonous case in a locality is not a rare event and often leads to dilemmas for operational teams as to whether transmission actually exists and whether the area should be classified as an active outbreak. While these isolated cases may often be relapses[4] (in the case of P. vivax), they could also be introduced cases, in a situation where the imported case has not been identified. Therefore, in situations of very few cases and very focused transmission, when there is doubt about the existence of transmission, it is recommended to include these localities with isolated cases in the foci register. Inclusion in the foci register will ensure that they are monitored and effective action is taken to prevent reintroduction.

3 World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/handle/10665/254761.

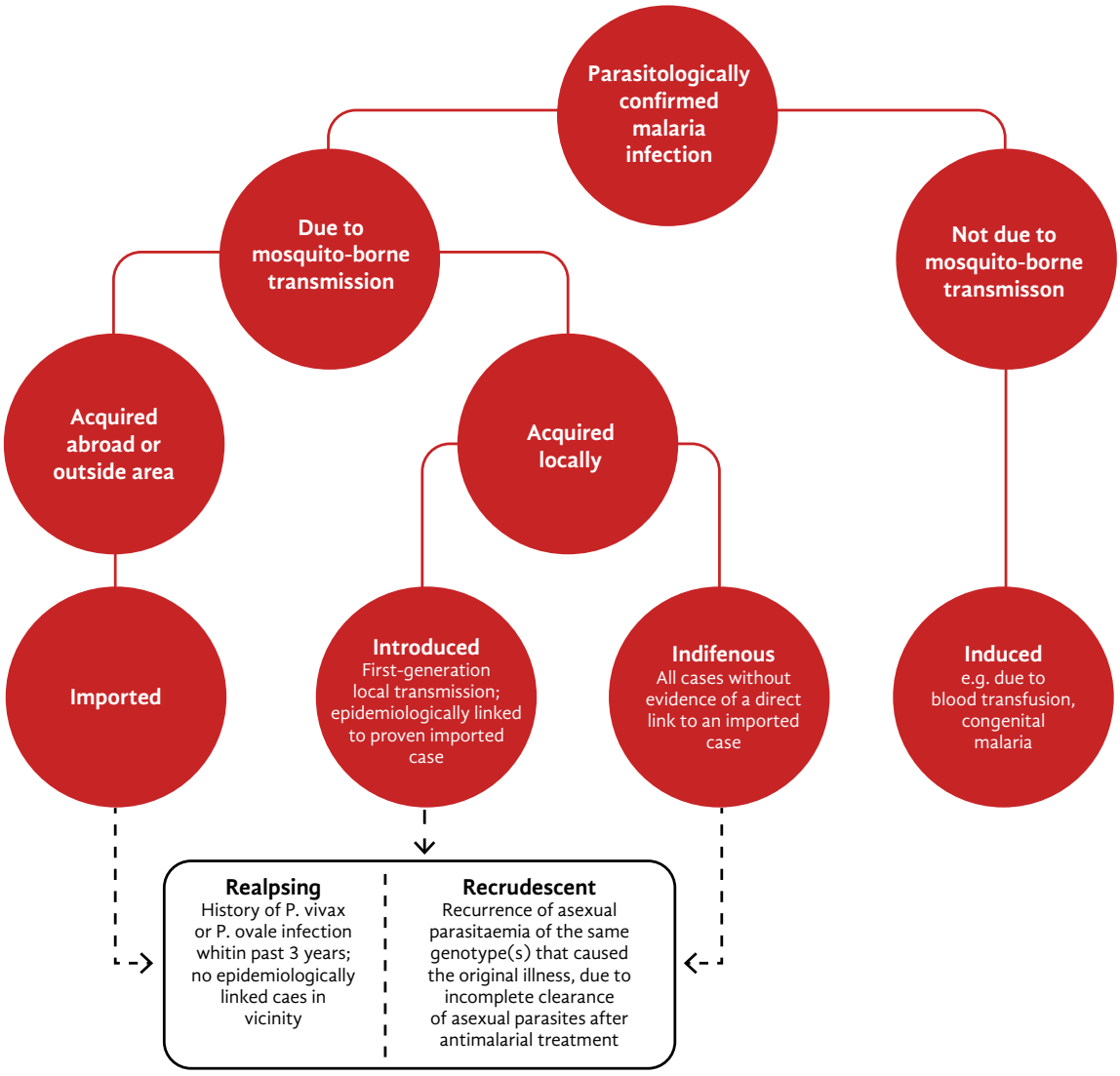
4 In the analysis of possible relapse cases, it is important to recognize that the period from first infection to relapse may be longer than the country's operational definition (usually 6 months), or to consider that *P. vivax* primary infection may have existed even if it was not diagnosed, i.e., because it was an oligosymptomatic episode or because it was treated elsewhere.

Case investigation

Case investigation is the "collection of information to allow classification of a malaria case by origin of infection, i.e., imported, indigenous, induced, introduced, relapse, or recrudescent."[5] Knowing the **origin of the infection** (probable place of infection) is especially important when countries are close to elimination and preventing reestablishment of transmission.

Case investigation should begin within three days from notification of the confirmed case. It begins at the point of care and ends in the community (patient's house or workplace) when feasible (if there are few cases). During this process, the patient's personal information is collected; current illness, including date of onset of symptoms, information on diagnosis and treatment; history of previous malaria infections; travel history; history of transfusions that could explain the infection; places where patient has spent the night; and other questions that help to: (i) determine how and where the patient could have contracted the infection; and (ii) inform response actions and transmission containment. Case classification is presented in Figure A2.

Figure A2. Classification of malaria cases



5 World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/handle/10665/254761.

Passive, reactive, and proactive case detection

There are several types of case detection actions:

- **Passive case detection**: The patient proactively visits a health center for diagnosis and treatment. This is the basis of malaria surveillance and requires health personnel to suspect or be aware of malaria. Passive case detection fails if people will not or cannot seek health services on their own, if health service coverage is very low, or if health personnel are not appropriately trained, do not suspect malaria, or do not have access to diagnostic tools.

- **Active case detection**: The health staff or community health worker takes the initiative to find the patient in the community. This involves an effort additional to that of passive case detection. It is important to conduct in areas of elimination, in order to detect: (i) symptomatic cases not diagnosed by passive case detection; and (ii) asymptomatic cases existing in the community, in the context of focus investigation. Active case detection is divided into proactive and reactive case detection.

- **Proactive case detection**: Conducted in at-risk populations (mobile populations, indigenous communities without access to health services, etc.), without being triggered by diagnosis of a confirmed case. Depending on the situation, it may be a one-time action or be conducted regularly, i.e., every 1-2 weeks, depending on whether it is a response action or a planned activity in scenarios where it has not been possible to implement passive detection. In the context of preventing the reestablishment of transmission, the analysis of the risk of parasite importation is a key element to guide such actions. Proactive case detection can be done with rapid diagnostic tests (RDT) or microscopy and scheduled during periods of greater transmission. To be successful, it should be done at a time when the population is traceable.

- **Reactive case detection**: Conducted after notification of a case or cluster of cases. The principle of reactive detection is the recognition that when transmission decreases, cases tend to be concentrated, so that the probability of getting infected would be higher for those living in the same household as a malaria case.[6] Reactive case detection should be conducted among cohabitants, in a radius around the index house (i.e., 200 meters in an urban area, 1–2 km. in a rural area), or in the entire focus. Reactive case detection is also conducted during foci investigations. If the focus is new, coverage of detection should be broader; if the focus is known, detection can be more targeted to the at-risk population. The purpose of reactive case detection is transmission containment and focus investigation. As previously mentioned, for reactive case detection to be successful, it must be conducted when the population is traceable.

DTI-R components

>Diagnosis

All suspected cases should be diagnosed using microscopy or RDT in the first 48 hours from onset of symptoms. The goal of prompt diagnosis and treatment is to reduce morbidity and mortality and interrupt transmission.[7] In low transmission contexts, with few confirmed cases each year, the objective of diagnosis and treatment within the first 48 hours from onset of symptoms remains

6 Van Eijk AM, Ramanathapuram L, Sutton PL, Kanagaraj D, Sri Lakshmi GP, Ravishankaran S, et al. What is the value of reactive case detection in malaria control? A case study in India and a systematic review. Malaria Journal 2016;15(67); UCSF Global Health Group, Background Paper. Screen and treat strategies for malaria elimination: a review of the evidence. San Francisco, United States. Institute for Global Health Sciences University of California; 2018.

7 World Health Organization. Global technical strategy for malaria 2016-2030. Geneva: WHO; 2015. Available at: https://apps.who.int/iris/handle/10665/342995; Ngwa C, Rosa T de A, Pradel G. Current topics in malaria. London: INTECH; 2016. Available at: https://www.intechopen.com/books/current-topics-in-malaria/the-biology-of-malaria-gametocytes.

the objective. Universal access to prompt diagnosis must be ensured, regardless of the number of cases the country is experiencing. Microscopy and RDT together can assure that a country reaches universal diagnostic coverage in remote areas and in any situation where it is not possible to ensure early diagnosis by microscopy. RDTs can bring diagnosis closer to the communities and prevent excessive workload for laboratories. The implementation of RDTs should be a programmatic action that ensures adequate quality and use, while maintaining the capacity and sustainability of the microscopy network, which continues to be the "gold standard".[8]

To achieve adequate access to diagnosis and treatment, determinants of access to health services and quality of care (coverage and effectiveness) are important. Universal coverage for diagnosis and treatment means that the entire population, including the migrant population and other minority groups, must have access to the services they need without financial risk to the family.[9] The extension and improvement of quality health services should be promoted whenever possible. When institutional health services are not available, the support of community health workers, mobile health services, and active case detection should be considered.[10]

Because parasitological diagnosis is a condition for treatment and case reporting, access to diagnosis is the trigger for the chain of elimination actions. Without proper diagnosis there is no treatment, no investigation, no information on malaria case distribution, no way to stratify risks or identify foci, and therefore, no guidance for vector control and no response. Access to prompt diagnosis continues to be a challenge in malaria-endemic countries in the Americas.

>Treatment

All positive malaria cases should receive appropriate treatment based on national protocols, beginning the same day that laboratory results are received. Health personnel are responsible for providing proper treatment. When health service coverage does not reach the entire population, efforts should be made to extend the services network. Because of the time this takes, countries should consider authorizing community health workers to prescribe treatment in order to avoid delays that could cause clinical complications and promote the persistence of transmission.[11]

>Investigation

Case investigation should be conducted within three days from diagnosis. Countries should establish criteria to determine where and when to conduct case investigation, as well as the roles within the health unit and procedures for conducting an investigation within the stipulated time. Details of case investigations and the team in charge will vary based on health service coverage and number of cases occurring in the community. When there are many cases, investigation starts and ends at the diagnostic point. If there are few cases, investigation ends in the community within three days from diagnosis. Reactive case detection (described in the response component below) also has an investigative component – focus investigation – to identify new cases that could be occurring in the community. Guidance is provided at the end of this annex to orient countries in establishing criteria for when and where to conduct malaria case investigation in the community in their surveillance guidelines.

8 World Health Organization. Policy brief on malaria diagnostics in low-transmission settings. Geneva: WHO; 2014. Available at: https://apps.who.int/iris/handle/10665/338353.

9 World Health Organization, World Bank. Tracking universal health coverage: 2017 global monitoring report. Geneva: WHO; 2018. Available at: https://www.who.int/healthinfo/universal_health_coverage/report/2017/en/.

10 World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/handle/10665/254761. Whitty C, Chandler C, Ansah E, Toby L, Staedke SG. Deployment of ACT antimalarials for treatment of malaria: challenges and opportunities. Malaria Journal. 2008;7(S1):S7.

11 Whitty C, Chandler C, Ansah E, Toby L, Staedke SG. Deployment of ACT antimalarials for treatment of malaria: challenges and opportunities. Malaria Journal 2008;7(S1):S7; Young M, Wolfheim C, Marsh DR, Hammamy D. World Health Organization/United Nations Children's Fund Joint Statement on Integrated Community Case Management: an equity-focused strategy to improve access to essential treatment services for children. American Society of Tropical Medicine and Hygiene. 2012;87(S5):6-10.

>Response

Reactive case detection

All malaria cases or cluster of cases should lead to prompt detection and treatment of other possible cases. This action can begin with case investigation (in the first three days from diagnosis) and always within seven days from onset of symptoms.[12] Local health services should be organized to respond in the specified time. As mentioned earlier, reactive case detection has an investigative component (detection of cases in the focus, barriers to access of health services, populations not protected by vector control actions, risk of importation of cases) and an intervention component (reducing the number of individuals with parasites). Each malaria case should be investigated, reactive case detection should be conducted for potential cases among the patient's contacts (cohabitants first, then close contacts), and all positive cases should be treated. The epidemiological situation should dictate the level and extent of reactive case detection.

Regardless of whether the case is classified as indigenous or imported, reactive detection should be performed, at a minimum, among co-travelers (if the case is imported) or among cohabitants of the index case (if the case is local), or co-workers (if transmission is considered to have occurred in the workplace), whether they are symptomatic or asymptomatic. The same person who diagnoses the index case and initiates the case investigation should perform reactive detection without waiting for a higher-level team. Where there are numerous malaria cases (more than 3 cases per investigation team per week), investigation and reactive case detection in response to each case loses epidemiological relevance and may place an operational burden that is impossible to take on. In such situations, the concept of DTI-R (as a programmatic activity to detect more cases) is also considered essential, but it translates into a set of systematic demand-stimulating actions (family members or cohabitants) and RCD operations triggered by the identification of clusters of cases (e.g., asking patients to bring any contacts that may have malaria to health services, or considering clusters of cases in higher prevalence areas for reactive case detection). Thus, RCD contributes to malaria surveillance, and consists of a systematic effort to analyze the dynamics of transmission and recognize clusters of cases, in order to identify gaps in passive case detection and other measures that together contribute to reducing transmission.

Reactive case detection should be carried out through the use of RDT or microscopy, always aiming to provide treatment in the field or as soon as possible. It is important to consider that, in areas of low transmission, infections with low parasitemias (200 parasites/μL) are frequent, and that the blood forms of *P. vivax* tend to have lower parasitemias than those of *P. falciparum*.[13] Although RDT for P. vivax tends to perform less well than for P. falciparum in detecting low parasitemias, the test has been improved so that, in round 7 of the WHO RDT performance evaluation program, six tests showed 100% ability to detect low parasitemias compared to microscopy.

In situations where there are very few malaria cases, it is necessary to conduct case investigation, focus investigation, and response in a more intense and detailed way. Several rounds of RCD can be planned, from a first action at the time the index case is diagnosed, in order to detect cases of the same generation, and subsequent actions with spaces of one to two weeks, seeking to detect cases of the second and third generation, as well as possible cases with late incubation periods in the case of *P. vivax*. If there are many cases, a single round administered to individuals with fever from a cluster of cases may be sufficient (Table A1). When conducting RCD, health personnel should take the opportunity to raise awareness about early seeking of health services, treatment

12 World Health Organization. Malaria surveillance, monitoring and evaluation: a reference manual. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/handle/10665/272284.

13 World Health Organization. WHO Evidence Review Group on Malaria Diagnosis in Low Transmission Settings. Geneva: WHO; 2013. Available at: https://www.who.int/publications/m/item/meeting-report-of-the-evidence-review-group-on-malaria-diagnosis-in-low-transmission-settings. World Health Organization, FIND and Centers for Disease Control and Prevention. Malaria rapid diagnostic test performance: results of WHO product testing of malaria RDTs: round 7 (2015-2016). Geneva: WHO; 2017. Available at: https://www.who.int/publications/i/item/978924151268.

adherence, and malaria prevention measures, mainly the use of long-lasting insecticidal nets (LLIN) and indoor residual spraying (IRS).

Table A1. Guidance on how to perform reactive case detection

Context	Trigger	Where	For whom	How many times
Many cases	• Cluster of cases. • High positivity rate in passive case detection.	Group of houses identified	Individuals with fever	Once (if there is diagnostic capacity)
Few cases (close to elimination)	Each case (if one to three cases per health unit per week)	• House of confirmed case and neighboring houses. • Fellow workers and travel companions.	• Individuals with fever and other mild symptoms. • Individuals without fever in certain contexts.	• Once for each case. • Weekly for 30-60 days after negativity of the case (based on context).
Preventing reestablishment	Index case	• Entire locality if area is receptive. • Only travel companions if area is not receptive.	• Individuals with fever and other mild symptoms. • Individuals without fever.	Weekly for 30-60 days after negativity of the case (based on context).

Vector control measures as a response to a case

In addition to RCD, vector control activities are a key component in the response to malaria foci. According to A framework for malaria elimination,[14] "optimum coverage of LLIN / IRS should be ensured and maintained in receptive and vulnerable areas". **Places with current malaria transmission should be targeted for vector control interventions (IRS or LLIN) and localities should be already protected when the "response" operation is triggered in the event of a case or cluster of cases.** This means that, in priority localities, vector control actions will not be undertaken as a "response" to the occurrence of cases. In situations where the affected population is not covered and analysis of the situation determines the need for vector control actions as part of the "response," vector control actions should comply with the recommended coverage and quality standards. Reactive case detection should not be delayed pending organization of the vector control operation. In fact, in most cases, the movement of vector control teams (IRS) will be subject to the findings of the investigation, which generally occurs concurrently with the initial RCD actions. To avoid delays in response, reactive case detection can begin immediately upon confirmation of the index case by the local team and the findings will guide the need for further action.

To achieve high LLIN and IRS coverage, malaria programs need to have the tools necessary to properly plan for needs (in areas with transmission, in receptive areas, and in areas at risk of importation of the parasite), select appropriate products, taking into account information about susceptibility of the vectors to insecticides, and develop programmatic actions to ensure comprehensiveness and quality in the different steps of the IRS and LLIN management cycle: procurement processes, distribution of LLINs in the communities, promotion of their use, waste management, as well as planned actions for monitoring and evaluation of the interventions. Tables A2 and A3 summarize DTI-R components and how they are implemented, based on their context.

14 World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/handle/10665/254761.

Table A2. Components of a DTI-R strategy

Component	Action	Rationale
Diagnosis: within two days from onset of symptoms	Diagnosis of suspected cases by microscopy or RDT	**1.** Reduction of complications and deaths from severe malaria, particularly by *P. falciparum*. **2.** Interruption of malaria transmission, especially due to *P. vivax*. *P. falciparum* gametocytes appear 7-14 days after first asexual cycle, usually shortly after onset of symptoms. The gametocytes of *P. vivax* appear one or two days after the first asexual cycle, in general near the onset of the symptoms.[1] **3.** Administer a single dose of primaquine for any infection by *P. falciparum* to reduce transmissibility. **4.** Provide radical cure treatment for *P. vivax* to prevent relapses that may be determinants of transmission dynamics.
Treatment: begin same day of diagnosis	Start treatment as early as possible. Actions to achieve good adherence to treatment	
Case investigation: within three days from diagnosis	Case is investigated and classified as indigenous, introduced, or imported	**1.** Indigenous and introduced cases signify active local transmission. Classification of a case as locally acquired (indigenous and introduced) or imported will guide the response. **2.** Case classification taking more than 72 hours could lead to a delay in response. In the context of preventing reestablishment of transmission, a timely response should seek to detect other undiagnosed cases before they disseminate gametocytes, or take preventative action before the end of the extrinsic incubation period.
Reactive case detection: within seven days from diagnosis	Reactive case detection among family members and neighbors of index case	**1.** Evidence of case clusters, especially in areas of low transmission.[2] **2.** Reduce the parasite reservoir, especially in low-transmission context where health team may not suspect malaria. **3.** WHO's "Malaria surveillance, monitoring, and evaluation: a reference manual"[3] emphasizes that active case detection is always carried out during epidemiological investigation of new cases and foci. **4.** In order to prevent a second generation of cases from index case, leading to transmission. These cases could already be symptomatic in the community or be in the incubation period. **5.** In order to prevent a second generation of cases from index case. Once the mosquito takes the patient's gametocytes, a minimum of seven days is necessary for the mosquito to be infective, that is, to have sporozoites in its salivary glands (extrinsic period). Once this infective mosquito bites a susceptible person, a minimum of seven more days is needed to complete the incubation period in the person (intrinsic period) and be part of the second generation of cases.[4] **6.** If a case is classified as imported, the aim is to find other imported cases that share an origin of infection with the index case. Introduced cases are not detected until a minimum extrinsic period of seven days and an intrinsic period of seven days are completed. Reactive detection can take up to approximately 120 days (two transmission cycles).
Vector control	All households in foci and areas with high potential for malaria transmission should be protected with LLIN or IRS	**1.** LLIN and IRS are cost-effective[5] interventions. **2.** LLIN and IRS have a greater impact on reducing vector capacity than other vector control interventions because they reduce vector population survival, the number of human bites per mosquito, and the number of female mosquitos. **3.** The WHO vector control guidelines[6] consider LLIN and IRS to be priority vector control actions, with larval control as complementary, and do not recommend spatial spraying. **4.** Countries' experiences indicate a resurgence of transmission when these interventions were interrupted.

14 Organización Mundial de la Salud. Terminología del paludismo. Ginebra: OMS; 2016. Actualizado en marzo de 2018. Disponible en https://apps.who.int/iris/bitstream/handle/10665/258964/WHO-HTM-GMP-2016.6-spa.pdf;jsessionid=A7F3C3ED065FFE-0CAE24D829721889A6?sequence=1.

DTI-R: diagnosis, treatment, investigation, and response; RDT: rapid diagnostic test; LLIN: long-lasting insecticidal nets; IRS: indoor residual spraying.

Sources:

1 Ngwa C, de A Rosa T, Pradel G. Current topics in malaria. London: INTECH; 2016.
2 van Eijk AM, Ramanathapuram L, Sutton PL, Kanagaraj D, Sri Lakshmi GP, Ravishankaran S, et al., What is the value of reactive case detection in malaria control? A case-study in India and a systematic review. Malaria Journal 2016;15(67). The Global Health Group, Background Paper. Screen and treat strategies for malaria elimination: a review of the evidence. San Francisco, US: Institute for Global Health Sciences, University of California; 2018.
3 World Health Organization. Malaria surveillance, monitoring and evaluation: a reference manual Geneva: WHO; 2018. Available at: https://apps.who.int/iris/bitstream/handle/10665/272284/9789241565578-eng.pdf.
4 Pampana E. Erradicación de la malaria. Mexico City: Centro Regional de Ayuda Técnica, Agency for International Development; 1996.
5 White MT, Conteh L, Cibulskis R, Ghani A. Costs and cost-effectiveness of malaria control interventions: a systematic review. Malaria Journal. 2011; 10(337).
6 World Health Organization. Guidelines for malaria vector control. Geneva: WHO; 2019. Available at: https://apps.who.int/iris/handle/10665/310862.

Table A3. How, when and who should implement different DTI-R components

DTI-R	What	When	How	Who
Diagnosis	With few or many cases: diagnose individuals with fever	**Within two days of onset of symptom**s	Microscopy or RDT in health units, community agents, volunteer collaborators at mobile points, or during active searches.	Health unit personnel, microscopists, community agents, or volunteer collaborators.
Treatment	With few or many cases: begin treatment	**Same day as diagnosis**	Treatment prescribed according to national protocols.	Health unit personnel, microscopists, community agents, or volunteer collaborators.
Case investigation	• Few cases: detailed case investigation • Many cases: classification of cases as imported or locally acquired (specifying probable place of infection).	**Within three days of diagnosis**	• Few cases: begin with diagnosis, end with house visit. • Many cases: begins and end with diagnosis.	• Few cases: begin with diagnostic team and end with epidemiology team. • Many cases: Diagnostic team (health unit personnel, microscopists, community agents, or volunteer collaborators).
Reactive case detection	• Detection of individuals with fever (and asymptomatic individuals, according to context) around index case. Consider work companions. • Few cases: several weekly rounds beginning as soon as possible, ideally in first seven days from onset of symptoms in index case. • Many cases: one round in a cluster of cases. • Repeat rounds weekly according to resources.	• Few cases: begin within seven days from onset of symptoms in index case. Continue weekly for 30 days after clearance of cases. Consider monthly rounds until sixth month if *P. vivax*.1 • Many cases: one round when a cluster of cases. • Many cases, with an outbreak: one round within seven days from onset of symptoms in index case. • Repeat rounds weekly according to resources.	• Few cases: RDT or microscopy.[2] Cohabitants and neighbors. • Define radius based on context. • Many cases, without outbreak: RDT or microscopy. • Cohabitants and neighbors (depending on resources). Define radius based on context. • Many cases, with outbreak: RDT or microscopy. • Cohabitants and neighbors. • Define radius based on context.	• Few cases: response team (health unit personnel, microscopists, community agents, or volunteer collaborators, vector control team). • Many cases: community agents, volunteer collaborators, malaria visitors.
Vector control	Protect population in active and residual foci and in areas of high transmission potential with LLIN or IRS.	• Routinely in active and residual foci and in areas of high transmission potential. • As response to one case (if area is receptive, not including routine activities).	• Two to three cycles according to insecticide used. • Ensure population is protected with LLIN or IRS during case and foci investigation.	Vector control team

LLIN: long-lasting insecticidal nets; IRS: inside residual spraying; RDT: rapid diagnostic test; PCR: polymerase chain reaction.

Sources:

1. Fontoura P, Finco B, Lima N, Carvalho J, Vinetz JM, Castro M, et al. Reactive case detection for Plasmodium vivax malaria elimination in rural Amazonia. PLOS Neglected Tropical Diseases 2016;10(12).
2. World Health Organization. A framework for malaria elimination. Geneva: WHO; 2017. Available at: https://apps.who.int/iris/handle/10665/254761.

Plasmodium vivax incubation, latency periods, and relapses and implications for case investigation

From the epidemiological perspective, perhaps the most important feature of the biology of *P. vivax*, compared to *P. falciparum,* is its ability to cause relapse in the weeks or months after primary parasitemia as well as late incubation periods, due to a hepatic stage of the parasite known as hypnozoite. There is great variability in the incubation and latency periods,[15, 16] as well as in the frequency of relapses; and while the causes of this are not well understood, they point to climate, type of strain, number of sporozoites inoculated, immunity, and factors that could trigger relapses, such as febrile episodes and the use of 8-aminoquinoline antimalarials. In other words, there are strains characterized by frequent relapses and short latency periods (tropical strains), others with longer latency periods and less frequent relapses (temperate strains), and yet others that combine frequent relapses and long latency periods.

Using as a reference the works of White[17] and Battle,[18] Figures A3 and A4 show which tropical and temperate strains are found in the Americas, the distribution of strains with late latency periods, in Central and South America, as well as the presence of strains characterized by frequent relapses, in South America. Comparing strains from Africa, Europe, and Asia with strains from the Americas (both temperate and tropical), the latter have longer latency periods.

Understanding the existence of these variations in *P. vivax* is important for epidemiology teams to properly guide the classification and investigation of cases and the interpretation of different situations in the classification and investigation of foci. Similarly, since the presence of frequent relapsing (tropical) strains in other endemic regions is associated with the existence of primaquine tolerance, requiring higher doses of primaquine, recognition of situations where such relapse patterns predominate may be of importance in clinical case management and follow-up.

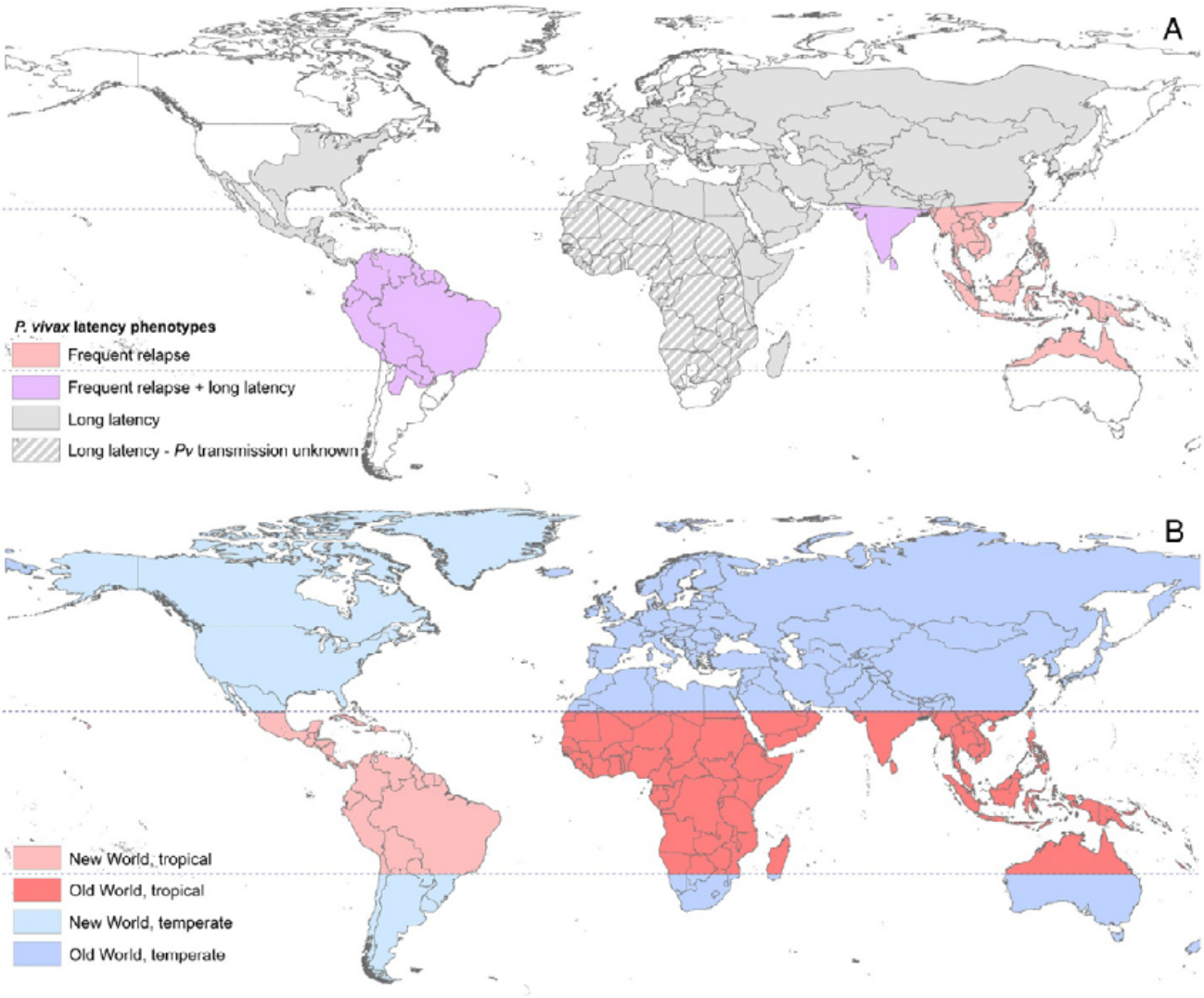
15 Incubation period: The period between the inoculation of sporozoites and the release of merozoites into the bloodstream (primary exo-erythrocytic cycle).

16 Latency period: The period between a primary attack and a relapse; in some strains, also the period between the inoculation of sporozoites and that of a patented primary attack, typically six months or more.

17 White, N. and M. Imwong, *Relapse*. Advances in Parasitology, Volume 80. 2012: Elsevier Ltd.

18 Battle, K., et al., *Geographical variation in Plasmodium vivax relapse*. Malaria Journal 2014. 13(144).

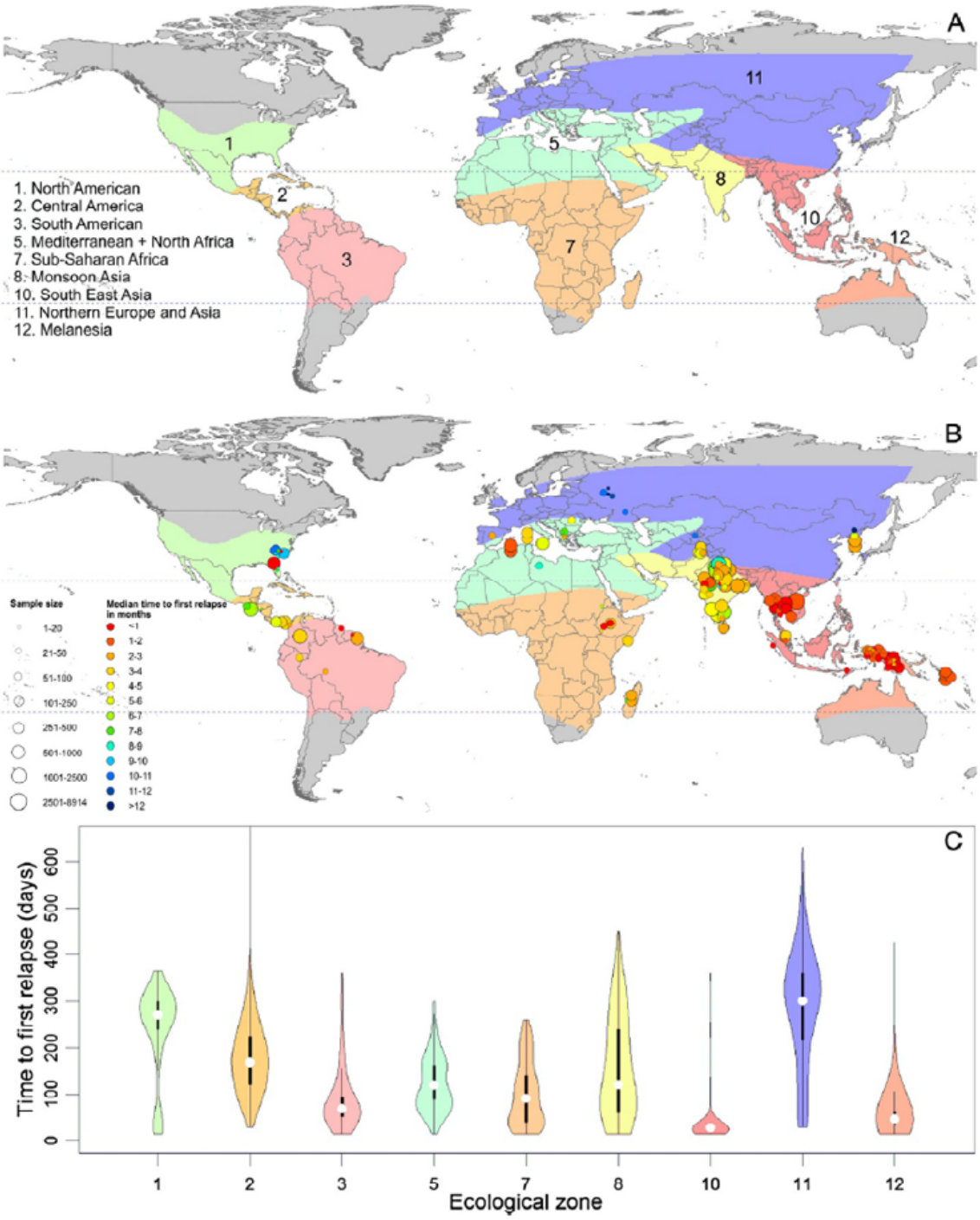
Figure A3. Proposed distribution of *Plasmodium vivax* relapse latency phenotypes



Note: This figure shows the distribution of *Plasmodium vivax* relapse and latency phenotypes. Panel A shows the distribution of strains characterized by frequent relapses and those with long latency periods. Tropical strains characterized by frequent relapses are in pink, while strains with long dormancy are in gray. Much of Africa is shown in a gray band because the influence of Duffy's negativity and its effect on *P. vivax* transmission in this part of the world are not yet understood. In the purple areas it is believed that both long latencies and frequent relapses occur. Panel B shows the classification system for Old World and New World. Tropical zones (red and pink) harbor strains that cause relapse more rapidly than those in temperate zones (light and dark blue). New World tropical strains (pink) cause relapse more slowly than Old World tropical strains (red), and Old World temperate strains (dark blue) cause relapse more slowly than New World temperate strains (light blue).

Source: Battle K, et al. Geographical variation in Plasmodium vivax relapse. Malaria Journal 2014;13(144).

Figure A4. Observed time to first relapse, based on different zooecological zones



Note: Panel A illustrates the zoogeographic areas used to describe the time of first relapse. Panel B shows the median time to relapse in each study used to obtain individual data. The size of each point varies with the size of the sample, while the time to first relapse is shown in a spectrum ranging from red (less than one month) to dark blue (more than 12 months). The graphs in panel C show time to first relapse for individuals in each area in panels A and B. The colored areas correspond to each zone and to a smoothed approximation of the frequency distribution (a core density graph) of the relapse time within each geographic region. The central black bar represents the interquartile range, while the white circles indicate the average values.

Source: Battle K, et al. Geographical variation in Plasmodium vivax relapse. Malaria Journal 2014;13(144).

Example of national guidelines for establishing the scope of case investigation

>Surveillance action

The objective of case investigation is to determine whether an infection was locally acquired and the likely location of infection, and thus whether there is indigenous transmission of malaria or factors that may lead to onward transmission.

The collection of a detailed history of an index case at a fixed point of care (health facility or community agent) is the basis of the initial case investigation. The investigation should be completed by the investigation team at the home or workplace of the index case within 1-3 days of notification of the malaria case.

The case investigation form is the surveillance tool that should be completed for each case investigated according to the above criteria.

>Areas where community case investigation should be conducted

All cases occurring in territories with very low malaria transmission should be investigated in the community.

To establish the areas where case investigation is mandatory, this standard follows the WHO-recommended criterion of investigating all cases in areas where fewer than three cases per week per "investigation team" occur.

Considering that, according to the national model for surveillance of events of public health concern, the basic unit responsible for epidemiological investigation is the [UNIT], this standard establishes that all [UNITS] with less than 3 cases per week should investigate all cases.

In the spirit of this standard, to promote timely actions for the interruption of malaria transmission, each [UNIT] should periodically analyze the weekly malaria behavior to adjust the local case investigation strategy.

According to the above criteria, [UNITS] that go from having many malaria cases to a stable situation of very low transmission (several weeks with less than 3 cases) should trigger systematic case investigation actions. Conversely, municipalities that go from having no cases or very few cases to an outbreak or epidemic situation do not need to continue to investigate all cases.

Similarly, in the spirit of the norm, those [UNITS] with a large territory with more than 3 cases per week, but where malaria is highly concentrated and there is an interest in preventing the reintroduction of malaria in areas already free of transmission but still receptive (urban areas, for example), should establish case investigation at the points of care that receive fewer than 3 cases per week.

>Action monitoring (case investigation)

For the purpose of supervision and monitoring of this public health action, at the beginning of each year, the Ministry of Health will establish the [UNITS] where epidemiological investigation of all cases is a priority. As a proxy to the criterion of 3 cases/week, [UNITS] with less than 150 cases in the immediately preceding year will be identified. This establishes a **minimum** parameter of surveillance units that must perform case investigation and that must be monitored during and at the end of the period for compliance with this action.

As an exception to this rule, priority in the monitoring of this action will also be given to those [UNITS] that, despite having more than 150 cases per year, present a markedly seasonal behavior with prolonged periods of very little transmission (less than 3 cases) where case investigation should be mandatory.

The central level will evaluate each year the indicator "% of cases investigated" (cases with investigation record/total number of cases to be investigated) for each of the [UNITS] established according to the two previous numerals.

Similarly, for the purpose of monitoring the malaria response, the central level will periodically evaluate malaria behavior to identify those [UNITS] with more than 150 cases in the previous year, but which during the period have shown a reduction of malaria to levels that justify the investigation of all cases (less than 3 cases per week).

ANNEX B. OPERATIONAL CHANGES TO REDUCE TRANSMISSION

In those situations where malaria transmission is elevated or reduction has stagnated, the strategies should be reviewed and operational changes in the field should be considered to achieve malaria elimination. The question that health teams must ask is "What can be done differently?". Ten operational elements of change are proposed to revitalize malaria interventions:

1. Organize the malaria operation at a more local level (focus, sector, micro-area). Sectorization of the territory is a key element for the malaria operation to respond to the specificities of the transmission dynamics and particularities of the affected communities. In contexts of stable and dispersed transmission settings, such sectorization may coincide with the territorial division of the health network, and in rural areas it usually corresponds to the river or land access routes, which normally also determine the patterns of population dynamics and malaria transmission. The proposed change is that the tools for analysis, technical capacity, and monitoring be installed at the local level. This involves:
    a. Defining micro-areas or operational areas within municipalities.
    b. Organizing a management model based on the basic team (health unit, vector control staff and basic health personnel) implements the response, and incorporates systematic analyses of the situation. The municipal team should be in charge of efforts to support the focus management model.
2. The objective of the intervention should be to transform active foci into cleared foci. Malaria elimination in the municipality will be the result of interrupting transmission in each of the foci.
3. Diagnosis and treatment must be accessible to the communities and therefore it is necessary to strengthen passive case detection. Brigades for active detection cannot replace passive detection. The creation of new diagnostic points with full involvement of the health network and other actors should be a priority and RDTs play a major role in this change.
4. Involve other actors (including the private sector, community, and actors linked to key economic activities), within the local municipality, around concrete solutions to improve detection, diagnosis, treatment, and use of LLIN.
5. Response to the detection of a case of malaria does not end with treatment. Each case or group of cases of malaria should trigger additional detection activities, including diagnosis and treatment of related cases. The timing and extent of these detection activities depend on the epidemiological situation.
6. Prioritize early case detection over other actions that consume operational capacity (such as case follow-up or directly observed treatment) in areas of high transmission.
7. Shift from routine reporting of data and indicators to analytical exercises focused on understanding the keys to transmission, triangulating epidemiological information with local observation, and understanding the social dynamics that explain malaria in order to propose hypotheses and guide solutions.
8. Ensure that inducing demand is a strategic and technically oriented action, establishing effective communication strategies with concrete messages about solutions to access

barriers, routes to access diagnosis and treatment, and solutions offered to the community, in line with improvements in the availability of diagnostics for passive search in health services.

9. Reduce relapses of *P. vivax* through a comprehensive, sustainable, and effective strategy. To this end, countries should, at a minimum, record relapses, ensure that primaquine is administered according to the patient's weight, and provide supervised or semi-supervised treatment.
10. Maintain broad coverage with LLIN or IRS in key localities, i.e., those with high malariogenic potential.

ANNEX C. EXAMPLES TO GUIDE REACTIVE DETECTION AND VECTOR CONTROL AS A RESPONSE TO A CASE

The WHO *Malaria surveillance, monitoring and evaluation: a reference manual* describes factors that help determine the extent and scope of RCD[1]:

Epidemiological situation: Index cases that are considered to be due to local transmission may trigger reactive case detection that is geographically more widespread. An apparently imported case, a relapse or a recrudescence, especially in an area with low receptivity, could trigger more limited case detection; however, it is always better to err on the side of caution; if local transmission is possible, it is advisable to carry out RCD, at least in the surrounding cluster of households.

Receptivity (presence of abundant anopheline vectors and other ecological and climatic factors favoring malaria transmission): Highly receptive areas should always be covered by RCD.

Type and degree of risk of parasite importation (proximity to a malarious area or frequent influx of infected individuals or groups or infecting anopheline): The risk of parasite importation guides both the type and extent of RCD in each area or sub-population.

Cluster type and extent: Local or national knowledge of the cluster pattern of infection and local experience with vector ecology and breeding sites will determine whether a geographically wider or narrower RCD should be planned.

Breeding sites: Knowledge of potential breeding sites in the area or locality may result in a more or less targeted RCD.

History of infection: The history of infection in the area and the type of outbreak (active, residual non-active and eliminated) will influence the type and extent of RCD. When the index case is the first in a new active focus, less will be known about the outbreak and its population, so a large-scale RCD of infected residents with or without fever will be necessary to fully characterize the situation and establish a baseline. If the index case is one of many cases from the same locality in the current transmission season in a well-known outbreak, the RCD can be more specific, because the populations at risk will already be known.

Location of infection: The hypothetical source of infection (workplace or residence) will influence the type and targeting of RCD.

Resources: The amount of resources available will guide the type of RCD; for example, selecting people with recent symptomatic disease for screening versus mass testing (mass diagnosis). The aim is to optimize the use of available resources and complete the investigation in a short time, e.g., seven days.

Parasitic species: There is currently no method to detect the liver stage of malarial infections. Radical cure of individuals with *P. vivax* malaria is necessary to eliminate the hepatic phase.

1 World Health Organization. Malaria surveillance, monitoring and evaluation: a reference manual. Geneva: WHO; 2018. Available at: https://apps.who.int/iris/handle/10665/272284.

Raising awareness: Regular repeat RCD will increase case detection and teach the population to use the free services offered at the local clinic for parasitological examination in all cases of fever, adhere to prescribed treatment and use preventive interventions.

Taking into account the factors outlined above, situations are described below that can help guide the organization of reactive case detection (RCD) actions according to the epidemiological context:

>In the context of stratum 4 with active foci and a large number of cases

In a context of stratum 4 with active foci and a high number of cases (more than three cases per week per investigation team), reactive case detection (RCD) actions for each diagnosed case will impose a heavy burden on the operation and may be of little relevance, especially in areas of known transmission, where passive and active detection efforts are already in place. In these situations, the following measures are suggested:

- Systematically inform all patients about the importance of encouraging family members and neighbors with similar symptoms to go to a health facility for a diagnostic malaria test.
- Perform RCD upon detection of a cluster of cases from localities or neighborhoods where there is no ongoing detection action in place or where there is a change in epidemiological behavior. The place where RCD should be carried out is where transmission is suspected to occur, or at the place where the respective cluster of people spend the night. In addition to the detection of new cases (intervention), the RCD in these conditions has an important "surveillance" objective, since the action serves to evaluate and correct key aspects of the response in this population (coverage with LLINs, barriers to access to diagnosis, and community awareness, among others).

>In the context of stratum 4, with active foci and less than three cases per week per investigation team

In a context of stratum 4 with less than three cases per week per investigation team, RCD can be performed for each new case diagnosed, provided that the RCD is not already covered by the response action to another recent case within the same cluster of cases. A reconnaissance of the area around a case (500 meters if an urban area, two kilometers if a rural area) will help identify houses and mosquito breeding sites and guide the radius of the RCD.[2] RCD will therefore be conducted around the case in the area delimited to all febrile cases.

If another case is found during this screening, weekly screening will continue until there are four to eight weeks without cases. In both contexts, the detected case(s) will be reported to the health units in the area so that they can be alert and intensify passive case detection. It is important to note that there is no single recommendation on the radius to be covered in RCD, which will often be determined by local geography, housing density, country experience and available resources. Whatever the radius covered, what is important is that there is good coverage. It will therefore be important to conduct RCD at times when the population is reachable.

>In the context of no active transmission but receptive

In a context without active transmission but receptive (either stratum 4 with non-active residual foci, or stratum 3 or 2), the history of recent travel to an area recognized as malaria-endemic should be investigated first (with special emphasis on the two weeks before the onset of symptoms):

2 For example, if the reconnaissance and entomological survey identifies a vector species with wide dispersal capacity and larval habitats far away from dwellings (e.g., *An. darlingi*), the RCD should cover a larger area than one where vector dispersal capacity is more limited and larval habitats are closer to dwellings (e.g., *An. albimanus*). This analysis should involve a local multidisciplinary team, if possible, with support from regional or national levels, composed of epidemiologists, entomologists and field technicians. Each situation should be analyzed under local conditions.

- Where there is a travel history, RCD should be performed to all travel companions. Also, it will be conducted in the community where the case stayed overnight from 14 days after arrival (eight days for *P. vivax* and seven days for *P. falciparum,* this being the minimum period of sporozoite development in the vector, with seven days as the minimum incubation period in humans), and up to 30 days after negativization of the index case begins. Recent modeling shows that the average interval between the first and second generation of *P. falciparum* is 49.1 (33.0-69.0) days;[3] thus, it is appropriate to extend case detection until day 69, if possible, counting from the onset of symptoms in the first case. RCD will be performed as described above (around the case found, and according to the delimited area) following time and place criteria such as the following:
    - In the first week, testing the entire population (individuals without fever and those with fever of unknown origin.
    - In the second, third and fourth week, only individuals with fever of unknown origin.

Finally, vector control measures will be applied in the delimited area. If the measure is IRS, a single cycle will be sufficient, unless transmission continues for several months.

- In the absence of a history of travel, RCD will be carried out in all areas where the person has stayed overnight during the 30 days prior to the date of onset of symptoms, and up to 30 days from post-treatment negativization, in the same manner as described above. The need for vector control actions at such sites will be considered on a situation-by-situation basis assessing receptivity and vulnerability and operational implications. If during these detections another case is found, weekly detections will continue until four weeks without cases are achieved. In this situation, weekly screening will be done in all four cycles as described in the no active transmission but receptive context. In addition, the detected case(s) will be communicated to the health units in the area so that they can be alert and intensify passive case detection. This intensified detection may include review of medical records with detection of fever of unknown origin or other symptoms compatible with malaria, such as anaemia or splenomegaly of unknown cause during the 30 days prior to case detection.

In a non-receptive area with no active transmission (stratum 1), RCD should be limited to all travel partners.

3 Huber J, Johnston G, Greenhouse B, Smith D, Perkins T. Quantitative, model-based estimates of variability in the generation and serial intervals of *Plasmodium falciparum* malaria. Malaria Journal 2016;15(490).

ANNEX D. SUPERVISION FORM FOR MALARIA POSTS

This form provides a general guide for supervision of malaria screening and diagnostic posts. It does not include specialized supervision of microscopy, which should be coordinated by the reference laboratory, as an integral component of the diagnostic quality assurance system.

1. Identification of the post

- → Post name
- → Type
- → Name of person in charge
- → Location
- → Date of current supervision
- → Date of last supervision
- → Person responsible for supervision

2. Detection and diagnosis

2.1 Data:

- → Number of cases examined: PD, AD (analyze weekly trend)
- → Number of positive cases: PD, AD (analyze weekly trend)
- → Positive slide rate: PD, AD (compare AD to PD)

2.2 Supplies and materials:

- → Number of RDT available, and estimate of time covered (months)
- → Slides, lancets, Giemsa stain, oil: estimate of time covered (months), problems
- → Personal protective equipment: estimated time covered (months)
- → Microscope (general condition[1]): observations of the microscopist or equipment supervisor
- → Form for sending slides to quality control: yes/no

2.3 Processes

- → Demand for care: variations in the number of tests conducted, comparison with other weeks, comparison with other posts, causes of low demand for care by the population, possible barriers experienced by the population.
- → Supply of care: schedules, station signage (yes/no), possible barriers (specify). Under-recording: does the staff of the health post believe there are cases that are not being captured?
- → Suspicion of malaria: knowledge and application of case definition. How negative cases are handled.
- → Febrile care flow (in health units): failures in flow leading to barriers and delays.
- → Rapid test procedure: quality of the procedure.
- → Slide preparation procedure: quality of the procedure.
- → Receipt of microscopy results (when applicable[2]): time from sending of slides; delays.

1 Microscopy supervision is specialized supervision that includes direct monitoring of reading, as well as the state and performance of materials and equipment handling. This supervision is organized by the reference laboratory of the respective network.

2 For slide pick-up points, without diagnosis.

- → Sending of slides for quality control (microscopist): yes/no, periodicity.
- → Receipt of quality control report (microscopist): result.

3. Treatment

3.1 Data

- → Number of treatments dispensed.
- → Number of cases with supervised treatment.
- → Number of recurrences.

3.2 Supplies and materials

- → Number of treatments available:
- → Record of supply of medications: yes/no. use and processing.
- → Table of treatment schemes by weight: yes/no, understanding and use.
- → Envelopes or materials to improve adherence and use (if applicable): yes/no, use.
- → Weight scale

3.3 Processes

- → Drug storage: assessment of storage condition.
- → Prescribing and dispensing treatment: knowledge of doses and tables, dispensing conditions, instructions and advice for the patient.
- → Treatment supervision: criteria, problems, limitations, and type of supervision.
- → Handling situations with pregnant women: knowledge and application.
- → Recognition of signs of severe malaria and related behavior: knowledge.
- → Managing recurrences: knowledge.

4. Investigation and response

4.1 Data

- → Number of cases investigated: review of files.
- → Number of cases that triggered RCD actions.

4.2 Processes

- → Questioning on key variables: ability to record place of residence, probable place of infection, and dates of onset of symptoms.
- → RCD procedure: criteria, coverage, periodicity, problems, and logistical constraints.
- → Case investigation: criteria, actions, and problems.

5. Information Management

5.1 Supplies and materials

- → Availability of records and forms (cases, persons examined, case investigation), estimate of time covered (months).

5.2 Processes

- → Case record: quality of key variables (place of residence [record quality], dates, and age).
- → Report: timely communication of information and problems.

→ Data analysis: trend analysis capacity, identification of new foci, warnings, and hypothesis.

6. Recommendations and tasks

Table D1 shows DTI-R components, recommendations for the station, and supervisor tasks.

Table D1. Components, recommendations, and DTI-R tasks

Component	Recommendations for the health posts	Supervisory tasks
Detection and diagnosis		
Treatment		
Investigation and response		
Information management		

ANNEX E. SUGGESTED INDICATORS FOR MALARIA PROGRAMS

N.°	Indicator	Numerator	Denominator	Breakdown	Standard or target	Data source
Impact						
1	Number and incidence rate (per 1,000 population) of malaria cases: • By species, classification, sex, age group. • By source (for example, imported, indigenous). • By active and passive case detection. • By sector.	Number of confirmed malaria cases identified through active and passive surveillance activities during a one-year period, per 1,000 population.	• Number of people at risk of malaria infection at mid-year during the reporting year. • When calculating national incidence, use the population of the entire country.	• Geographic area and focus, risk group, active versus passive case detection, age, sex, and species. • When approaching elimination: autochthonous, introduced, imported by nationality, induced.	Annual target to be projected by the program.	Malaria database. Verification at local and national level.
2	Number of foci by classification.	Number of foci, by classification (active, residual inactive, eliminated).			Annual target to be projected by the program.	Malaria database.
3	Number of people and percentage of population living in an active focus.	• Number of people in the foci, by classification (active, residual inactive, eliminated). • Number of people living in an active focus.	Total population of the country.		Annual target to be projected by the program.	Malaria database.
4	Number of malaria deaths by species and by classification (imported or locally acquired).	Number of malaria deaths, by species and by classification.			Annual target to be projected by the program.	Malaria database.

Surveillance						
5	Annual rate of blood tests per district and per focus, and by rapid diagnostic tests or microscopy.	Number of patients who underwent parasitological testing during a year.	Number of people at risk for malaria at mid- year.	Geographic area or focus, risk group, active versus passive, time (year and month).	• No target, based on context. • Surveillance follows clear criteria.	Malaria database. Verification at local and national level.
6	Percentage of monthly or periodic reports received from health facilities (with number of malaria diagnostic tests performed and number of positive patients).	Number of periodic reports received from health facilities (with number of malaria diagnostic tests performed and number of positive patients).	Number of periodic reports received from health facilities (with number of diagnostic tests performed and number of positive patients).		100%	Malaria case and case detection databases.
7	Percentage of patients with suspected malaria who received a malaria diagnostic test.	Number of suspected malaria cases receiving a diagnostic test. (Define suspected cases: fever of unknown origin [FUO], fever, and epidemiological link such as travel to an endemic region).	Number of suspected malaria cases.	Geographic area, type of health facility, time (year and month).	100%	Systematic information, facility or community surveys.
8	Percentage of cases reported within 24 hours of detection.	Number of case reports received within 24 hours of detection.	Total number of malaria case notifications.	Geographic area and focus, risk group, time (year and month), type of facility.	100%	Malaria case and case detection databases.
Diagnosis						
9	Percentage of microscopy results validated by the national reference laboratory (indirect control).	Number of validated positive and negative microscopy results.	Number of validated positive and negative microscopy results.	Microscopy post	100% of positive results, 10% of negative results.	Database of the reference laboratory. Verification at local and national level.
10	Percentage of laboratories participating in WHO-recommended diagnostic quality assurance assessments (direct quality control, national and external proficiency assessments).	Number of laboratories participating in quality assurance assessments.	Number of malaria laboratories.		100%	Laboratory reference database.

11	Proportion of health facilities without diagnostic stock-outs.	Number of health facilities without diagnostic stock-outs (in countries with very few cases, it will be necessary to define which facilities should have diagnostic supplies).	Number of health facilities that should have diagnostic supplies for malaria.	Geographic area, type of facility, time (year and month).	100%	Systematic information and health facility surveys.
Case management						
12	Percentage of patients with confirmed malaria receiving first-line antimalarial treatment according to national policy.	Number of patients with confirmed malaria receiving first-line antimalarial treatment according to national policy.	Total number of confirmed malaria cases.		100%	Malaria case and case detection databases.
13	Proportion of cases going to health services in first 48 hours from onset of symptoms.	Number of cases going to health services (including community workers) in first 48 hours from onset of symptoms.	Total number of malaria cases passively detected.	Geographic area and focus, risk group, time (year and month), type of facility.	Target values to be projected by the program each year.	Systematic information.
14	Median time between onset of symptoms and initiation of treatment, by type of surveillance.	Median number of days malaria cases were treated since onset of symptoms.		Geographic area and focus, risk group, time (year and month), type of facility, type of surveillance.	Target values to be projected by the program year after year.	Systematic information.
15	Proportion of cases with supervised treatment.	Number of cases receiving supervised treatment.	Total number of confirmed malaria cases.	Most important for countries with very few cases.	100%	Systematic information.
16	Proportion of months in health facilities where first-line treatment was out of stock.	Number of months in health facilities where first-line treatment was out of stock (in countries with very few cases it will be necessary to define which facilities should have treatment supplies).	Number of months	Geographic area, type of facility, time (year and month).	100%	Systematic information and health facility surveys.

Investigation						
17	Percentage of cases investigated and classified.	Total number of malaria cases in the national registry of cases investigated and classified in the previous year.	Total number of confirmed malaria cases.	Geographic area and focus, risk group, time (year and month), type of facility.	100%	Malaria case and case detection databases. Verification at local and national level.
18	Percentage of cases investigated and classified.	Total number of malaria cases in the national registry of cases investigated and classified within the previous year.	Total number of confirmed malaria cases.	Geographic area and focus, risk group, time (year and month), type of facility. Most important for countries with very few cases.	100%	Malaria case and case detection databases.
19	Percentage of foci investigated.	Total number of new foci in the national focus registry investigated during the previous year.	Total number of new foci in the national focus registry.	Geographic area and focus, time (year).	100%	Malaria database.
20	Percentage of foci investigated and classified	Total number of new foci in the national focus registry investigated and classified in the previous year.	Total number of new foci in the national focus registry.	Geographic area and focus, time (year). Most important for counties with very few cases.	100%	Malaria database.
Vector control						
21	Proportion of risk group sleeping under an insecticidal net or living in a house that has been sprayed in the past 12 months.	Number of people living in risk areas sleeping under an insecticidal net or living in a house that has been sprayed in the past 12 months.	Number of people living in risk areas. (Define population at risk: population living in active, residual inactive, or very vulnerable and receptive areas.)		100% of target population.	Record of operations or household surveys.
22	Percentage of active and residual non-active foci protected by indoor residual spraying (IRS), by year.	Number of active and residual non-active foci protected by IRS, by year.	Number of active and residual non-active foci protected by IRS, by year.		100% of target foci.	Surveys

23	Percentage of population living in active and residual inactive foci protected by IRS, by focus and year.	Number of people who live in inactive active and residual foci protected by IRS, by focus and year.	Population living in active and residual inactive foci, by focus and year.	100% of target population.	Surveys.
24	Percentage of active and residual inactive foci protected by insecticidal nets (LLIN), by year	Number of active and residual inactive foci protected by LLIN, by year.	Number of active and residual inactive foci protected by LLIN, by year.	100% of target foci.	Surveys.
25	Percentage of population living in active and residual inactive foci protected by LLIN, by focus and year.	Number of people living in active and residual inactive foci protected by LLIN, by focus and year.	Population living in active and residual inactive foci, by focus and year.	100% of target population.	Surveys.
26	Percentage of active and residual inactive foci with larval control activities.	Number of active and residual inactive foci with larval control activities.	Total active and residual inactive foci.	According to national objective.	Activity records.
Program milestones					
27	Malaria spending by source (internal, external).			Annual program target.	
28	Per capita expenditure for malaria control elimination.			Annual program target.	Systematic reports.
29	Malaria is a notifiable disease in the first 24 hours.			Yes	Policy documents.
30	Standard operating procedures exist for all surveillance components.			Yes.	Evaluation of the surveillance and information systems.
31	There is a national reference laboratory for malaria diagnosis that implements the quality assurance system.			Yes.	Evaluation of the quality assurance system for malaria diagnosis.
32	A record of foci exists and has been updated in the last 12 months.			Yes.	Malaria records.
33	An independent national committee for the elimination of malaria has been established.			Yes.	Malaria records.

34	An annual malaria report is prepared and distributed to all district health offices.		Yes.	Malaria records.
35	The national plan for malaria elimination has been approved by the minister of health.		Yes.	Malaria records.
36	Functional intersectoral collaboration exists in all districts concerned.		Yes.	Malaria records.
37	There is an updated list of all public and private health facilities and community health workers providing malaria diagnosis and treatment.		Yes.	Evaluation of the surveillance and information systems.
38	Each health facility is registered to receive appropriate supervision.		Yes.	Evaluation of the surveillance and information systems.

All malaria-endemic countries in the Region of the Americas have taken on the challenge of eliminating the disease and implementing interventions to guide their health programs and strategies in that direction.

This manual provides guidance on how to implement basic malaria elimination actions. It proposes to change the malaria operation with the focus on addressing the foci and organizing the operation at the most local level. The document begins with the need to identify and define an operational area (the focus or micro-area) where a specific programmatic intervention of diagnosis, treatment, investigation, and response (DTI-R) is implemented, which, although standardized at the national level, must be guided above all by an understanding of the dynamics of transmission at the local level.

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