





Challenges in Elimination

Studies concerning the complex shifts in malaria transmission and epidemiology, or other emerging issues and barriers that the present control interventions and strategies are unlikely able to fully address (modified definition [\[ref\]](#)).



Response Strategies

Studies concerning the actions required to achieve malaria control and elimination [\[ref\]](#).



Basic Science

Studies addressing our understanding of the biology of the *Plasmodium* species, and of the relationships between human populations and the different species of mosquito and parasite [\[ref\]](#).



Epidemiology

Studies concerning the distribution of health-related states by occurrence of events or determinants (including disease transmission or incidence), and the understanding of which can be applicable towards control and intervention of such health factors [\[ref\]](#).



Health Systems & Operational Research

Studies that address the structure (health system) or programme that englobes all the activities whose primary purpose is to promote, restore or maintain health (modified definition [\[ref\]](#)). In the specific context of the Health Systems area, subcategory definitions are drawn from the WHO framework of six building blocks* [\[ref\]](#).

*Note: products/technologies as a subarea is not included under this theme, as the development and access of different product types are described under the “Response Strategies” theme. In the context of Operational Research, studies (and subcategories) concern areas of important focus in the search for management and optimization knowledge on malaria interventions, strategies, or tools to enhance quality, effectiveness and access or coverage [\[ref, ref\]](#).

(See also subcategories below on significant areas of the challenges identified or of emerging focus)



Challenges in Elimination

Drug Resistance: Studies concerning the ability of a parasite strain to survive and/or multiply despite the absorption of a medicine given in doses equal to or higher than those usually recommended [\[ref\]](#). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- the epidemiology and risk factors of drug resistance
- the use of mathematical models to predict drug resistance
- mechanisms and molecular basis of drug resistance
- the genetic diversity of drug resistant parasites
- developing technologies to detect parasite resistance
- monitoring drug resistance
- evaluating strategies to contain and/or mitigate drug resistance
- developing effective drugs against malaria resistant parasites
- measuring impact of drug resistance on malaria transmission

Indigenous & Imported Cases: Studies concerning the investigation of the cases contracted locally with no evidence of importation and no direct link to transmission from an imported case (indigenous) and the malaria cases or infections in which the infection was acquired outside the area in which it is diagnosed (imported) (modified definition [\[ref\]](#)). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- identifying and/or characterizing pockets of transmission
- reducing transmission and/or eliminating malaria foci
- detecting outbreaks, responding & preventing onward transmission
- developing malaria transmission maps

Insecticide Resistance: Studies concerning the property of mosquitoes to survive exposure to a standard dose of insecticide [\[ref\]](#). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- epidemiology and sources of insecticide resistance
- mechanisms and molecular basis of insecticide resistance
- genetic diversity of insecticide resistance mosquitoes
- the use of mathematical models to predict insecticide resistance
- developing technologies to detect mosquito resistance
- monitoring insecticide resistance
- evaluating strategies to contain and/or mitigate insecticide resistance
- developing effective insecticides against resistant mosquitoes
- the effectiveness of vector tools in areas of insecticide resistance
- measuring the impact of insecticide resistance on malaria transmission

***P. vivax*:** Studies concerning any primary investigation (trial or discovery), or secondary research (review) on the species *Plasmodium vivax*.

Vulnerable populations: Studies concerning groups of people who are particularly at considerably higher risk of contracting or will likely suffer greater burden subsequent to malaria infection in certain situations or contexts (modified definition [\[ref\]](#)). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into understanding risk factor or targeting intervention on:



- pregnant women, infants and children
- people suffering from HIV/AIDS or patients with other mutually effective co-infections
- high-risk groups, including indigenous communities
- non-immune migrants, and mobile or displaced populations
- populations out of catchment or coverage of the health system or established intervention

Response Strategies

Combination interventions: Studies concerning any combination of intervention tools and strategies and their evaluation [\[ref\]](#).

Drug-based Strategies: Studies concerning the use of medicines either in absence of or in combination with other interventions to treat malaria infections and their consequences (modified definition [\[ref\]](#)). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) on implementing and evaluating:

- artemisinin-based combination therapies (ACTs) or any other regimen to treat *P. falciparum* and *P. vivax* infections.
- chloroquine or any other regimen to treat *Plasmodium* infections
- drug delivery and targeting approaches, including any form of mass drug administration

Modelling: Studies concerning and not limited to any primary investigation (trial or discovery), or secondary research (review) into understanding and applying the role of mathematics and mathematical models in providing an explicit framework for understanding the disease transmission dynamics within and between hosts and parasites [\[ref\]](#).

Tools for Elimination: Studies concerning the development or evaluation of any product, device, technique, or other tools for direct application including and not limited to diagnosis, clinical treatment (drugs), vaccination, and vector control to achieve and maintain malaria elimination [\[ref\]](#). The activities listed here are broadly categorized as **Vaccines (Immune Correlates)**, **Diagnostics**, and **Product Development**.

- **Vaccines (Immune Correlates):** Studies concerning the measurable signs associated with vaccine-induced protection [\[ref\]](#). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:
 - the development and mechanisms of malaria immunity
 - malaria antigens that activate the immune system
 - identifying vaccine targets
 - safety and immunogenicity of vaccine candidates
 - antibodies that confer protection against malaria infection
 - the relationship between immunity and malaria transmission
- **Diagnostics:** Studies concerning tools and methods used in the process of establishing the cause of an illness (modified definition [\[ref\]](#)). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:
 - evaluating different screening tools and/or strategies to detect malaria infections
 - developing new diagnostic methods
 - improvement on the sensitivity and specificity of existing diagnostic methods
 - developing new methods to identify asymptomatic/sub-microscopic infections
 - implementing tools to detect infections
- **Product Development:** Studies concerning the research, development and testing of new drugs or commodities. Activities listed here may include and are not limited to any primary



investigation (trial or discovery) or secondary research (review) into the establishment of product development partnerships (PDPs), research and development of new drugs, diagnostics, vaccines, etc.

Vector-based Strategies: Studies concerning the deployment of any countermeasure against malaria-transmitting mosquitoes, intended to limit their ability to transmit the disease [\[ref\]](#). Activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- the effectiveness of vector tools, such as LLINs or IRS
- testing new vector control tools
- the effectiveness of different vector control strategies
- testing new vector control strategies in the field



Basic Science

Enabling Technologies & Assays: Studies concerning the testing of new technologies and laboratory procedures. The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into biological platforms, DNA sequencing, etc.

Parasite Genetic Diversity: Studies concerning the targeting of the genetic characteristics of the parasite. The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- genetic characteristics of the *Plasmodium* species
- population genetics structure, complexity and diversity
- genetic diversity of drug resistant parasites
- genetic diversity of asymptomatic/sub-microscopic infections



Epidemiology

Asymptomatic Reservoir: Studies concerning the presence of parasites in the blood of infected humans without symptoms of illness [\[ref\]](#). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into the characteristics, infection mechanisms, and strategies of targeting asymptomatic/sub-microscopic infections, including:

- their epidemiology and risk factors
- gametocyte carriage
- their genetic diversity
- their mechanism(s) in contributing to transmission
- innovative approaches (e.g. molecular methods, serology, etc.) to identify such infections
- identifying individuals who harbour hypnozoites
- evaluation of strategies to prevent, detect and/or treat such infections
- non-human hosts of *Plasmodium* parasites that can act as reservoirs of infection

Measurement of Transmission: Studies concerning the measurement and understanding of malaria transmission [\[ref\]](#). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- assessment of the determinants of transmission



- characterizing malaria vector species and investigating their capacity to transmit malaria infection
- serological markers of infection and their role in monitoring transmission
- development and/or implementation of tools to measure transmission
- malaria patterns of transmission and/or its epidemiology in a given area
- development of malaria transmission maps
- modelling aimed at evaluating the impact of malaria interventions on malaria transmission
- monitoring patterns of malaria transmission in relation to coverage and use of interventions

Residual Transmission: Studies concerning the persistence of transmission after good coverage has been achieved with high-quality vector control interventions to which local vectors are fully susceptible [\[ref\]](#). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- identifying and/or characterizing pockets of such transmission
- reducing and/or eliminating such transmission

Targeting Foci: Studies concerning the definition and understanding of circumscribed areas situated in currently or formerly malarious areas that contain the epidemiological and ecological factors necessary for malaria transmission (modified from [\[ref\]](#)). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- identifying and/or characterizing such pockets of transmission
- reducing transmission and/or eliminating foci
- detecting outbreaks, responding & preventing onward transmission
- developing malaria transmission maps



Health Systems & Operational Research

Financing & Economics: Studies concerning the financing function of a health system, particularly with the mobilization, accumulation and allocation of money to cover the health needs of the people, individually and collectively. The purpose of health financing is to make funding available, as well as to set the right incentives to providers, to ensure that all individuals have access to effective public and personal health care [\[ref\]](#). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into targeting the value, effectiveness, efficiency or the resources needed to achieve the coverage and service delivery objectives (e.g. *budgeting of services, cost-effectiveness of interventions, estimation of the costs, economic impact, etc.*)

Health Workforce: Studies concerning all people engaged in actions whose primary intent is to enhance health. These human resources include clinical staff, such as physicians, nurses, pharmacists and dentists, as well as management and support staff [\[ref\]](#). The activities listed here may include and are not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- the knowledge, skills, motivation and deployment of the health workforce
- the relationship between number of health workers and population health outcomes
- assessing the adequacy of the workforce to respond to the health-care needs of a given population

Information Systems: Studies concerning information systems (physical or procedural) and processes that collect data from health and other relevant sectors, which altogether provide the underpinnings for decision-making and have four key functions: data generation, compilation, analysis and synthesis, and



communication and use [\[ref\]](#). The activities listed here may include and not limited to any primary investigation (trial or discovery), or secondary research (review) into the analysis of the data to ensure overall quality, relevance and timeliness, and into effective conversion from data to information for health-related decision-making.

Leadership & Governance: Studies concerning the leadership and management structures and approaches in building and governing a health system to ensure that strategic policy frameworks exist and that are combined with effective oversight, coalition-building, regulation, attention to system design and accountability [\[ref\]](#).

Monitoring & Evaluation: Studies concerning the gathering and using of data on programme implementation (on a regular basis: weekly, monthly, quarterly or annually) with the aim of ensuring that programmes are proceeding satisfactorily or, if necessary, requiring adjustments. The overall goal of M&E is to improve programme effectiveness, efficiency and equity [\[ref\]](#). The activities listed here may include and not limited to any primary investigation (trial or discovery), or secondary research (review) into the routine measuring of programmatic effectiveness, or more strategic review of impact by interventions (which is further categorized as follows):

- **Impact of interventions:** Studies concerning the outcomes, consequences and repercussions of the strategies and programmes when they are implemented in the field. The activities listed here may include and not limited to any primary investigation (trial or discovery), or secondary research (review) into:
 - estimation and/or determination of the repercussions or effects of the strategies or programmes
 - implementation and/or evaluation of new combination of interventions or approaches

Service Delivery: Studies concerning the availability and delivery mechanisms of health services and products that meet a minimum quality standard and securing access [\[ref\]](#).

Social Science: Studies concerning the society and how populations behave and interact with each other and with the environment, in order to understand the effects of the habits, traditions and/or sociodemographic characteristics of the people and the communities, role of religion, rituals, etc. in the context of health and healthcare.

Surveillance: Studies concerning the continuous and systematic collection, analysis and interpretation of disease-specific data and use in planning, implementing and evaluating public health practice [\[ref\]](#). The activities listed here may include and not limited to any primary investigation (trial or discovery), or secondary research (review) into:

- different strategies for case investigation
- different approaches for data collection and/or reporting
- improvement of the malaria surveillance system
- approaches for outbreak detection or detecting malaria re-introduction
- case management
- implementation and/or evaluation of new surveillance approaches