MASS DRUG ADMINISTRATION FOR MALARIA: RESEARCH LANDSCAPE

PRE-READ FOR THE WHO GMP EVIDENCE REVIEW GROUP ON MASS DRUG ADMINISTRATION FOR MALARIA

11-13 September 2018, Geneva, Switzerland

SUMMARY

Mass Drug Administration (MDA), the strategy of administrating antimalarials to an entire population at the same time regardless of infection status, has been a key component of many malaria control and elimination efforts.

Currently, several studies are being implemented in order to evaluate and define the role that MDA, in combination with other strategies, plays in the path towards malaria control and elimination.

With the aim of facilitating the discussions at the Evidence Review Group (ERG) on Mass Drug Administration for Malaria, the Malaria Eradication Scientific Alliance (MESA) has mapped the landscape of current research in MDA for malaria by collecting, quality checking and validating information related to ongoing and closed research activities.

A total of 31 projects related to malaria MDA have been identified. Of these, seven are ongoing and 23 are closed. In terms of malaria transmission intensities, 16 studies are in areas of low and very low transmission, four are located in moderate transmission areas, three are set in areas of high transmission, and two are taking place in both high and low transmission intensity regions. We have identified six projects responding to complex emergencies; one ongoing and four closed. The additional study deploying MDA in complex emergencies that has been identified is still in the planning phase.

Out of the 31 projects compiled, we have identified peer-reviewed publications for 19 of them and obtained additional information and/or preliminary results from personal communication with the PIs and researchers, or from abstracts and presentations at conferences, for 21 of them.

BACKGROUND AND OBJECTIVES

Mass Drug Administration (MDA), defined by WHO as *the administration of antimalarial treatment to all age groups of a defined population or every person living in a defined geographical area (except those for whom the medicine is contraindicated) at approximately the same time and often at repeated intervals*(1), has been historically a key component of malaria control and elimination strategies.

With the aim of facilitating the discussions at the upcoming Evidence Review Group (ERG) in September 2018, this report describes the landscape of recent and ongoing research in antimalarial MDA and provides an overview of the projects' main characteristics. The document builds on the landscape of research that was presented at the WHO ERG on MDA, MSAT and FSAT held on April 2015(2).

METHODOLOGY

Creation of a database of research in MDA

In order to review the current landscape of research in MDA, we systematically collected data on funded and active research projects.

Following the MESA terminology[1], a project was defined as a research or development study with defined objectives that contributes to the malaria elimination and eradication agenda. All the projects identified were entered into the MESA Track database and also compiled in an Excel file for the ERG pre-read package (see attached).

ELIGIBILITY CRITERIA

In line with the objectives of the ERG, the inclusion criteria for the projects were the following:

- ✓ Funded research projects
- ✓ Active from 2012 onwards
- ✓ Studies administering antimalarials to a population in a defined area regardless of infection status
- ✓ Age-targeted MDA (studies administering antimalarials to all children in a defined area regardless of infection status)
- ✓ MDA in complex emergencies

The exclusion criteria were:

- ⊗ Studies administering intermittent preventive treatment (IPT) to sub-populations (pregnant women, infants)
- ⊗ MDAs not administering antimalarials (e.g. ivermectin alone)
- ⊗ Seasonal malaria chemoprophylaxis (SMC)
- ⊗ MDA at the household level (focal MDA)
- ⊗ Mass Screen and Treat (MSAT)
- ⊗ Focal Screen and Treat (FSAT)

[1] http://www.malariaeradication.org/mesa-track/methodology-definitions

We did not systematically search for modelling projects, but if a modelling study was identified and met the inclusion criteria, it was also included in the compilation.

SYSTEMATIC DATA COLLECTION

From March to August 2018, we systematically compiled information on research projects and grants. We pursued the information, as a first step, from public sources using the following search terms: *mass drug administration AND malaria, MDA AND malaria, targeted parasite elimination, targeted malaria elimination.*

All the projects were collected from:

- Research grants databases:
  - Bill & Melinda Gates Foundation (BMGF)
  - Department for International Development UK (DFID)
  - Medical Research Council of the United Kingdom (RCUK)
  - National Institutes of Health (NIH)
  - President's Malaria Initiative (PMI)
  - Regional Artemisinin-resistance Initiative (RAI)
  - Wellcome Trust
- Clinical trials registries databases:
  - Clinicaltrials.gov
  - WHO International Clinical Trials Registry Platform (ICTRP)
- Other sources of information:
  - American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting 2017, symposia videos
  - Doctors Without Borders (MSF) website
  - MESA Track database
  - PubMed

As a second step to ensure quality control and validation of the information collected, we contacted the Principal Investigators of the projects and other expert researchers via e-mail.

Communication with PIs and researchers is an ongoing process. Hence, the data presented in this report reflects on the feedback received up to September 6th, 2018. To this date, 25 researchers and PIs have been contacted and 21 have responded (See Annex 2 for more details).

Categorization of Projects

The projects collected were charted according to the intensity of transmission (as described in the project abstract or country level in the 2017 WHO World Malaria Report(3)) or categorised as MDA in complex emergencies. Transmission intensities were those defined by the WHO Framework for malaria elimination(4):

- Very low transmission: Annual parasite incidence of <100 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* malaria >0 but <1%.
- Low transmission: Annual parasite incidence of 100-250 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* of 1-10%.
- Moderate transmission: Annual parasite incidence of 250-450 cases per 1000 population and a prevalence of *P. falciparum/P. vivax* malaria of 10-35%.

- High transmission: Annual parasite incidence of about 450 or more cases per 1000 population and a *P. falciparum* prevalence rate of ≥35%.

LANDSCAPE ANALYSIS

Overview

A total of 31 projects related to malaria MDA have been identified. Of these, seven are ongoing and 23 are closed. In terms of malaria transmission intensities, 16 studies are in areas of low and very low transmission, four are located in moderate transmission areas, three are set in areas of high transmission, and two are taking place in both high and low transmission intensity regions. We have identified six projects responding to complex emergencies; one ongoing and four closed. The additional study deploying MDA in complex emergencies that has been identified is still in the planning phase.

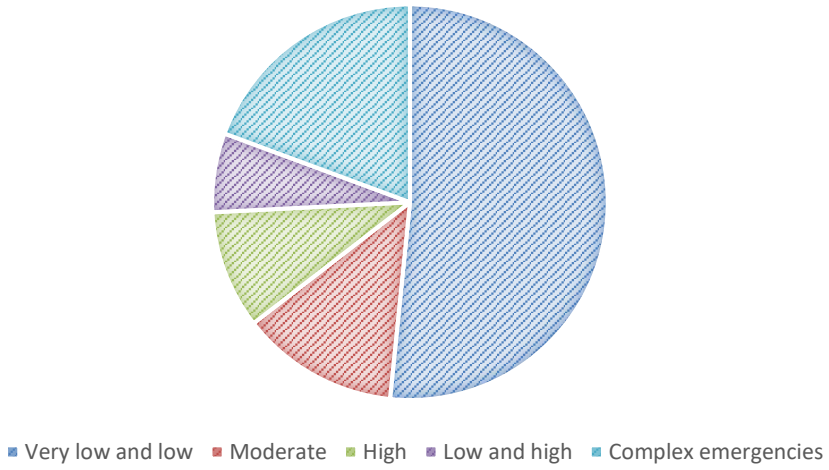

Figure 1. Proportion of projects by transmission intensity/complex emergencies.

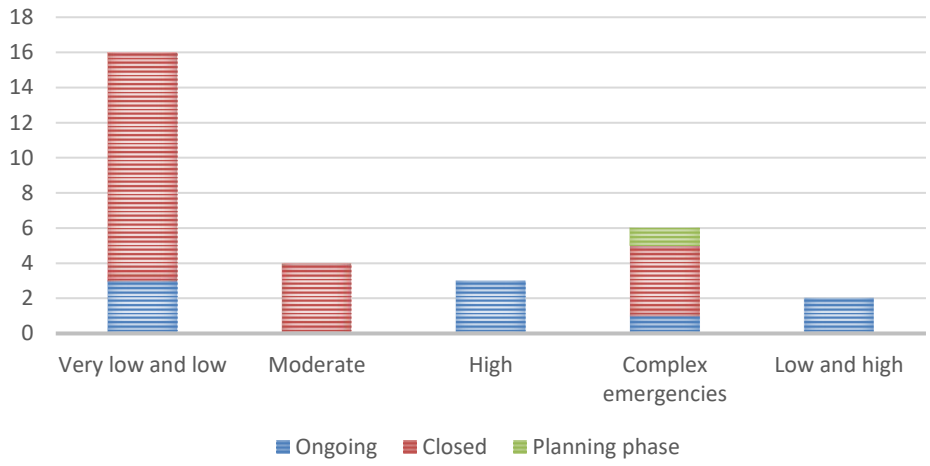

Figure 2. Number of projects by transmission intensity/complex emergencies and timeline.

Areas of low and very low transmission

From the 18 studies identified that are taking place in areas of low and very low transmission, three are ongoing and 15 are closed.

Ongoing

- In The Gambia, a cluster-randomized trial led by the Medical Research Council Unit and with expected end in August 2020, aims to determine whether MDA combining an antimalarial with ivermectin can reduce or interrupt malaria transmission over two years in an area with high coverage of standard malaria control interventions (*id 23*).
- In Haiti (*id 10*), a study led by the CDC Foundation and with planned ending in 2020 aims to assess the performance of MDA/TME (Targeted Malaria Elimination). Antimalarials are administered together with Indoor Residual Spraying (IRS) in identified hotspots on top of other concomitant interventions in order to assess the effectiveness, feasibility and acceptability of this package of interventions(5).
- A modelling study that will end in September 2018 (*id 9*) aims to develop an integrated strategy for *Plasmodium falciparum* elimination in Laos using the combination of MDA and mass vaccination. First results show that the addition of MDA may accelerate the reduction in malaria prevalence and incidence(6).

Closed

- A randomized trial in Zambia led by PATH-MACEPA which ended March 2018 (*id 2*), aimed to assess the effectiveness of MDA in areas of high and low malaria transmission by comparing MDA, focal MDA and standard of care (LLINs, IRS, passive case detection, enhanced case management and surveillance). The first results show a decrease in parasite prevalence after MDA in the low transmission area(7).
- The Oxford University-led multi-country project entitled *Targeted Chemo-Elimination (TCE/TME) to eradicate malaria in areas of suspected or proven artemisinin resistance in Southeast Asia and South Asia* (*id 1 and subprojects*) aimed to conduct and evaluate the efficacy of an MDA approach in selected areas with the goal of eliminating malaria. A total of 16 villages (eight control and eight intervention) with an approximate population of 500 people per village were targeted. The first available results show a lower parasite prevalence in the intervention villages (Cambodia, *id 1.1* and Myanmar/Thailand, *id 1.3*)(8,9).
- A cluster-randomized trial in Zanzibar led by the Karolinska Institute (*id 27*) aimed to determine the effectiveness of two rounds of MDA for reducing malaria transmission in 16 hotspot *shehias*.
- In Senegal, between 2013 and 2014 (*id 15*), the London School of Hygiene and Tropical Medicine conducted a randomized trial which evaluated the effect of the combination of IRS and chemotherapy (MSAT or MDA) compared to the National Malaria Control Policies(10).
- A cluster-randomized trial led by AFRIMS (*id 4*) aimed to quantify the relative effectiveness of targeted MDA in Cambodian soldiers(11).

Six closed non-randomized studies have been identified:

- A study in The Gambia led by the MRC Unit aimed to understand the dynamics of malaria transmission in high and low transmission areas (*id 12*) and conducted two yearly rounds of MDA at the start of the transmission season in 2014 and 2015. After the first round of MDA, a reduction in malaria incidence and prevalence was observed in both low and high transmission areas; whereas

after the second round of MDA, the effect was longer and the incidence decreased more in the low transmission region (results presented at ASTMH 2017(12,13)).

- A project in Eastern Myanmar (*id 26*) was a scale-up of the work developed in project *1* from 2014 to 2017. Three monthly MDA rounds were administered in the malaria posts in four villages identified as hotspots.
- A Doctors Without Borders-led study that took place in 2015 in Cambodia (*id 22*) aimed to assess the acceptability, feasibility and impact of MDA on clinical malaria and RDT-positivity among febrile patients in eight intervention villages. Three rounds of MDA were planned, but the intervention stopped after the first round due to the low coverage achieved(14).
- Also in Cambodia, project *11,* led by PSI, took three different approaches to assess malaria elimination efforts among mobile migrant workers in plantation settings. The first two approaches were to test different screen and treat models and the third approach was to do MDA if epidemiological data demonstrated that the majority of workers harboured malaria parasites. However, the results of the study showed very low level of parasitaemia across the population, so finally MDA was not deployed(15).
- In June 2013, RTI International (*id 14*) conducted MDA in four *shehias* of Zanzibar identified as hotspots which exceeded the epidemic alert threshold after having received mass screening and treatment(16).
- The Mahidol-Oxford Research Unit (MORU) led a project in the bordering areas of Thailand and Myanmar (*id 24*) which investigated the possibility of offering supervised chemoprevention to the whole community and monitored the intervention acceptability and effects(17).

Areas of moderate transmission

The four identified studies located in moderate transmission areas are closed, with the most recent one ending in 2017.

- In Myanmar, a randomized trial administered three monthly rounds of antimalarial in 2015 and assessed the feasibility, acceptability, safety and effect of the intervention in hotspots with artemisinin resistance and high migration rates (*id 13*). Preliminary results show a drop of *P. falciparum* prevalence from 14.2% at baseline to 1.4% (three months post-MDA) in the intervention group (results presented at ASTMH 2017(18)).
- The Barcelona Institute for Global Health and the Manhiça Health Research Centre conducted a non-randomized trial in Southern Mozambique which ended in 2017 and aimed to assess the feasibility and impact of a malaria elimination intervention package consisting of IRS and MDA on top of LLINs and standard case management (*id 7*).
- Two additional studies have been identified in Comoros, both led by the Guangzhou University of Chinese Medicine (*id 20.1 and 20.2*). The former took place in Anjouan Island during October and December 2012 with the aim of investigating the therapeutic effect of the method of Fast Elimination of Malaria by Source Eradication (FEMSE), consisting of three monthly rounds of antimalarial administered to approximately 85-93% of the island inhabitants. The results show a decrease of the malaria parasite rates among the population, with rates among randomly selected children decreasing from 13.5% before the MDA to 0.5% 18 months after the MDA(19). In 2013, the same intervention was conducted in the neighbouring island of Grande Comore (*id 20.2*)(20).

Areas of high transmission

A total of five projects located in high transmission areas have been identified. From these, two have activities in both high and low transmission areas (*id 2 and 12*).

Ongoing

- In Uganda, a study led by Pilgrim Africa aims to establish the impact of population-based Indoor Residual Spraying (IRS) in combination with chemotherapy on key malaria indicators in a high transmission setting in North-eastern Uganda (*id 16*). The first phase of the study is planned to end in December 2018(21).
- Project *17* is a newly funded protocol that uses data and samples leveraged from the above-mentioned study to investigate the impact of IRS and MDA on the malaria infectious reservoir, host immunity and drug resistance. It is expected to end in May 2022.
- In Togo, a study led by the Guangzhou University of Chinese Medicine aims to compare MDA to the current antimalarial measures in the country (*id 25*). The expected ending date is March 2019.

Closed

- The PATH-MACEPA cluster randomized trial in Zambia (*id 2*) showed no difference between the treatment groups (MDA compared to focal MDA and standard of care) in the high transmission region(7).
- The study conducted in The Gambia (*id 12*) showed a decrease in malaria incidence and prevalence in both high and low transmission areas after the first round of MDA, but this decrease was not observed in the high transmission region after the second round, with incidence and prevalence restoring to baseline levels (results presented at ASTMH 2017(12,13)).

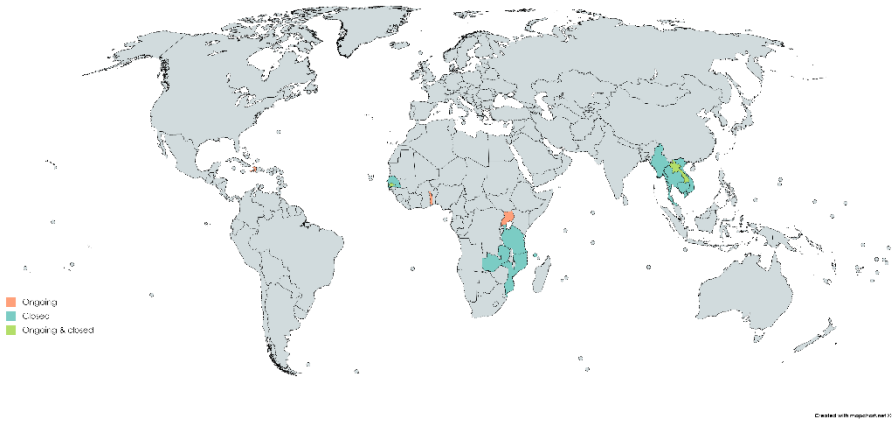

Figure 3. Identified ongoing and closed MDA studies in very low and low, moderate and high transmission areas.

Complex emergencies

We have identified six studies deploying MDA in exceptional complex emergencies. One is currently ongoing, four are closed, and one is in the planning phase.

The ongoing study is taking place in Nigeria in 2017 and 2018 with the aim of targeting child mortality caused by malaria, together with malnutrition and other comorbidities (*id E1*). Community health workers are administering the antimalarials for five monthly rounds during the high transmission season. According to WHO, 1.2 million children under five have been reached and the preliminary results show significant declines in malaria incidence and mortality in the target areas(22).

In Sierra Leone, MDA was used with the objective of reducing malaria transmission in Ebola affected areas between January 2014 and December 2015 (*id E4*). After two rounds of MDA, the number of RDT positive cases and malaria clinical cases decreased significantly(23). Another MDA was deployed in Liberia during the Ebola outbreak (October and December 2014) (*id E5*). Two rounds of MDA were carried out by delivering the antimalarials at fixed points in four neighbourhoods of Monrovia resulting in a decrease of the self-reported fever cases after the first MDA round(24). In 2015, three rounds of MDA were delivered in two refugee camps in Northern Uganda, targeting children aged six months to 14 years (*id E6*). Incidence of malaria decreased both in children less than five years and children aged between five and 14 years(25). Finally, an MDA program was considered in Greece between 2012 and 2014 as an additional measure to prevent reestablishment of malaria in the country (*id E7*). The total population of young male immigrants originating from malaria endemic countries who resided in the area was targeted and no malaria cases were recorded in the country in 2013 and 2014(26).

The study identified which is currently in planning phase is expected to take place in South Sudan as an emergency malaria response intervention(22) (*id E2*).

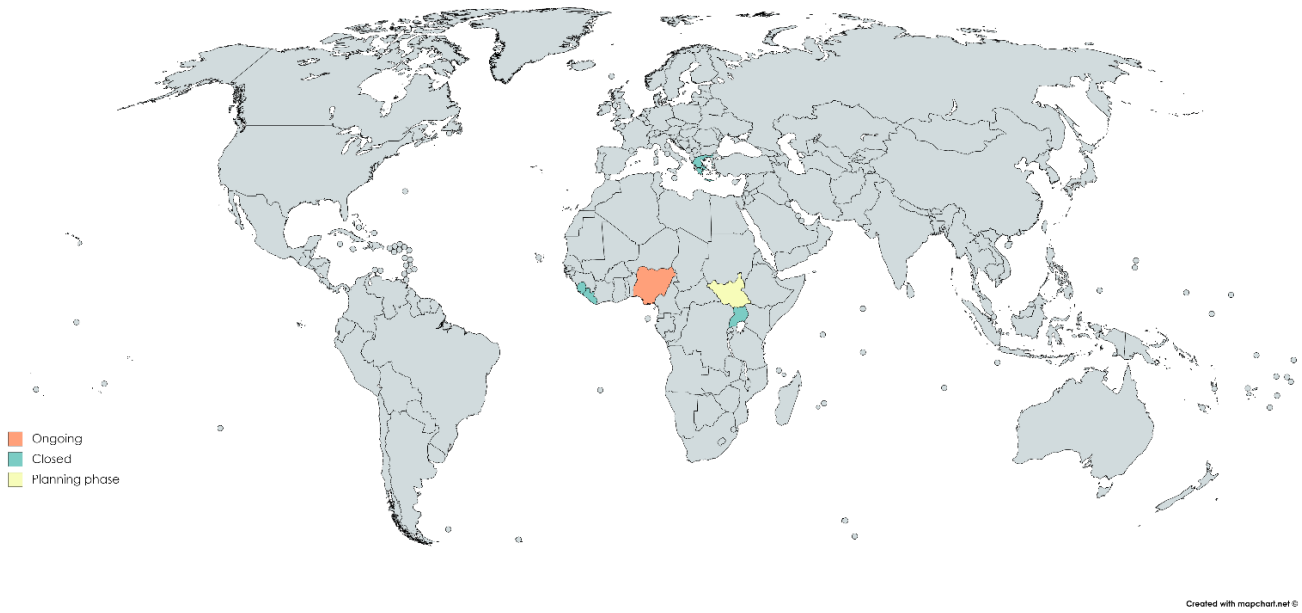

Figure 4. Projects deploying MDA in complex emergencies.

Projects timeline

Closed

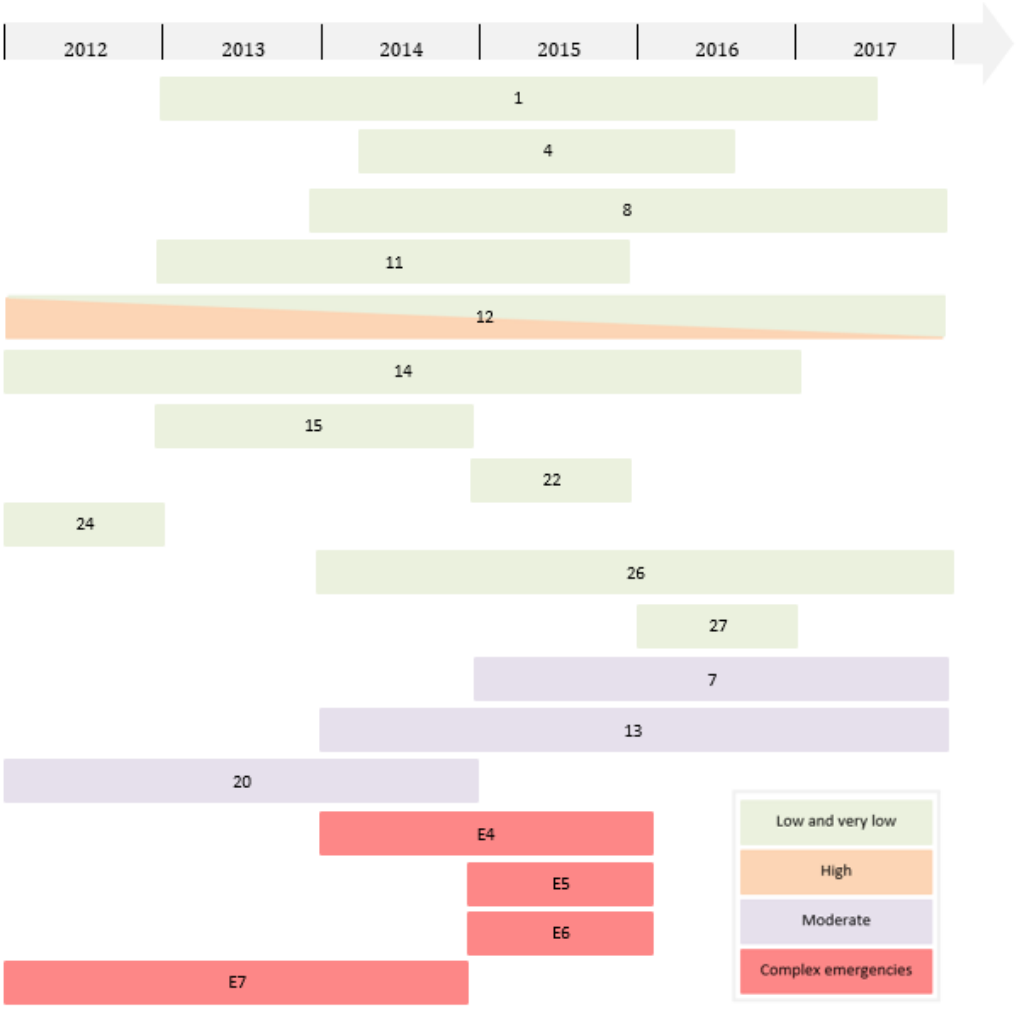

Figure 5. Closed projects by category.

Ongoing

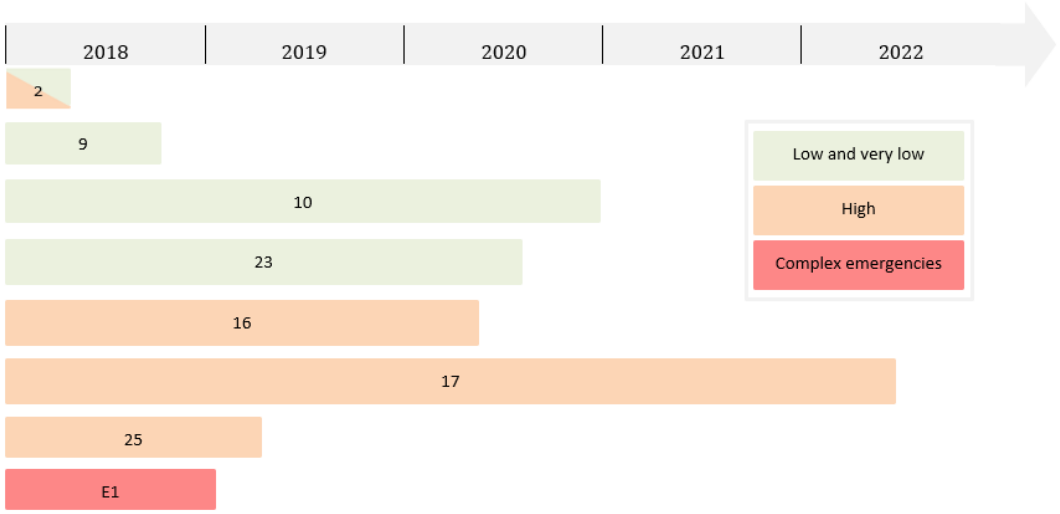

Figure 6. Ongoing projects by category.

Study design

From the 31 studies compiled, ten are randomized trials (one ongoing, nine closed; eight in areas of low and very low transmission, one with work in both high and low transmission areas, one in a moderate transmission region) (Table 1), 18 are non-randomized interventions (four ongoing, 13 closed, one in planning phase; seven in areas of low and very low transmission, three in moderate transmission regions, seven in high transmission areas, one in both high and low transmission areas) (Table 2), and there is one modelling study in Laos, one preparatory work taking place in Myanmar and one impact assessment study that uses data and samples leveraged from another study (Table 3).

Regarding the comparisons, MDA compared to no intervention or to standard malaria control interventions (mainly LLINs and IRS) is the most common situation, but there are also studies comparing MDA to focal MDA, or MDA to MSAT.

The studies compiled use a variety of MDA regimens, rounds of MDA and modes of delivery. The combination most frequently used is dihydroartemisinin-piperaquine (with or without primaquine) and the number of rounds ranges from three monthly rounds to two yearly rounds, five monthly rounds or four rounds. The most common mode of delivery is through directly-observed therapy (DOT), but the studies are also testing house-to-house campaigns, delivery in the malaria posts or delivery at fixed distribution sites.

Randomized trials

Id	Country (transmission intensity)	Drug	Rounds of MDA	Mode of delivery (MOD)
Ongoing				
23	The Gambia (low)	DP, Ivermectin	3 monthly rounds	^
Closed				
1.1	Cambodia (low)	DP	3 monthly rounds	DOT
1.2	Laos (low)	DP + PQ	3 monthly rounds	DOT
1.3	Myanmar/Thailand (low)	DP + PQ	3 monthly rounds	DOT
1.4	Vietnam (low)	DP + PQ	3 monthly rounds	DOT
2	Zambia (high and low)	DP	2 rounds	DOT (first and last dose)
4	Cambodia (low)	DP + PQ	3 monthly rounds	^
15	Senegal (low)	DP	2 rounds	DOT (first dose)
27	Tanzania (low)	DP + PQ	2 rounds	House-to-house campaigns
13	Myanmar (moderate)	DP + PQ	3 monthly rounds	^

Table 1. Randomized trials: overview of drug & regimen. DP: Dihydroartemisinin-Piperaquine; PQ: Primaquine; DOT: Directly-observed therapy; ^: data unavailable at the time this report was finalised.

Non-randomized interventions

Id	Country (transmission intensity)	Drug	Rounds of MDA	Mode of delivery
Ongoing				
10	Haiti (low)	SP + PQ	1 round	DOT during a house-to-house campaign
16	Uganda (high)	DP	4 rounds	DOT (first dose), house-to-house
25	Togo (high)	AP	^	^
E1	Nigeria (high)	AA	5 monthly rounds	Community health workers
Closed				
11	Cambodia (low)	DP	n/a	n/a
12	The Gambia (high and low)	DP	2 yearly rounds	DOT
14	Tanzania (low)	DP (main drug) AP (due to shortages) AA (children)	^	House-to-house
22	Cambodia (very low)	DP	3 rounds planned (but just 1 delivered)	DOT House-to-house
24	Thailand/Myanmar (low)	DP	3 monthly rounds	^
26	Myanmar (low)	DP + PQ	3 monthly rounds	Malaria posts
7	Mozambique (moderate)	DP	2 yearly rounds	DOT (first dose), house-to-house
20.1	Comoros (moderate)	AP + PQ (2 districts) AP (5 districts)	3 monthly rounds	DOT
20.2	Comoros (moderate)	AP	3 monthly rounds	DOT
E4	Sierra Leone (high)	AA	2 rounds	DOT (first dose), house-to-house
E5	Liberia (high)	AA	2 rounds	Distribution sites
E6	Uganda (high)	DP	3 rounds	Distribution sites
E7	Greece (very low – zero)	Chloroquine + PQ	1 round	DOT
Planning phase				
E2	South Sudan (high)	^	^	^

Table 2. Non-randomized interventions: overview of drug & regimen. SP: Sulfadoxine-Pyrimethamine; DP: Dihydroartemisinin-Piperaquine; PQ: Primaquine; AP: Artemisinin-Piperaquine; AA: Artesunate-Amodiaquine; DOT: Directly-observed therapy; ^: data unavailable at the time this report was finalised.

Other

Id	Country (transmission intensity)	Drug	Rounds of MDA	Mode of delivery

Ongoing				
9	Laos (low)	DP	3 monthly rounds	^
17	Uganda (high)	n/a	n/a	n/a
Closed				
8	Myanmar (low)	n/a	n/a	n/a

Table 3. Other study designs: overview. DP: Dihydroartemisinin-Piperaquine; ^: data unavailable at the time this report was finalised.

Population studied

The targeted population of the studies compiled varies largely depending on the setting and type of study (Tables 4-8).

Pregnant and lactating women are one of the main exclusion criteria for the studies. Some studies excluded both all trimesters pregnant women and lactating women, but others considered the pregnancies by trimesters; excluding only first trimester pregnancies when administering dihydroartemisinin-piperaquine, and excluding all pregnant women when giving ivermectin or primaquine.

The inclusion criteria regarding age also varies considerably across studies, ranging from children older than two months up to 75 years. In some studies, the weight was also considered to decide whether a child was included or not in the study.

Areas of low and very low transmission

Id	Country	Target & Size	Inclusion criteria	Exclusion criteria
Ongoing				
9	Laos (modelling)	Savannakhet province	n/a	n/a
10	Haiti	Foci in 5 communes Target population: 46000	≥6 months	Pregnant women (first trimester) (for SP) Pregnant women (for PQ)
23	The Gambia	32 villages EE: 6400	>6 months	Pregnant women (for ivermectin) Pregnant women first trimester (for DP)
Closed				
1.1	Cambodia	4 villages EE (intervention arm): 729	≥6 months	Pregnant or lactating women
1.2	Laos	4 villages EE (intervention arm): 1036	≥6 months	Pregnant or lactating women
1.3	Myanmar/Thailand	4 villages EE (intervention arm): 1131	≥6 months	Pregnant women (first trimester)

1.4	Vietnam	EE (intervention arm): 1527	≥6 months	Pregnant or lactating women
4	Cambodia	Target population: 1200 EE: 1050	>2 years	Pregnant or lactating women
8	Myanmar (preparatory work)	6 regions	n/a	n/a
11	Cambodia	40 plantations in 5 provinces	>5 years	^
14	Tanzania (Zanzibar)	4 shehias EE: 8816	>2 months	Pregnant women (first trimester)
15	Senegal	40 clusters EE (intervention arm): 80000	≥3 months	Pregnant women
22	Cambodia	8 intervention villages Target population: 7583	>5 years > 5 kg	Pregnant women >65 years
24	Myanmar/Thailand	3 villages targeted, but only 1 accessible	>14 years	Pregnant women
26	Myanmar	4 townships Target population: 12465	>6 months	Pregnant women (first trimester) Pregnant or lactating women (for primaquine)
27	Tanzania (Zanzibar)	16 shehias EE: 24000	>6 months	Pregnant women (first trimester) Pregnant or lactating women (for primaquine)

Table 4. Population studied in low and very low transmission areas. SP: Sulfadoxine-Pyrimethamine; PQ: Primaquine; EE: Estimated Enrolment, DP: Dihydroartemisinin-Piperaquine; ^: data unavailable at the time this report was finalised.

Areas of moderate transmission

Id	Country	Target & Size	Inclusion criteria	Exclusion criteria
Closed				
7	Mozambique	Target population: 50000	>6 months or >5 kg	Pregnant women (first trimester)
13	Myanmar	16 clusters Target population: 8721	>1 year	Pregnant women (first trimester) Pregnant women (for primaquine)
20.1	Comoros	Target population: 273700 - 309120	≥6 months	Pregnant women (first trimester)
20.2	Comoros	Target population: 420000	≥6 months	Pregnant women (first trimester)

Table 5. Population studied in moderate transmission areas.

Areas of high transmission

Id	Country	Target & Size	Inclusion criteria	Exclusion criteria
Ongoing				

16	Uganda	3 sub-counties Target population: 49762	≥6 months	Less than 6 months Less than 5 kg
17	Uganda (impact assessment)	n/a	n/a	n/a
25	Togo	Target population: 150000 (control area) 155350 (intervention)	>6 months	Less than 6 months

Table 6. Population studied in high transmission areas.

Areas of high and low transmission

Id	Country	Target & Size	Inclusion criteria	Exclusion criteria
Closed				
2	Zambia	10 districts 56 health facility catchment areas EE: 5640	≥3 months	Pregnant women (first trimester)
12	The Gambia	12 villages EE: 3725 (year 1) 3198(year 2)	>6 months	Pregnant women Less than 5 kg >75 years

Table 7. Population studied in the projects located in high and low transmission areas. EE: Estimated Enrolment.

Complex emergencies

Id	Country	Target & Size	Inclusion criteria	Exclusion criteria
Ongoing				
E1	Nigeria	5 areas in Borno State EE: 1.2M	All children under 5	^
Closed				
E4	Sierra Leone	7 high burden districts Target population: 1.6M	>6 months	Pregnant women (first trimester) Malnourished children
E5	Liberia	4 neighbourhoods Target population: 300000	>6 months	^
E6	Uganda	EE (intervention arm): 40611	Children 6 months to 14 years	Less than 6 months
E7	Greece	Target population: 1270 EE (intervention arm): 1094	Young male adults	Moderate or severe G6PD deficiency

Table 8. Population studied in complex emergencies. EE: Estimated Enrolment; ^: data unavailable at the time this report was finalised.

Concomitant interventions

The majority of the studies are implementing concomitant interventions to accompany the MDA strategy. LLINs, IRS, community engagement strategies, improved case management, and surveillance are the interventions most frequently implemented. Other strategies identified are health promotion to encourage health seeking for fever (*id 15*), sensitization meetings (*id 12*), or larval source management (*id 10*).

DISCUSSION

The studies included in this landscape analysis have been conducted in different settings and use different designs, drug regimens, drug doses, number of rounds, concomitant interventions and eligibility criteria, among others. They also assess different outcome measures. Hence, this variability hinders the process of drawing generalized conclusions and interpreting the results obtained.

For ongoing and unpublished projects, the details and preliminary results compiled in this report reflect on what the researchers have shared up to August 2018. Some of this data may change until the end of the studies.

We also acknowledge that the studies deploying MDA with the objective of interrupting transmission are not suited for joint evaluation with studies implementing MDA campaigns in the context of complex emergencies. Therefore, the studies *E1 – E7* should be examined and interpreted separately from the other studies compiled.

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ANNEX 1

All of the project details can be consulted in the attached Excel file.

ANNEX 2

List of researchers that have responded

- Amanda Tiffany, Centers for Disease Control and Prevention (CDC)
- Beatriz Galatas, Barcelona Institute for Global Health
- Daniel Parker, University of California, Irvine
- Dorothy Echodu, Pilgrim Africa
- James Eliades, PSI Myanmar
- Jianping Song, Guangzhou University of Chinese Medicine
- Joaniter Nankabirwa, Infectious Diseases Research Collaboration, Uganda
- Julia Mwesigwa, MRC Unit The Gambia at LSHTM
- Lisa White, Mahidol Oxford Tropical Medicine Research Unit
- Lorenz Von Seidlein, Mahidol Oxford Tropical Medicine Research Unit
- Maria Tseroni, University of Thessaly, Greece
- Mariusz Wojnarski, Armed Forces Research Institute of Medical Sciences (AFRIMS)
- Martin De Smet, Doctors Without Borders
- Matthew Coldiron, Doctors Without Borders
- Michelle Chang, Centers for Disease Control and Prevention (CDC)
- Myaing Myaing Nyunt, Duke University
- Paul Milligan, London School of Hygiene and Tropical Medicine (LSHTM)
- Ricki Orford, PSI
- Stefan Hoyer, Global Malaria Programme, World Health Organization
- Thomas Eisele, Tulane University
- Ulrika Morris, Karolinska Institute