Supplemental Materials

Mass Testing and Treatment to Accelerate Malaria Elimination: A Systematic Review and Meta-Analysis

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Supplementary Table 1. Search strategy

	Search term
1.	*malaria/ or Antimalarials/
2.	exp malaria, falciparum/ or exp malaria, vivax/
3.	malaria ovale.mp. or Plasmodium ovale/
4.	plasmodium malariae.mp. or Plasmodium malariae/
5.	1 or 2 or 3 or 4
6.	“mass test and treat” or Mass testing and treatment “. tw or MTAT.tw
7.	mass screening.tw or Mass screening/
8.	(screening or screened or diagnosed or diagnostics or test*).adj2 mass
9.	(“case detection” or PACD or ACD).tw
10.	“Population-wide” or “Community-wide” adj2 (test* or treat* or screen*)
11.	“household screen*”.tw
12.	“community case management”.tw or CCM .tw
13.	“monthly screening and treatment”.tw or MSAT.tw
14.	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13
15.	5 and 1

Supplementary Table 2. List of studies excluded after full review and primary reasons for exclusion

Study	Reference	Reason for exclusion
Bal (2020)	[1]	Not retrieved
Balogh (2014)	[2]	Not retrieved - Abstract presented in 63rd Annual ASTMH meeting
Batwala (2011)	[3]	Intervention: febrile illness
Bennett (2019)	[4]	Not retrieved
Bousema (2013)	[5]	Crossed Referenced Article
Bousema (2016)	[6]	Excluded for Contextual Factors (Intervention: hotspot-targeted interventions with larviciding, distribution of long-lasting insecticide-treated nets, indoor residual spraying, and focal mass drug administration)
Briet (2017)	[7]	Not retrieved
Chaturvedi (2017)	[8]	Intervention: Mass screening to determine prevalence
Collins (2019)	[9]	Study protocol
Cisse (2013)	[10]	Study protocol – no publication found – contacted PI but no response
Conner (2020)	[11]	Intrevention: combination strategies i.e., MTaT with PECADOM++ (weekly fever screening, testing and treatment
Cook (2015)	[12]	Study focus area: testing RDTs vs PCR in MTaT
Crowell (2011)	[13]	Not retrieved
Crowell (2012)	[14]	Crossed Referenced Article-Primary article already included
Daniels (2020)	[15]	Outcomes: parasite relatedness and genomic diversity
Desai (2015)	[16]	Not retrieved
Dhiman (2011)	[17]	Intervention: fever screening/no assessment of impact of intervention
Diallo (2014)	[18]	Not retrieved
Diallo (2015)	[19]	Not retrieved
Drakeley (2018)	[20]	No output reported yet
Faye (2015)	[21]	Not retrieved
Griffin (2010)	[22]	Excluded for Mathematical Modelling (Intervention: MTaT using single dose of ACT)
Griffin (2012)	[23]	Not retrieved
Grueninger (2011)	[24]	Not retrieved
Guelbeogo (2011)	[25]	Not retrieved
Hamainza (2014)	[26]	Population: Monthly household visit by CHWs for screening in health facility

		catchment area, not whole population residing in delimited area/Excluded for Contextual Factors
Hamer (2020)	[27]	Crossed Referenced Article
Hennessee (2013)	[28]	Not retrieved
Kinzer (2010)	[29]	Study design: Only included those who tested negative in initial recruitment screening for follow-up in incidence study and treatment evaluation
Krishnamoorthy (1985)	[30]	Not retrieved
Landier (2018)	[31]	Intervention: testing febrile cases in communitty for early detection of cases
Larsen (2012)	[32]	Not retrieved
Larsen (2013)	[33]	Not retrieved/CRA
Liew (2018)	[34]	Study design: RCD, followed with active case detection through test and treat post outbreak; not a study
Lover (2018)	[35]	Not retrieved
Lover (2019)	[36]	Not retrieved
Macauley (2005)	[37]	Study focus area: Case studies review
Maude (2009)	[38]	Excluded for Contextual Factors (Study focus area: commentary)
Mlacha (2020)	[39]	Intervention: This is a reactive strategy conducting MTaT based on weekly data from HF and only targeting villages with higher incidences in previous week
Minja (2019)	[40]	Not retrieved
Mosha (2013)	[41]	Intervention: Screen and treat approach vs tMDA/MDA
Mwanga (2015)	[42]	Excluded for Mathematical Modelling (Intervention: combination strategies that does not include MTaT)
Mwesigwa (2019)	[43]	Not retrieved
Nankabirwa (2010)	[44]	Not retrieved
Nct (2016)	[45]	Not retrieved
Nikolov (2015)	[46]	Not retrieved
Nosten (2019)	[47]	Study protocol
Pactr (2013)	[48]	Not retrieved
Pang (2001)	[49]	Excluded for Contextual Factors Intervention: symptoms-based test and treat in target village)
Pradhan (2022)	[50]	Intervention-Comprehensive Case Management
Ndong (2017)	[51]	Crossed Referenced Article
Ndong (2020)	[52]	Study protocol
Samuels (2014)	[53]	Not retrieved

Samuels (2015)	[54]	Not retrieved/CRA
Samuels (2017)	[55]	Crossed Referenced Article
Samuels (2021)	[56]	Crossed Referenced Article
Scott (2015)	[57]	Not retrieved
Scott (2016)	[58]	Study design: Cross sectional study determining the risk factors for malaria and RDT positivity
Shirayama (2008)	[59]	Study design: survey
Silal (2014)	[60]	Excluded for Mathematical Modelling (Intervention: MDA and FTaT)
Silal (2018)	[61]	Not retrieved
Silumbe (2012)	[62]	Not retrieved
Slater (2018)	[63]	Not retrieved
Stresman (2020)	[64]	Intervention: Reactive strategies
Stuckey (2014)	[65]	Not retrieved
Stuckey (2016)	[66]	Excluded for Mathematical Modelling (CRA)
Sutanto (2015)	[67]	Not retrieved
Sutcliffe (2012)	[68]	Study design: Longitudinal cohort & Cross-sectional survey
Tairou (2015)	[69]	Not retrieved
Thanh (2015)	[70]	Intervention implementation criteria: Time frame does not include 1-24 months after the start of the intervention
Tiono (2013)	[71]	Crossed Referenced Article
Tiono (2014)	[72]	Study focus area: evaluation of diagnostics
Villegas (2010)	[73]	Not retrieved
Vitor-Silva (2016)	[74]	Study design: prospective cohort
Wenger (2013)	[75]	Not retrieved
Wenger (2014)	[76]	Not retrieved

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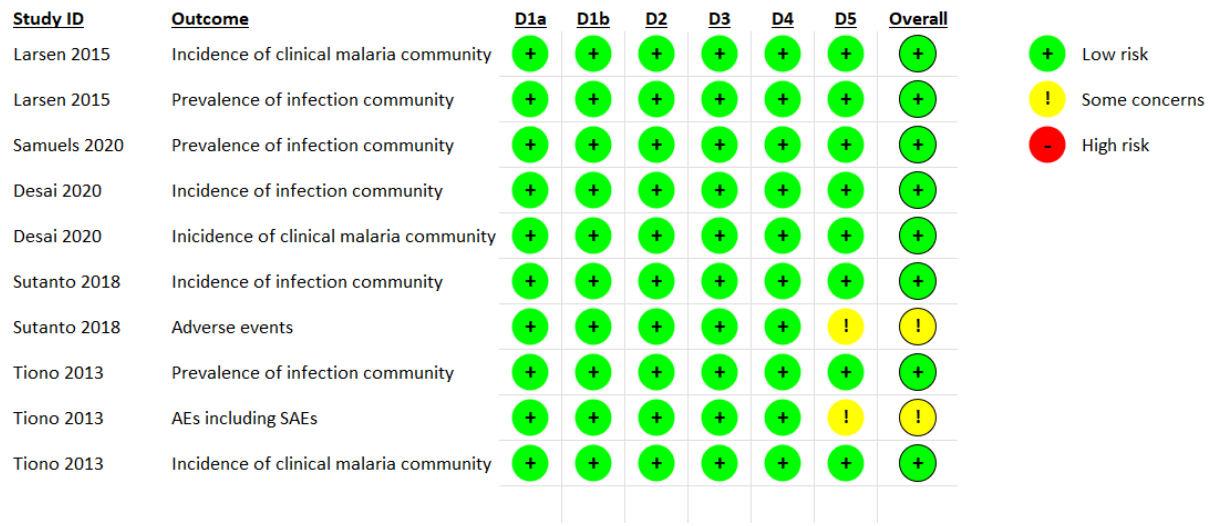
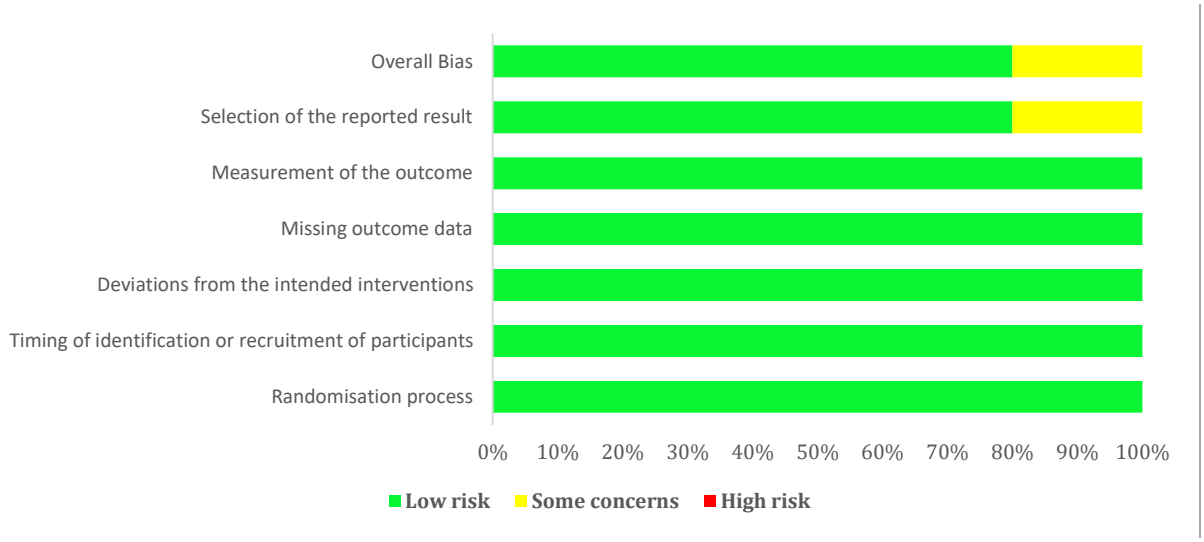
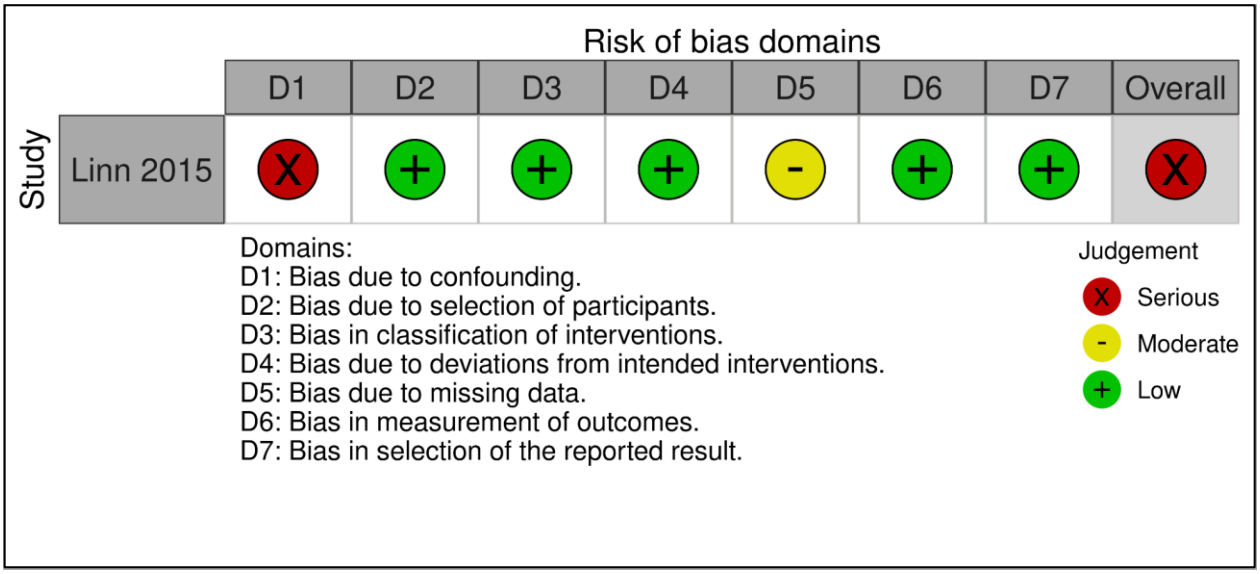
Supplementary Figure 1. Risk of Bias summary for the outcomes assessed in the cRCTs



Supplementary Figure 2: Risk of Bias summary for the cRCTs by percentage



Supplementary Figure 3: Risk of Bias summary for the controlled before and after study



Supplementary Table 3. Data extracted from included studies

Study 1 Desai et al. and Samuels et al. (2020)

Study characteristics	
METHODS	
Study dates	2013-2015
Location	Siaya district, western Kenya
Peak transmission season	May to July November to December
Baseline transmission intensity	High, baseline incidence rate 0.20 cases/p-y in intervention and 0.21 cases/p-y in control cluster parasite prevalence (median) was 33.9% in the intervention group and 36.8% in the control group
Parasite species	Plasmodium falciparum
Vector species	Anopheles arabiensis, Anopheles funestus,
Study design	Cluster-randomized controlled trial
Statistical power calculation	Incidence- Assuming a baseline incidence of 1.6 infections per person per year, a type I error rate of 5%, and 80% power to detect a difference in malaria incidence between intervention and control arms of at least 30%. The study required 220 per arm each year and author adjusted the sample size to 330 per arm for an expected 18% loss. Prevalence- assuming a malaria infection prevalence of 40% in the control arm, a type I error rate of 5%, and 80% power to detect a relative difference in malaria prevalence of 50% between arms, 20 compounds per cluster were selected to attain calculated sample size
Clusters	Unit of randomization: MTaT-wedges consisting of villages Incidence- Cohort of residents from 400 compunds Prevalence- 20 compounds from 20 clusters Features of the clusters: Buffer areas, restricted randomization Number of clusters selected: 30 Number of clusters analyzed: 20 Average cluster size: 10 villages
PARTICIPANTS	
Targeted population	Total: all residents of 10 HF catchment area Intervention: Incidence- Longitudinal cohort study: 330 participants Prevalence-Cross-sectional surveys: 20 compounds from the core area per cluster (857 participants) Comparison: Incidence: Longitudinal cohort study: 330 participants Prevalence: Cross-sectional surveys: 20 compounds from the core area per cluster (857 participants)
Participant characteristics	MTaT: all inhabitants >1 month Longitudinal cohort studies: ≥1 year old Cross-sectional studies: ≥1 month old

INTERVENTION	
Intervention	Mass testing and treatment
Comparator	Standard of care
Background interventions	Long lasting insecticide nets (in both arms)
Drug and manufacturer	Dihydroartemisinin–piperaquine (DP; Duocotexcin, Holy-Cotec, China, or Eurartesim, Sigma-Tau, Italy); children aged 1-3 months treated with artemether–lumefantrine (AL): pregnant women with quinine
Dosage	40 mg dihydroartemisinin and 320 mg piperaquine for 6 years and above; 20mg dihydroartemisinin and 160mg for children > 3 months to 5 years
Number of rounds per season or year	3
Treatment interval	Every 4 months
Duration of the intervention	2 months
Treatment adherence	Round 1: 350/371 (94.34%), Round 2: 323/341 (94.72%), Round 3: 291/318 (91.51%), Round 4: 331/347 (95.39%), Round 5: 363/382 (95.03%), Round 6: 303/325 (93.23%)
OUTCOMES	
Incidence of malaria infection at the community level	Measurement: Longitudinal cohort, measured by microscopy/RDT Timepoints: 0-12 months Sample size: year 1: 516 (MTaT 253 & Control 263) year 2: 550 (MTaT 272 & Control 278)
Incidence of clinical malaria at the community level	Measurement: Passive surveillance, measured by RDT Timepoints: 0-12 months Sample size: N/A
Prevalence of infection at the community level	Measurement: Cross-sectional survey Timepoints: 2 months post intervention (third round of MTaT) Sample size: year 1: MTaT 179 (896 individuals) compounds & control 183 compounds (1016 individuals) year 2: MTaT 179 (841 individuals) compounds & control 190 compounds (907 individuals)

Study 2 Larsen et al. (2015)

Study characteristics	
METHODS	
Study dates	Dec 2011-July 2013
Location	Gwembe, southern Kalomo, Siavonga, and Sinazongwe districts in southern Zambia
Peak transmission season	March-May
Baseline transmission intensity	Moderate, malaria parasite prevalence in children 1–59 months of age was 34.5% in the MTAT and 38.5% in control

	monthly confirmed case incidence in the preintervention period was 33.4 per 1,000 catchment population in control areas and 36.2 per 1,000 catchment population in intervention areas
Parasite species	Plasmodium falciparum
Vector species	Anopheles arabiensis and Anopheles funestus
Study design	Cluster randomized step-wedge control trial
Statistical power calculation	total sample size of 3,000 children < 5 years of age in 2,100 households > 2 rounds were sought to effectively measure a 50% reduction in malaria parasite prevalence between intervention and control groups, from an assumed 10% malaria parasite prevalence at baseline with a design effect of two.
Clusters	Unit of randomization: 46 HFCA, organized into 18 contiguous randomization group Features of the clusters: Satellite imagery from google earth Number of clusters selected: 18 Number of clusters analyzed: 18 Average cluster size: 2-3 HFCA
PARTICIPANTS	
Targeted population	MTaT & Incidence: All inhabitants of selected districts Prevalence: 3000 in 2100 households
Participant characteristics	Prevalence: children 1-59 months
INTERVENTION	
Intervention	Mass testing and treatment
Comparator	Standard of care
Background interventions	ITNs and IRS
Drug and manufacturer	Artemether-lumefantrine (AL) as per recommendation by MOH
Dosage	As per national guidelines provided by MOH
Number of rounds per season or year	3
Treatment interval	Every other month
Duration of the intervention	1 year
Treatment adherence	No monitoring was done for treatment adherence
OUTCOMES	
Incidence of clinical malaria at the community level	Measurement: HMIS based outpatient malaria case incidence Timepoints: 0-12 months Sample Size: All inhabitants of HFCA
Prevalence of infection at the community level	Measurement: Malaria indicator household survey, by RDT Timepoints: 6 months post-intervention Sample size: 513 (intervention); 511 (control)

Study 3 Sutanto et al. (2018)

Study characteristics	
METHODS	
Study dates	2013
Location	Wesiku district, West Timor, Indonesia
Peak transmission season	April-November
Baseline transmission intensity	Low, SPR in MST3 vs MST2 was 7.4% vs 8.7%
Parasite species	Plasmodium falciparum, Plasmodium vivax & Plasmodium malariae
Vector species	Anopheles barbirostris, Anopheles subpictus and Anopheles vagus
Study design	open-label, community-wide cluster-randomized controlled trial
Statistical power calculation	The recruitment target was 1029 subjects per arm, considering a cluster design effect of 1.5, 5% significance, 80% power, and a 1:1 sample size ratio between intervention and control arms. A target of 115 children per arm would yield a power of 82% in detecting an estimated 50% reduction in malaria incidence following MST.
Clusters	Unit of randomization: Households Features of the clusters: Stratified Number of clusters selected: 16 Number of clusters analyzed: 11 for prevalence & 16 for incidence Average cluster size: Average Households in clusters MST3-28, MST2-20, MST0-37 Average Resident in clusters MST3-89, MST2-71, MST0-124
PARTICIPANTS	
Targeted population	Total: All inhabitants for selected disctrict Intervention: Prevalence 1029, Incidence 115 children Comparison: Prevalence 1029, Incidence 115 children
Participant characteristics	Prevalence: all inhabitants Incidence: school children
INTERVENTION	
Intervention	Mass Testing and Treatment (MST)
Comparator	Standard of care
Background interventions	None
Drug and manufacturer	DHP (fixed-dose tablets of 40 mg dihydroartemisinin, 320 mg piperaquine; D-ARTEPP, Guilin Pharmaceutical Co, China, 6 December 2014 expiry); primaquine (15-mg primaquine base tablets; PT Phapros Tbk, Jakarta, Indonesia, October 2014 expiry)
Dosage	DHP regimen was daily based on patients' weight. For P. falciparum, primaquine was given as a single dose on day 1 as per patients' weight. For P. vivax infection the primaquine dose daily for 14 days as per patient weight

Number of rounds per season or year	MST3- 3 rounds MST2- 2 rounds
Treatment interval	MST3-5 weeks MST2-10 weeks
Duration of the intervention	6 months
Treatment adherence	Drug adherence was defined as taken completely as prescribed with witnessing, and occurred with >90% of cases
OUTCOMES	
Incidence of malaria infection at the community level	Measurement: Microscopy and PCR Timepoints: 0-6 months Sample size: 124 (MST3); 57 (MST2); 143 (MST0)
AEs	Drug administration during this study did not prompt withdrawal of any subject, and no serious AEs occurred. The most common AEs during treatment were fever (0.023/person-day), headache (0.008/person-day), vomiting (0.006/person-day), cough (0.004/person-day), shivering (0.003/person-day), and nasal congestion (0.002/person-day).

Study 4 Tiono et al. (2013)

Study characteristics	
METHODS	
Study dates	January 2011 to January 2012
Location	Saponé district, Burkina Faso
Peak transmission season	June-November
Baseline transmission intensity	High, mean prevalence of asymptomatic carriers intervention 42.8% & control 47.5%
Parasite species	Plasmodium falciparum
Vector species	Not mentioned
Study design	single-centre, controlled, parallel, cluster-randomized
Statistical power calculation	Not provided
Clusters	Unit of randomization: Villages Features of the clusters: Stratified randomization Number of clusters selected: 118 Number of clusters analyzed: 18 Average cluster size: 1 village
PARTICIPANTS	
Targeted population	Total: All inhabitants for selected district Intervention: 6817 Comparison: 7258
Participant characteristics	Prevalence: all inhabitants Incidence: children <5 years
INTERVENTION	

Intervention	Community-wide screening and treatment
Comparator	Standard of care
Background interventions	LLINs
Drug and manufacturer	AL/AL dispersible (20 mg artemether and 120 mg lumefantrine)
Dosage	twice a day for three consecutive days as per body weight
Number of rounds per season or year	3
Treatment interval	Every month
Duration of the intervention	1 year
Treatment adherence	Not quantified- AL adherence was good in those identified as asymptomatic carriers and in individuals with symptomatic malaria.
OUTCOMES	
Incidence of clinical malaria at the community level	Measurement: Microscopy/RDT Timepoints: 0-12 months Sample size: intervention: 5897, control: 6510
AEs including SAEs	There were no notable differences in AEs or SAEs between the intervention arm and the control arm at either the cluster or individual level and no new or unexpected safety findings were recorded. In total, 0.3% of treated asymptomatic carriers reported at least one AE within 7 days of starting treatment.
Prevalence of infection at the community level	Measurement: Microscopy Timepoints: 9 months post-intervention Sample size: intervention: 5897, control: 6510

Study 5 Linn et al. (2015)

Study characteristics	
METHODS	
Study dates	July to November 2013
Location	Saraya health district, South-east Senegal
Peak transmission season	July-November
Baseline transmission intensity	High, mean parasite prevalence of symptomatic malaria-intervention 1.88% and control 1.58%
Parasite species	Plasmodium falciparum
Vector species	Not mentioned
Study design	Quasi-experimental study design
Statistical power calculation	Not applicable
Clusters	N/A
PARTICIPANTS	

Targeted population	Total: 8954 Intervention: 4217 Comparison: 8954
Participant characteristics	All individuals of intervention households with symptoms of malaria
INTERVENTION	
Intervention	ProACT
Comparator	Passive community case management
Background interventions	LLINs & SMC
Drug and manufacturer	ACT
Dosage	As per national malaria control programme (NMCP)
Number of rounds per season or year	21
Treatment interval	Weekly
Duration of the intervention	21 weeks
Treatment adherence	Not mentioned
OUTCOMES	
Prevalence of infection at the community level	Measurement: symptomatic screening with RDT Timepoints: 21 weeks Sample size: 3762

Study 6 Ndong et al. (2019)

Study characteristics	
METHODS	
Study dates	2017-2018
Location	Pakro sub-district, Ghana
Peak transmission season	Perennial
Baseline transmission intensity	In July 2017, the prevalence of asymptomatic parasitemia was 36.3%
Parasite species	Plasmodium falciparum
Vector species	Not mentioned
Study design	Uncontrolled before and after
Statistical power calculation	Not applicable
Clusters	Not applicable
PARTICIPANTS	
Targeted population	Total: 5000

Participant characteristics	All inhabitants of selected area
INTERVENTION	
Intervention	Mass testing, treating and tracking (MTTT)
Comparator	Not applicable
Background interventions	Community case management
Drug and manufacturer	ACT
Dosage	As per the guidelines of National malaria control programme (NMCP)
Number of rounds per season or year	4
Treatment interval	4 months
Duration of the intervention	1 year
Treatment adherence	No data provided
OUTCOMES	
Prevalence of infection (asymptomatic parasitemia)	Measurement: RDT Timepoints: Every four months at each round Sample size: Round 1: 3891 & Round 4: 4941
Prevalence of infection (symptomatic parasitemia)	Measurement: RDT Timepoints: 1 year

Study 7 Bharti et al. (2020)

Study characteristics	
METHODS	
Study dates	2017 to 20020
Location	Mandla, Madhya Pradesh, India
Peak transmission season	June to September
Baseline transmission intensity	Varied with different annual parasitic incidence (API); Malaria prevalence 123 per 100,000
Parasite species	Plasmodium falciparum
Vector species	Not mentioned
Study design	Uncontrolled before and after
Statistical power calculation	Not applicable
Clusters	Not applicable
PARTICIPANTS	
Targeted population	Total: 63,194

Participant characteristics	All inhabitants of selected area
INTERVENTION	
Intervention	Mass Screening and Treatment (MSAT)
Comparator	Not applicable
Background interventions	ITN, IRS, active case management
Drug and manufacturer	ACT
Dosage	As per the national drugs policy
Number of rounds per season or year	3
Treatment interval	-
Duration of the intervention	-
Treatment adherence	-
OUTCOMES	
Prevalence of infection	Measurement: RDT Three rounds of MTaT were conducted to determine prevalence in the asymptomatic reservoir. MTaT was compared with detection through passive surveillance prevalence. 1st round-moderate to high burden areas - 50/28,527 i.e. 0.18% vs 0.06% from passive surveillance; 2nd round-low to high burden areas - 7/11,363 i.e. 0.06% vs 0.03% from passive surveillance; 3rd round- RCD of cryptic cases in 50 households -3/8,467 i.e. 0.03%