Supplementary Appendix

Supplement to: Roh et al, Dihydroartemisinin-piperaquine versus sulfadoxine-pyrimethamine for intermittent preventive treatment of malaria in pregnancy: a systematic review and individual participant data meta-analysis

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Appendix 1. PRISMA 2020 Checklist

Section and	Item	Checklist item	Location where
TITLE	#		item is reported
Title	1	Identify the report as a systematic review.	Paper title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	N/A
INTRODUCTION	-		
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Paragraphs 2-3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Paragraph 4
METHODS	-		
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	"Search strategy
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	and selection criteria" section
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	"Data extraction and quality assessment" section
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	"Study endpoints" section; Appendices 2-4
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Appendices 2-4
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	"Data extraction and quality assessment" section; Appendix 5

Appendix

Section and Topic	ltem #	Checklist item	Location where item is reported
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	"Statistical analysis" section
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	N/A
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	"Statistical analysis" section
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	"Statistical analysis" section
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	"Statistical analysis" section
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	"Statistical analysis" section; Appendix 4
RESULTS	-		
Study selection 1		Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	"Description of studies" section; Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	"Description of studies" section
Study characteristics	17	Cite each included study and present its characteristics.	"Description of studies" section; Appendix 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	"Description of studies" section
Results of	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b)	Figures 2-6; Results

Section and Topic	ltem #	Checklist item	Location where item is reported	
individual studies		an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	section	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	"Description of studies" section	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	All pooled estimates are presented with 95% CIs and <i>I</i> ² statistic for in Results section + Figures 2-6	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	95% CIs are presented with all outcomes	
DISCUSSION	-			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Paragraph 1-3	
	23b	Discuss any limitations of the evidence included in the review.	Paragraph 4	
	23c	Discuss any limitations of the review processes used.	Paragraph 4	
	23d	Discuss implications of the results for practice, policy, and future research.	Paragraph 5	
OTHER INFORMAT	ΓΙΟΝ	r		
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	"Data extraction and quality assessment"	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	section of Methods	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Summary, "Role of funding source" section of Methods, "Acknowledgement"	

Section and Topic	ltem #	Checklist item	Location where item is reported
			section
Competing interests	26	Declare any competing interests of review authors.	"Declaration of interests" section
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	"Data sharing statement" section

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Study Information	Desai 2015 ¹	Kakuru 2016 ²	Kajubi 2019 ³	Mlugu 2021⁴	Madanitsa 2023⁵ studies	Gutman unpublished ⁶
Study Details				·		
Source	PMID: 26429700	PMID: 26962728	PMID: 30910321	PMID: 33891721	PMID: 36913959	ClinicalTrials.Gov: NCT03009526
Study site(s)	4 health facilities in Siaya County, Kenya	Tororo District Hospital in Tororo District, E. Uganda	Masafu General Hospital in Busia District, E. Uganda	Kibiti District Center in Kibiti District, SE. Tanzania	12 ANC clinics in W. Kenya (n=4) S. Malawi (n=5), NE Tanzania (n=3)	Machinga District Hospital in Liwonde, S. Malawi
Prevalence of PfDHPS 540E mutation, %*	96%	85%	98%	90%	Kenya: 65%; Malawi: 90%; Tanzania: 52%	99%
Prevalence of PfDHPS 581G mutation, %*	6%	0%	3%	1%	Kenya: 11%; Malawi: 8%; Tanzania: 40%	8%
Number of Participants Randomized (Among Singleton Pregnancies)	1012	194	769	956	Kenya: 992; Malawi: 938; Tanzania: 1192	593
Sulfadoxine-Pyrimethamine	508	104	381	478	Kenya: 495; Malawi: 469; Tanzania: 597	297
Dihydroartemisinin-Piperaquine	504	90	388	478	Kenya: 497; Malawi: 469; Tanzania: 595	296
IPTp dosing regimen	every ANC	every 8 weeks	every 4 weeks	every 4 weeks	every 4 weeks	every 4 weeks
Number of IPTp doses, median (IQR)	2 (2-3)	3 (3-3)	6 (5-6)	3 (2-4)	Kenya: 4 (4-5); Malawi: 4 (4-5); Tanzania: 5 (4-6)	4 (3-5)

Appendix 2. Description of study characteristics and outcomes for each study

Study Information	Desai 2015 ¹	Kakuru 2016 ²	Kajubi 2019 ³	Mlugu 2021⁴	Madanitsa 2023⁵ studies	Gutman unpublished ⁶
PCR positivity at enrolment, %	32%	58%	81%	14%	Kenya: 15%; Malawi: 11%; Tanzania: 18%	11%
Birth outcomes		•	•			
Foetal Loss	Available	Available	Available	Available	Available	Available
Small-for-Gestational Age	Available [†]	Available	Available	Available [†]	Available	Available
Preterm Delivery	Available [†]	Available	Available	Available [†]	Available	Available
Low Birthweight	Available	Available	Available	Available	Available	Available
Neonatal Death	Available	Available	Available	Available (no cases)	Available	Available
Continuous Birth Outcomes						
Mean Birthweight	Available	Available	Available	Available	Available	Available
Mean Gestational Age at Delivery	Available [†]	Available	Available	Available [†]	Available	Available
Mean Birthweight-for-Gestational Age Z-scores	Available [†]	Available	Available	Available [†]	Available	Available
Malaria Outcomes						
Incidence of Clinical Malaria Episodes in Pregnancy	Available	Available	Available	Available	Available	Available
Any Evidence of Pigment Only in Placental Tissue by Histopathology	Available	Available	Available	Available	Available	Available

Study Information	Desai 2015 ¹	Kakuru 2016 ²	Kajubi 2019 ³	Mlugu 2021⁴	Madanitsa 2023⁵ studies	Gutman unpublished ⁶
Any Evidence of Parasites in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Available	Available; RDT not done on placental blood	Available; RDT not done on placental blood	Available; RDT not done on placental blood	Available	Available
Any Evidence of Parasites or Pigment in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Available	Available; RDT not done on placental blood	Available; RDT not done on placental blood	Available; RDT not done on placental blood	Available	Available
Any Evidence of Parasites in Maternal Peripheral Blood at Delivery by RDT, Microscopy, or PCR	Available	Available; RDT not done on maternal blood	Available; RDT and PCR not done on maternal blood	Available	Available	Available; PCR not done on maternal blood
Maternal Outcomes		·	•			•
Any Evidence of Severe Anaemia (Hb <7 g/dl) During Pregnancy	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Not Available; Measured at Delivery Only
Any Evidence of Moderate Anaemia (Hb <9 g/dl) During Pregnancy	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Not Available; Measured at Delivery Only
Any Evidence of Mild Anaemia (Hb <11 g/dl) During Pregnancy	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Available; Assessed at routine visits	Not Available; Measured at Delivery Only
MUAC at Delivery	Available; but unadjusted estimates b/c enrolment data was unavailable	Not available	Not available	Not available	Available	Available
Maternal weight gain per week [‡]	Available	Available	Available	Available	Available	Available

Study Information	Desai 2015 ¹	Kakuru 2016 ²	Kajubi 2019 ³	Mlugu 2021⁴	Madanitsa 2023⁵ studies	Gutman unpublished ⁶
Infant Outcomes						
Any Evidence of Stunting (LAZ <2 SD) from Birth to 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks
Any Evidence of Underweight (WAZ <2 SD) from Birth to 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks
Any Evidence of Wasting (WLZ <2 SD) from Birth to 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks
Mean LAZ at 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks
Mean WAZ at 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks
Mean WLZ at 2 Months of Life	Available; Follow up data up to 6-8 weeks	Available; Follow-up data up to 8 weeks	Available; Follow-up data up to 8 weeks	Not available	Available; Follow up data up to 6-8 weeks	Available; Follow up data up to10 weeks

Abbreviations: ANC = antenatal care visit; Hb = haemoglobin; IQR = interquartile range; LAZ = length-for-age z-score; MUAC = mid-upper arm circumference; WAZ = weight-for-age z-score; WLZ = weight-for-length z-score

* Prevalence of polymorphisms were reported as part of the published findings of the trial, except for the Kakuru et al (2016) and Kajubi et al (2019) studies which were reported separately in Conrad et al (2017)⁷ NS Nayebare et al (2020)⁸, respectively. Data were not available from Gutman et al (unpublished) and we therefore used estimates from a separate study (Gutman et al (2015)⁹) which was conducted at the same site eight years earlier.

† Gestational age dating not confirmed by ultrasound

 \ddagger Maternal weight gain per week calculated using the following formula: $\frac{Weight_{last ANC visit before delivery} - Weight_{enrollment}}{\# of weeks between enrollment and last ANC v sit}$

Appendix 3. Definition of outcomes

Outcome	Description
Birth outcomes	
Any Adverse Pregnancy Outcome	Binary variable defined as a composite outcome of any one of the following conditions: miscarriage (stillbirth (foetal loss ≥28 gestational weeks), preterm birth (PTB; delivery <37 gestational weeks), small-for-gestational age (SGA; birthweight <10 th percentile for gestational age using the INTERGROWTH-21 st standard ¹⁰); low birthweight (LBW; birthweight <2,500 grams), and neonatal loss (newborn death within the first 28 days of life).
Foetal Loss	Binary variable defined as a composite outcome of miscarriage or abortion that occurred at less than 28 gestational weeks
Small-for-Gestational Age	Binary variable defined as birthweight below the 10 th percentile for a given gestational age and sex using the INTERGROWTH-21 st standard ¹⁰
Preterm Delivery	Binary variable defined as delivery occurring less than 37 gestational weeks among live births
Low Birthweight	Binary variable defined as newborn birthweight that was less than 2500 grams. Birthweights were assessed among live births. Corrected birthweights were used when available.
Neonatal Death	Defined as a binary variable indicating the death of live newborn within the first 28 days of life
Continuous Birth Outcomes	-
Birthweight	Continuous measure of newborn birthweight in grams. Birthweights were assessed among live births. Corrected birthweights were used when available.
Gestational Age at Birth	Continuous measure of duration of gestation in weeks. Gestational age at birth was estimated using the gestational age at enrolment assessed by ultrasound, except for Desai 2015 and Mlugu 2021. Desai 2015 used the Ballard score, while Mlugu 2021 used last menstrual period to estimate gestational age at delivery.
Birthweight-for-Gestational	Continuous measure of birthweight-for-gestational age z-scores. Z-
Age Z-scores	scores were calculated based on INTERGROWTH-21 st standards ¹⁰
Malaria outcomes	
Incidence of Clinical Malaria Episodes in Pregnancy	Count outcome defined as the number of symptomatic malaria episodes experienced during the pregnancy follow-up period. Clinical malaria was defined as presence of documented fever (≥37.5°C or defined by study-specific definitions) or recent history of fever in the last 48 hours (or as defined by study-specific definitions) and a positive diagnosis of malaria by either rapid diagnostic test or blood smear microscopy.
Any Evidence of Pigment Only in Placental Tissue by Histopathology	Binary variable defined as the presence of pigment (but not parasites) in the placental tissue assessed by histopathology. For this outcome, active and chronic placental infections as defined by Rogerson et al ¹¹ were excluded from the analysis.

Any Evidence of Parasites in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Binary variable defined as the presence of parasites in the placental tissue or blood assessed by histopathology, PCR, microscopy, or RDT. For this outcome, samples containing pigment with no indication of parasites in the placental tissue or blood were considered in the "No" category.
Any Evidence of Parasites or Pigment in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Binary variable defined as the presence of parasites or pigment in the placental tissue or blood assessed by histopathology, PCR, microscopy, or RDT. For this outcome, samples containing pigment with no indication of parasites in the placental tissue or blood were considered in the "Yes" category.
Any Evidence of Parasites in Maternal Peripheral Blood at Delivery by RDT, Microscopy, or PCR	Binary variable defined as the presence of parasites detected in maternal peripheral blood at delivery by PCR, microscopy, or RDT.
Maternal outcomes	
Any Evidence of Severe Anaemia (Hb <7 g/dl) During Pregnancy	Binary variable defined as the incidence of a severe anaemic episode detected during routine and/or unscheduled visits during pregnancy follow-up period. Severe anaemia was defined as a haemoglobin measurement that fell below 7 g/dL.
Any Evidence of Moderate Anaemia (Hb <9 g/dl) During Pregnancy	Binary variable defined as the incidence of a moderate anaemic episode detected during routine and/or unscheduled visits during pregnancy follow-up period. Moderate anaemia was defined as a haemoglobin measurement that fell below 9 g/dL.
Any Evidence of Mild Anaemia (Hb <11 g/dl) During Pregnancy	Binary variable defined as the incidence of a moderate anaemic episode detected during routine and/or unscheduled visits during pregnancy follow-up period. Moderate anaemia was defined as a haemoglobin measurement that fell below 11 g/dL.
MUAC at Delivery	Continuous measure of maternal mid-upper arm circumference measured at delivery.
Maternal weight gain per week [‡]	Continuous variable defined as the average weight gained per week from enrolment to last day of antenatal care visit before delivery. The following formula was used to define this outcome: $\frac{Weight_{last ANC visit before delivery} - Weight_{enrollment}}{\# of weeks between enrollment and last ANC visit}$
Infant Outcomes	
Any Evidence of Stunting (LAZ <2 SD) from Birth to 2 Months of Life	Binary variable defined as a length-for-age z-score that fell below two standard deviations below the median 2006 WHO Child Growth Standards ¹² at birth and at routine scheduled neonatal care visits up to approximately two months of life. Infant follow-up periods varied between studies: six-eight weeks in the Desai 2015 and Madanitsa 2023 studies, eight weeks in the Kakuru 2016 and Kajubi 2019 studies, and ten weeks in the Gutman unpublished study.
Any Evidence of Underweight (WAZ <2 SD) from Birth to 2 Months of Life	Binary variable defined as a weight-for-age z-score that fell below two standard deviations below the median 2006 WHO Child Growth Standards ¹² at birth and at routine scheduled neonatal care visits up to approximately two months of life. Infant follow-up

	periods varied between studies: six-eight weeks in the Desai 2015
	and Madanitsa 2023 studies, eight weeks in the Kakuru 2016 and
	Kajubi 2019 studies, and ten weeks in the Gutman unpublished
	study.
	Binary variable defined as a weight-for-length z-score that fell
	below two standard deviations below the median 2006 WHO Child
Any Evidence of Marting	Growth Standards ¹² at birth and at routine scheduled neonatal care
Any Evidence of Wasting	visits up to approximately two months of life. Infant follow-up
(VVLZ <2 SD) from Birth to 2	periods varied between studies: six-eight weeks in the Desai 2015
Months of Life	and Madanitsa 2023 studies, eight weeks in the Kakuru 2016 and
	Kajubi 2019 studies, and ten weeks in the Gutman unpublished
	study.
1 AZ at 2 Months of Life	Continuous variable defined as a length-for-age z-score based on
LAZ at 2 Months of Life	2006 WHO Child Growth Standards. ¹²
MAZ at 2 Months of Life	Continuous variable defined as a weight-for-age z-score based on
WAZ at 2 Months of Life	2006 WHO Child Growth Standards. ¹²
M/1 7 at 2 Mantha of Life	Continuous variable defined as a weight-for-length z-score based
WLZ at 2 Months of Life	on 2006 WHO Child Growth Standards. ¹²

Appendix 4. Details of causal mediation analyses methods

Causal mediation analyses were performed to quantify the contributions of placental malaria, gestational weight gain (GWG), and maternal mid-upper arm circumference (MUAC) on the differential impact of IPTp regimens on birthweight-for-gestational age z-scores.

Brief summary of causal mediation analysis. Mediation analyses were conducted following the "potential outcomes" framework as described by Rubin¹³ and Pearl^{14,15} and extended for mediation analyses by Imai.¹⁶ Under this framework, potential outcomes are defined for each individual based on their counterfactual treatment condition. Let A, Y, and W denote the treatment, outcome, and confounder for each individual *i*. In the scenario where treatment is binary, an individual would have two potential outcomes: one had they been treated ($Y_i(a=1)$) and another if they had not been treated ($Y_i(a=0)$). The causal effect of the treatment on the outcome for individual *i* is defined as $Y_i(a=1) - Y_i(a=0)$ and $E[Y_i(a=1) - Y_i(a=0)]$ is defined as the average causal effect.

For mediation analyses, this framework is extended to further decompose the above causal effect (also known as the "total effect") into effects that are mediated and not mediated through some intermediate variable of interest, M. This requires the specification four potential outcomes for each individual:

<i>Y_i(a</i> =0, <i>M_i(a</i> =0))	$Y_i(a=0, M_i(a=1))$
<i>Y_i(a</i> =1, <i>M_i(a</i> =0))	$Y_i(a=1, M_i(a=1))$

where $Y_i(a, M_i(a))$ represents the outcome value for individual *i* had treatment been set to some value *a* and the mediator value was set to the value it would have taken on under *a*. For example, $Y_i(a=1, M_i(a=1))$ represents the outcome value for individual *i* had they been treated and their mediator value takes on what it would have "naturally" taken on had the individual been treated. By estimating potential mediator values, $M_i(a=0)$ and $M_i(a=1)$, we can separately estimate the **natural indirect effect (NIE)**, where NIE = $Y_i(a, M_i(a=1)) - Y_i(a, M_i(a=0))$ and is defined as the effect of the treatment on the outcome that is mediated through M (i.e., mediated effect). The **natural direct effect (NDE)** is defined as the effect of the treatment on the outcome via pathways not through mediator M (i.e., non-mediated effect), where NDE = $Y_i(a=1, M_i(a)) - Y_i(a=0, M_i(a))$.

Of these four potential outcomes, two can never be observed under real world conditions (i.e., $Y_i(a=1, M_i(a=0))$ and $Y_i(a=0, M_i(a=1))$) and depending the individual's actual treatment value, either one of the two remaining potential outcome values are actually observed ($Y_i(a=1, M_i(a=1))$) or $Y_i(a=0, M_i(a=0))$). However, these values are needed to derive NIE AND NDE; therefore, unobserved values must be estimated from data.

Required assumptions. To interpret NIE and NDE estimates causally, several assumptions need to be met¹⁷, including:

- No unmeasured confounding between treatment-outcome, treatment-mediator, and mediatoroutcome
- Treatment and mediator positivity
- Well-defined treatment and mediator
- Mediator and outcome values are unaffected by another individual's treatment and mediator condition
- No presence of a mediator-outcome confounder that is itself affected by the treatment

Targeted Maximum Likelihood Estimation Approach to Causal Mediation Analysis. We used the semiparametric, doubly robust targeted maximum likelihood estimation (TMLE) approach to estimate NIE and NDE. TMLE offers advantages over traditional parametric approaches by imposing fewer assumptions about the underlying data generating process. It does so by allowing data-adaptive, ensemble machine-learning approaches (e.g., SuperLearner via the sl3 package¹⁸) to flexibility accommodate interactions and non-linear relationships between variables, thereby reducing the risk of model misspecification.

A detailed description of the TMLE approach is provided in Zheng and van Der Laan (2012).¹⁹ In brief, the observed data is used to generate an initial outcome model estimating the expected outcome conditional on treatment, mediator, and confounders (i.e., Q[Y|A, M, W]). The initial outcome estimates are then updated using "clever covariates" derived from two propensity score models: one estimating the conditional probability given confounders (g(A|W)) and one estimating the conditional probability of treatment given mediator and confounders (g(A|W)). This process, known as the "targeting step" of TMLE, is performed to ensure that the final estimates optimize the bias-variance trade-off, thereby enhancing the precision, efficiency, and robustness of causal effect estimates. Finally, this updated estimate is used to generate updated estimates of the four potential outcomes and NIE and NDE are calculated as the mean difference across these potential outcomes (using prior formulas).

Mediation analysis methods. The directed acyclic graph (DAG) on the right was used to represent our assumptions of the causal relationships between treatment mediator, outcome, and confounders. Mediators were analyses separately to prevent overly complex models given our small sample size and to reduce the risk of violating the treatment and mediator positivity assumption.



The medout con package in R²⁰ was used to estimate NIE, NDE, and the corresponding 95% confidence intervals. Definitions of the treatment, mediator, outcome, and confounders used in the analyses are provided in the table below. The algorithm library for the initial outcome model included elastic net regularization, lasso (L-1 penalized) regression, generalized linear regression, generalized additive models, and extreme gradient boosting. The algorithm library for propensity score models included simple intercept models, generalized additive models, and gradient boosted decision tree models. 10-fold cross-validation was used all applications. Observations with missing values were excluded from the analysis.

Variable	Description
Treatment (A)	Randomized assignment to IPTp with sulfadoxine-pyrimethamine (A=1) or
	dihydroartemisinin-piperaquine (A=0)
Mediators (M)	• Placental malaria, defined as any evidence of pigment or parasites in
	the placental tissue or blood detected by histopathology, RDT,
	microscopy, and/or PCR
	• Gestational weight gain, defined as mean weight gain per week from
	enrolment to last antenatal care visit before delivery
	• Maternal mid-upper arm circumference in cm measured at delivery
Outcome (Y)	Birthweight-for-gestational age z-score using INTERGROWTH-21 st
	birthweight standards
Confounders (W)	Maternal age, BMI, weight, and gestational age; highest schooling level
measured at enrolment	completed by mother (none, primary, secondary, or higher); and infant sex

Variable definitions

Appendix 5. Bias assessment using the Cochrane Risk of Bias Tool 2.0

Appendix

Summary. The Cochrane risk of bias tool for randomized trials (RoB 2.0) was applied to each study. As the primary outcome of the individual trials often differed from the primary outcome of our meta-analysis and varied between studies, we conducted the risk of bias assessment based on the primary outcome of the meta-analysis. Overall, six of the eight trials were considered to have a low risk of bias; two studies (Desai et al, 2015 and Mlugu et al, 2021) had some concerns regarding the primary outcome because gestational age dating was not confirmed by ultrasound. This may have resulted in misclassification of small-for-gestational age and preterm birth, both of which are included as components in the composite primary outcome. Detailed visualizations from the RoB 2.0 assessment are provided below. Plots were generated using the robvis package in R.²¹



Risk of bias traffic light plot

Appendix 6. Participant characteristics at enrolment by arm

Table S-1. Desai et al, Kenya (2015)

Enrolmont observatoristics	Total	IPTp-SP	IPTp-DP	
	N=1,012	N=508	N=504	
Maternal age in years, mean (SD)	23·4 (5·7)	23·5 (5·9)	23·4 (5·5)	
Gestational age in weeks, mean (SD)	22.9 (4.8)	22.8 (4.9)	23.0 (4.8)	
Gravidity categories, n/N (%)				
Primigravidae	336/1012 (33%)	178/508 (35%)	158/504 (31%)	
Secundigravidae	215/1012 (21%)	112/508 (22%)	103/504 (20%)	
Multigravidae (3+)	461/1012 (46%)	218/508 (43%)	243/504 (48%)	
Weight in kg, mean (SD)	61.6 (9.2)	61.5 (9.1)	61.7 (9.4)	
Height in cm, mean (SD)	164·3 (6·8)	164·3 (6·9)	164·3 (6·7)	
Maternal MUAC in cm, mean (SD)				
Highest level of schooling completed, n/N	N (%)			
None	229/1004 (23%)	114/505 (23%)	115/499 (23%)	
Primary	569/1004 (57%)	283/505 (56%)	286/499 (57%)	
Secondary	183/1004 (18%)	96/505 (19%)	87/499 (17%)	
Higher	23/1004 (2%)	12/505 (2%)	11/499 (2%)	
Wealth index tertiles, n/N (%)				
Lowest tertile	328/1006 (33%)	172/505 (34%)	156/501 (31%)	
Middle tertile	331/1006 (33%)	164/505 (32%)	167/501 (33%)	
Highest tertile	347/1006 (34%)	169/505 (33%)	178/501 (36%)	
Slept under a bed net last night, n/N (%)	725/1012 (72%)	364/508 (72%)	361/504 (72%)	
Microscopy positivity, n/N (%)	154/984 (16%)	79/499 (16%)	75/485 (15%)	
PCR/LAMP positivity, n/N (%)	322/1002 (32%)	167/504 (33%)	155/498 (31%)	

Table S-2. Kakuru et al, Uganda (2016)

Enrolment characteristics	Total	IPTp-SP	IPTp-DP
	N=194	N=104	N=90
Maternal age in years, mean (SD)	21.7 (4.0)	21.3 (3.6)	22·2 (4·3)
Gestational age in weeks, mean (SD)	15·3 (2·0)	15·2 (2·0)	15·4 (2·0)
Gravidity categories, n/N (%)			
Primigravidae	73/194 (38%)	42/104 (40%)	31/90 (34%)
Secundigravidae	58/194 (30%)	30/104 (29%)	28/90 (31%)
Multigravidae (3+)	63/194 (32%)	32/104 (31%)	31/90 (34%)
Weight in kg, mean (SD)	55.6 (6.9)	55·5 (6·8)	55·7 (7·1)
Height in cm, mean (SD)	162·7 (6·8)	162·8 (6·8)	162·5 (6·9)
Maternal MUAC in cm, mean (SD)			
Highest level of schooling completed, n/N	N (%)		
None	9/194 (5%)	6/104 (6%)	3/90 (3%)
Primary	143/194 (74%)	74/104 (71%)	69/90 (77%)
Secondary	39/194 (20%)	22/104 (21%)	17/90 (19%)
Higher	3/194 (2%) 2/104 (2%)		1/90 (1%)
Wealth index tertiles, n/N (%)			
Lowest tertile	67/194 (35%)	38/104 (37%)	29/90 (32%)
Middle tertile	66/194 (34%)	31/104 (30%)	35/90 (39%)
Highest tertile	61/194 (31%)	35/104 (34%)	26/90 (29%)
Slept under a bed net last night, n/N (%)	174/194 (90%)	91/104 (88%)	83/90 (92%)
Microscopy positivity, n/N (%)			
PCR/LAMP positivity, n/N (%)	111/193 (58%)	58/104 (56%)	53/89 (60%)

Table S-3. Kajubi et al, Uganda (2019)

Enrolmont observatoriation	Total	IPTp-SP	IPTp-DP
Enrotment characteristics	N=769	N=381	N=388
Maternal age in years, mean (SD)	23.7 (5.8)	23.8 (5.9)	23.7 (5.6)
Gestational age in weeks, mean (SD)	15·5 (2·4)	15·5 (2·4)	15·4 (2·3)
Gravidity categories, n/N (%)			
Primigravidae	193/769 (25%)	100/381 (26%)	93/388 (24%)
Secundigravidae	187/769 (24%)	83/381 (22%)	104/388 (27%)
Multigravidae (3+)	389/769 (51%)	198/381 (52%)	191/388 (49%)
Weight in kg, mean (SD)	55·9 (7·6)	56·1 (7·7)	55.6 (7.6)
Height in cm, mean (SD)	158-6 (6-0)	158·8 (6·2)	158·4 (5·9)
Maternal MUAC in cm, mean (SD)			
Highest level of schooling completed, n/N	N (%)		
None	63/769 (8%)	37/381 (10%)	26/388 (7%)
Primary	512/769 (67%)	248/381 (65%)	264/388 (68%)
Secondary	175/769 (23%)	89/381 (23%)	86/388 (22%)
Higher	19/769 (2%)	19/769 (2%) 7/381 (2%)	
Wealth index tertiles, n/N (%)			
Lowest tertile	251/740 (34%)	122/366 (33%)	129/374 (34%)
Middle tertile	248/740 (34%)	116/366 (32%)	132/374 (35%)
Highest tertile	241/740 (33%)	128/366 (35%)	113/374 (30%)
Slept under a bed net last night, n/N (%)	242/740 (33%)	122/366 (33%)	120/374 (32%)
Microscopy positivity, n/N (%)	394/769 (51%)	192/381 (50%)	202/388 (52%)
PCR/LAMP positivity, n/N (%)	622/769 (81%)	313/381 (82%)	309/388 (80%)

Table S-4. Mlugu et al, Tanzania (2021)

Enrolmont observatoristics	Total	IPTp-SP	IPTp-DP
	N=956	N=478	N=478
Maternal age in years, mean (SD)	26.6 (7.1)	26.5 (7.1)	26.6 (7.1)
Gestational age in weeks, mean (SD)	21.5 (3.4)	21.4 (3.5)	21.7 (3.3)
Gravidity categories, n/N (%)			
Primigravidae	243/956 (25%)	128/478 (27%)	115/478 (24%)
Secundigravidae	213/956 (22%)	105/478 (22%)	108/478 (23%)
Multigravidae (3+)	500/956 (52%)	245/478 (51%)	255/478 (53%)
Weight in kg, mean (SD)	55·2 (8·9)	54.8 (8.5)	55.6 (9.3)
Height in cm, mean (SD)	152·2 (3·1)	152·1 (3·1)	152·4 (3·0)
Maternal MUAC in cm, mean (SD)			
Highest level of schooling completed, n/N	N (%)		
None	183/956 (19%)	94/478 (20%)	89/478 (19%)
Primary	657/956 (69%) 336/478 (70%)		321/478 (67%)
Secondary	116/956 (12%) 48/478 (10%)		68/478 (14%)
Higher	0/956 (0%)	0/956 (0%) 0/478 (0%)	
Wealth index tertiles, n/N (%)			
Lowest tertile	251/740 (34%)	122/366 (33%)	129/374 (34%)
Middle tertile	248/740 (34%)	116/366 (32%)	132/374 (35%)
Highest tertile	241/740 (33%)	128/366 (35%)	113/374 (30%)
Slept under a bed net last night, n/N (%)	695/956 (73%)	345/478 (72%)	350/478 (73%)
Microscopy positivity, n/N (%)			
PCR/LAMP positivity, n/N (%)	136/956 (14%)	63/478 (13%)	73/478 (15%)

Table S-5. Madanitsa et al, Kenya (2023)

Enrolmont observatoriation	Total	IPTp-SP	IPTp-DP
Enroument characteristics	N=992	N=495	N=497
Maternal age in years, mean (SD)	23.8 (5.3)	23.8 (5.4)	23.8 (5.3)
Gestational age in weeks, mean (SD)	21.5 (3.6)	21.8 (3.7)	21.3 (3.4)
Gravidity categories, n/N (%)			
Primigravidae	355/992 (36%)	178/495 (36%)	177/497 (36%)
Secundigravidae	268/992 (27%)	131/495 (26%)	137/497 (28%)
Multigravidae (3+)	369/992 (37%)	186/495 (38%)	183/497 (37%)
Weight in kg, mean (SD)	65·1 (11·2)	66.1 (11.1)	64.1 (11.2)
Height in cm, mean (SD)	162·7 (6·8)	163·4 (6·7)	162.0 (6.9)
Maternal MUAC in cm, mean (SD)	27.0 (3.2)	27·2 (3·3)	26.8 (3.2)
Highest level of schooling completed, n/N	N (%)		
None	57/992 (6%)	28/495 (6%)	29/497 (6%)
Primary	454/992 (46%) 218/495 (44		236/497 (47%)
Secondary	334/992 (34%)	334/992 (34%) 170/495 (34%)	
Higher	147/992 (15%)	79/495 (16%)	68/497 (14%)
Wealth index tertiles, n/N (%)			
Lowest tertile	46/992 (5%)	17/495 (3%)	29/497 (6%)
Middle tertile	473/992 (48%)	242/495 (49%)	231/497 (46%)
Highest tertile	473/992 (48%)	236/495 (48%)	237/497 (48%)
Slept under a bed net last night, n/N (%)	895/900 (99%)	440/445 (99%)	455/455 (100%)
Microscopy positivity, n/N (%)	127/981 (13%)	61/490 (12%)	66/491 (13%)
PCR/LAMP positivity, n/N (%)	127/865 (15%)	61/434 (14%)	66/431 (15%)

Table S-6. Madanitsa et al, Malawi (2023)

Enclmont observatoriation	Total	IPTp-SP	IPTp-DP	
Enrotment characteristics	N=938	N=469	N=469	
Maternal age in years, mean (SD)	24.5 (5.9)	24·3 (5·9)	24.7 (5.9)	
Gestational age in weeks, mean (SD)	21.3 (3.1)	21.2 (3.1)	21.3 (3.1)	
Gravidity categories, n/N (%)				
Primigravidae	287/936 (31%)	151/469 (32%)	136/467 (29%)	
Secundigravidae	238/936 (25%)	112/469 (24%)	126/467 (27%)	
Multigravidae (3+)	411/936 (44%)	206/469 (44%)	205/467 (44%)	
Weight in kg, mean (SD)	58.7 (9.1)	58.4 (8.8)	59.0 (9.4)	
Height in cm, mean (SD)	157·3 (6·3)	157·2 (6·1)	157.5 (6.6)	
Maternal MUAC in cm, mean (SD)	26·3 (3·1)	26·2 (3·1)	26·4 (3·1)	
Highest level of schooling completed, n/N	N (%)			
None	90/938 (10%)	42/469 (9%)	48/469 (10%)	
Primary	586/938 (62%) 306/469 (65%		280/469 (60%)	
Secondary	236/938 (25%)	107/469 (23%)	129/469 (28%)	
Higher	26/938 (3%)	14/469 (3%)	12/469 (3%)	
Wealth index tertiles, n/N (%)				
Lowest tertile	649/938 (69%)	331/469 (71%)	318/469 (68%)	
Middle tertile	165/938 (18%)	78/469 (17%)	87/469 (19%)	
Highest tertile	124/938 (13%)	60/469 (13%)	64/469 (14%)	
Slept under a bed net last night, n/N (%)	580/597 (97%)	283/293 (97%)	297/304 (98%)	
Microscopy positivity, n/N (%)	104/934 (11%)	52/467 (11%)	52/467 (11%)	
PCR/LAMP positivity, n/N (%)	159/867 (18%)	79/433 (18%)	80/434 (18%)	

Table S-7. Madanitsa et al, Tanzania (2023)

Enrolmont observatoriation	Total	IPTp-SP	IPTp-DP
Enrotment characteristics	N=1,192	N=597	N=595
Maternal age in years, mean (SD)	26·5 (6·5)	26·5 (6·6)	26·5 (6·5)
Gestational age in weeks, mean (SD)	20.0 (3.4)	19·9 (3·3)	20.1 (3.5)
Gravidity categories, n/N (%)			
Primigravidae	324/1187 (27%)	164/594 (28%)	160/593 (27%)
Secundigravidae	260/1187 (22%)	130/594 (22%)	130/593 (22%)
Multigravidae (3+)	603/1187 (51%)	300/594 (51%)	303/593 (51%)
Weight in kg, mean (SD)	59·5 (12·1)	59·5 (12·4)	59·5 (11·8)
Height in cm, mean (SD)	155·9 (6·1)	155·8 (6·0)	156·1 (6·3)
Maternal MUAC in cm, mean (SD)	27.5 (3.9)	27.6 (4.0)	27.5 (3.9)
Highest level of schooling completed, n/N (%)		
None	128/1189 (11%)	65/596 (11%)	63/593 (11%)
Primary	702/1189 (59%)	366/596 (61%)	336/593 (57%)
Secondary	326/1189 (27%) 147/596 (25%)		179/593 (30%)
Higher	33/1189 (3%)	1189 (3%) 18/596 (3%) 15/5	
Wealth index tertiles, n/N (%)			
Lowest tertile	336/1192 (28%)	177/597 (30%)	159/595 (27%)
Middle tertile	415/1192 (35%)	200/597 (34%)	215/595 (36%)
Highest tertile	441/1192 (37%)	220/597 (37%)	221/595 (37%)
Slept under a bed net last night, n/N (%)	932/956 (97%)	451/466 (97%)	481/490 (98%)
Microscopy positivity, n/N (%)	70/1192 (6%)	38/597 (6%)	32/595 (5%)
PCR/LAMP positivity, n/N (%)	114/1082 (11%)	56/543 (10%)	58/539 (11%)

Table S-8. Gutman et al, unpublished

Envolment observatoriation	Total	IPTp-SP	IPTp-DP	
	N=593	N=297	N=296	
Maternal age in years, mean (SD)	24.6 (6.2)	24.5 (6.4)	24.7 (6.1)	
Gestational age in weeks, mean (SD)	20.1 (3.2)	20.1 (3.2)	20.1 (3.1)	
Gravidity categories, n/N (%)				
Primigravidae	184/589 (31%)	102/295 (35%)	82/294 (28%)	
Secundigravidae	146/589 (25%)	73/295 (25%)	73/294 (25%)	
Multigravidae (3+)	259/589 (44%)	120/295 (41%)	139/294 (47%)	
Weight in kg, mean (SD)	58·4 (10·0)	58.6 (9.4)	58·3 (10·6)	
Height in cm, mean (SD)	157·4 (6·2)	157·3 (6·6)	157.5 (5.7)	
Maternal MUAC in cm, mean (SD)	26·2 (3·1)	26.4 (3.2)	26.1 (3.1)	
Maternal education level, n/N (%)				
None	286/593 (48%)	146/297 (49%)	140/296 (47%)	
Primary	209/593 (35%)	97/297 (33%)	112/296 (38%)	
Secondary	89/593 (15%) 49/297 (16%)		40/296 (14%)	
Higher	9/593 (2%) 5/297 (2%)		4/296 (1%)	
Wealth index tertiles, n/N (%)				
Lowest tertile	200/593 (34%)	93/297 (31%)	107/296 (36%)	
Middle tertile	196/593 (33%)	105/297 (35%)	91/296 (31%)	
Highest tertile	197/593 (33%)	99/297 (33%)	98/296 (33%)	
Slept under a bed net last night, n/N (%)	932/956 (97%)	451/466 (97%)	481/490 (98%)	
Microscopy positivity, n/N (%)				
PCR/LAMP positivity, n/N (%)	143/593 (24%)	66/297 (22%)	77/296 (26%)	

Appendix 7. Forest plot of study-specific estimates

Figure S-1. Any composite adverse birth outcome

	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value Weight
Overall Desai et al. Kenya, 2015	74/453 (16 3%)	65/452 (14 4%)] :	0 88 [0 65: 1 20]	0.415 10.8%
Kakuru et al. Uganda 2016	33/100 (33%)	21/85 (24 7%)		0.75 [0.47:1.19]	0.222 6.0%
Kajubi et al. Uganda, 2019	82/328 (25%)	98/346 (28.3%)		1.13 [0.88: 1.46]	0.331 13.4%
Mugu et al. Tanzania, 2021	94/478 (19.7%)	70/478 (14.6%)		0.74 [0.56: 0.99]	0.041 11.8%
Madanitsa et al. Kenva. 2023	72/462 (15.6%)	85/474 (17.9%)		1.15 [0.86: 1.53]	0.337 11.6%
Madanitsa et al. Malawi, 2023	108/424 (25.5%)	127/430 (29.5%)		1.16 [0.93: 1.44]	0.185 15.3%
Madanitsa et al. Tanzania. 2023	153/549 (27.9%)	183/539 (34%)	· · ·	1.22 [1.02; 1.46]	0.030 17.9%
Gutman et al, Malawi, unpublished	78/281 (27.8%)	88/274 (32.1%)		1.16 [0.90; 1.49]	0.263 13.2%
Random effects model				1.05 [0.92; 1.19]	0.505 100.0%
Prediction interval	0.00 [0.00, 0.15]	0.061		-[0.74; 1.48]	
Heterogeneity: $T = 48\% [0\%, 77\%], \tau =$	0.02[0.00; 0.15], p =	0.061	0.5 1 2		
			Favors DP Favors SP		
	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value Weight
Primigravidae			1		
Desai et al, Kenva, 2015	32/155 (20.6%)	32/133 (24.1%)		1.17 [0.76: 1.79]	0.487 10.8%
Kakuru et al, Uganda, 2016	18/38 (47.4%)	10/29 (34.5%)		0.73 [0.40: 1.33]	0.302 6.2%
Kajubi et al, Uganda, 2019	34/85 (40%)	34/77 (44.2%)		1.10 [0.77: 1.59]	0.592 14.0%
Mlugu et al, Tanzania, 2021	33/128 (25.8%)	22/115 (19.1%)		0.74 [0.46; 1.20]	0.220 9.2%
Madanitsa et al, Kenya, 2023	36/165 (21.8%)	37/161 (23%)		1.05 [0.70; 1.58]	0.801 11.9%
Madanitsa et al, Malawi, 2023	43/131 (32.8%)	46/120 (38.3%)		1.17 [0.84; 1.63]	0.362 15.6%
Madanitsa et al, Tanzania, 2023	55/148 (37.2%)	68/141 (48.2%)		1.30 [0.99; 1.70]	0.059 20.2%
Gutman et al, Malawi, unpublished	39/93 (41.9%)	25/76 (32.9%)		0.78 [0.53; 1.17]	0.235 12.1%
Random effects model	,	()	\diamond	1.04 [0.90; 1.22]	0.583 100.0%
Prediction interval				-[0.77; 1.41]	
Heterogeneity: $I^2 = 18\% [0\%; 61\%], \tau^2 =$	< 0.01, <i>p</i> = 0.289				
Multigravidae					
Desai et al, Kenya, 2015	42/298 (14.1%)	33/319 (10.3%)		0.73 [0.48; 1.13]	0.156 9.4%
Kakuru et al, Uganda, 2016	15/62 (24.2%)	11/56 (19.6%)		0.81 [0.41; 1.62]	0.553 4.3%
Kajubi et al, Uganda, 2019	48/243 (19.8%)	64/269 (23.8%)		1.20 [0.86; 1.68]	0.272 13.6%
Mlugu et al, Tanzania, 2021	61/350 (17.4%)	48/363 (13.2%)		0.76 [0.54; 1.08]	0.120 12.7%
Madanitsa et al, Kenya, 2023	36/297 (12.1%)	48/313 (15.3%)		1.27 [0.85; 1.89]	0.251 10.4%
Madanitsa et al, Malawi, 2023	65/293 (22.2%)	80/308 (26%)		1.17 [0.88; 1.56]	0.279 16.3%
Madanitsa et al, Tanzania, 2023	98/398 (24.6%)	115/396 (29%)	+=	1.18 [0.94; 1.49]	0.161 20.5%
Gutman et al, Malawi, unpublished	39/186 (21%)	63/198 (31.8%)		1.52 [1.07; 2.14]	0.018 12.8%
Random effects model			$\langle \rangle$	1.09 [0.91; 1.29]	0.349 100.0%
	0.00 - 0.000			-[0.68; 1.73]	
Heterogeneity: $I^{-} = 47\% [0\%; 76\%], \tau^{-} =$	0.03, p = 0.069		r		
Test for subgroup differences: $\chi_1^2 = 0.12$,	df = 1 ($p = 0.734$)		0.5 1 2		
·····, // ····-,	V 7		Favors DP Favors SP		

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; LBW = low birthweight; RR = risk ratio; SGA = small-forgestational age; SP = sulfadoxine-pyrimethamine

Figure S-2. Foetal loss

	SP	DP								
Author, Country, Year	n/N (%)	n/N (%)		R	isk Rat	io		RR [95% CI]	p-value	Weight
Overall										
Desai et al, Kenya, 2015	17/508 (3.3%)	7/504 (1.4%)		_	•			0.42 [0.17; 0.99]	0.048	18.2%
Kakuru et al, Uganda, 2016	3/104 (2.9%)	0/90 (0%)			_			0.16 [0.01; 3.15]	0.231	2.1%
Kajubi et al, Uganda, 2019	8/381 (2.1%)	12/388 (3.1%)						1.47 [0.61; 3.56]	0.390	17.8%
Mlugu et al, Tanzania, 2021	7/478 (1.5%)	0/478 (0%)						0.07 [0.00; 1.16]	0.063	2.2%
Madanitsa et al, Kenya, 2023	7/495 (1.4%)	8/497 (1.6%)			-			1.14 [0.42; 3.11]	0.801	14.6%
Madanitsa et al, Malawi, 2023	6/469 (1.3%)	8/469 (1.7%)						1.33 [0.47; 3.81]	0.592	13.7%
Madanitsa et al, Tanzania, 2023	10/597 (1.7%)	13/595 (2.2%)			- 			1.30 [0.58; 2.95]	0.524	20.0%
Gutman et al, Malawi, unpublished	5/297 (1.7%)	6/296 (2%)			-	-		1.20 [0.37; 3.90]	0.757	11.4%
Random effects model					\diamond			0.94 [0.61; 1.46]	0.797	100.0%
Prediction interval					-			-[0.40; 2.22]		
Heterogeneity: $l^2 = 32\% [0\%; 70\%], \tau^2 = 0.$	07 [0.00; 4.18], p = 0.	.170								
			0.01	0.1	1	10	100			

Favors DP Favors SP

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigravidae						
Desai et al, Kenya, 2015	5/178 (2.8%)	1/158 (0.6%)		0.23 [0.03; 1.91]	0.172	14.2%
Kakuru et al, Uganda, 2016	3/42 (7.1%)	0/31 (0%)		0.19 [0.01; 3.60]		7.6%
Kajubi et al, Uganda, 2019	2/100 (2%)	4/93 (4.3%)		2.15 [0.40; 11.47]	0.370	23.1%
Mlugu et al, Tanzania, 2021	2/128 (1.6%)	0/115 (0%)		0.22 [0.01; 4.59]		7.1%
Madanitsa et al, Kenya, 2023	1/178 (0.6%)	3/177 (1.7%)		3.02 [0.32; 28.73]	0.337	12.8%
Madanitsa et al, Malawi, 2023	1/151 (0.7%)	3/136 (2.2%)		3.33 [0.35; 31.64]	0.295	12.8%
Madanitsa et al, Tanzania, 2023	1/164 (0.6%)	6/160 (3.8%)		6.15 [0.75; 50.51]	0.091	14.6%
Gutman et al, Malawi, unpublished	5/102 (4.9%)	0/82 (0%)		0.11 [0.01; 2.01]		7.8%
Random effects model			\diamond	0.99 [0.34; 2.89]	0.985	100.0%
Prediction interval				-[0.06; 15.40]		
Heterogeneity: $I^2 = 41\% [0\%; 74\%], \tau^2 = 0.96, \mu$	0 = 0.106					
Multigravidae						
Desai et al, Kenya, 2015	12/330 (3.6%)	6/346 (1.7%)		0.48 [0.18; 1.26]	0.134	22.9%
Kakuru et al, Uganda, 2016	0/62 (0%)	0/59 (0%)				0.0%
Kajubi et al, Uganda, 2019	6/281 (2.1%)	8/295 (2.7%)		1.27 [0.45; 3.61]	0.654	19.7%
Mlugu et al, Tanzania, 2021	5/350 (1.4%)	0/363 (0%)		0.09 [0.00; 1.58]		2.6%
Madanitsa et al, Kenya, 2023	6/317 (1.9%)	5/320 (1.6%)		0.83 [0.25; 2.68]	0.749	15.5%
Madanitsa et al, Malawi, 2023	5/318 (1.6%)	5/331 (1.5%)		0.96 [0.28; 3.29]	0.949	14.2%
Madanitsa et al, Tanzania, 2023	9/430 (2.1%)	7/433 (1.6%)		0.77 [0.29; 2.06]	0.605	22.5%
Gutman et al, Malawi, unpublished	0/193 (0%)	6/212 (2.8%)		- 11.84 [0.67; 208.75]		2.6%
Random effects model	· · ·		\diamond	0.81 [0.51; 1.28]	0.365	100.0%
Prediction interval			-	-[0.44; 1.48]		
Heterogeneity: $I^2 = 21\% [0\%; 64\%], \tau^2 = < 0.01$, <i>p</i> = 0.271					
2						
Test for subgroup differences: $\chi_1^c = 0.12$, df = 1 (p = 0.732)		0.01 0.1 1 10 10	00		
			Favors DP Favors SP			

Figure S-3. Small-for-gestational age (<10th percentile for birthweight-for-gestational age)

Author Country Year	SP n/N (%)	DP n/N (%)	Bisk Batio	BR [95% Cl]	p-value Weight
Aution, Country, Tear		1011 (70)	Then Halle		p raide freight
Overall					
Desai et al, Kenya, 2015	36/412 (8.7%)	39/415 (9.4%)		1.08 [0.70; 1.66]	0.741 7.8%
Kakuru et al, Uganda, 2016	22/97 (22.7%)	15/85 (17.6%)		0.78 [0.43; 1.40]	0.403 4.3%
Kajubi et al, Uganda, 2019	52/320 (16.2%)	70/327 (21.4%)		1.32 [0.95; 1.82]	0.096 13.2%
Mlugu et al, Tanzania, 2021	73/410 (17.8%)	64/400 (16%)		0.90 [0.66; 1.22]	0.494 14.6%
Madanitsa et al, Kenya, 2023	45/444 (10.1%)	57/452 (12.6%)		1.24 [0.86; 1.80]	0.245 10.4%
Madanitsa et al, Malawi, 2023	69/406 (17%)	88/406 (21.7%)		1.28 [0.96; 1.69]	0.093 16.6%
Madanitsa et al, Tanzania, 2023	113/532 (21.2%)	146/523 (27.9%)		1.31 [1.06; 1.63]	0.012 26.5%
Gutman et al, Malawi, unpublished	30/252 (11.9%)	31/253 (12.3%)		1.03 [0.64; 1.65]	0.904 6.6%
Random effects model			\diamond	1.17 [1.03; 1.32]	0.016 100.0%
Prediction interval				-[0.95; 1.44]	
Heterogeneity: $I^2 = 3\% [0\%; 69\%], \tau^2 < 0$	0.01 [0.00; 0.11], <i>p</i> =	0.404			
			0.5 1 2		
			Favors DP Favors SP		
	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value Weight
Primigravidae					
Desai et al Kenva 2015	23/147 (15.6%) 21/126 (16.7%)		1.07 [0.62: 1.83]	0.819 10.0%
Kalum at al Usanda 0010	10/05 (00.6%)	7/00 (04 10/)		0.04 [0.07, 1.04]	0.001 4.00/

Desai et al, Kenya, 2015	23/147 (15.6%)	21/126 (16.7%)	_			1.07 [0.62; 1.83]	0.819	10.0%
Kakuru et al, Uganda, 2016	10/35 (28.6%)	7/29 (24.1%)				0.84 [0.37; 1.94]	0.691	4.3%
Kajubi et al, Uganda, 2019	23/83 (27.7%)	24/72 (33.3%)		-		1.20 [0.75; 1.94]	0.448	13.0%
Mlugu et al, Tanzania, 2021	29/105 (27.6%)	19/95 (20%)				0.72 [0.44; 1.20]	0.213	11.4%
Madanitsa et al, Kenya, 2023	25/159 (15.7%)	27/153 (17.6%)		-	_	1.12 [0.68; 1.84]	0.649	11.9%
Madanitsa et al, Malawi, 2023	29/127 (22.8%)	31/111 (27.9%)		-		1.22 [0.79; 1.89]	0.367	15.4%
Madanitsa et al, Tanzania, 2023	43/145 (29.7%)	53/134 (39.6%)			_	1.33 [0.96; 1.85]	0.084	27.6%
Gutman et al, Malawi, unpublished	18/83 (21.7%)	11/71 (15.5%)				0.71 [0.36; 1.41]	0.332	6.4%
Random effects model				\diamond		1.09 [0.92; 1.30]	0.320	100.0%
Prediction interval						-[0.87; 1.37]		
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = < 0$	0.01, <i>p</i> = 0.510							
Multigravidae								
Desai et al, Kenya, 2015	13/265 (4.9%)	18/289 (6.2%)	_			1.27 [0.63; 2.54]	0.500	5.0%
Kakuru et al, Uganda, 2016	12/62 (19.4%)	8/56 (14.3%) -		*	-	0.74 [0.33; 1.67]	0.467	3.6%
Kajubi et al, Uganda, 2019	29/237 (12.2%)	46/255 (18%)				1.47 [0.96; 2.27]	0.077	13.0%
Mlugu et al, Tanzania, 2021	44/305 (14.4%)	45/305 (14.8%)				1.02 [0.70; 1.50]	0.909	16.2%
Madanitsa et al, Kenya, 2023	20/285 (7%)	30/299 (10%)				1.43 [0.83; 2.46]	0.196	8.2%
Madanitsa et al, Malawi, 2023	40/279 (14.3%)	57/293 (19.5%)				1.36 [0.94; 1.96]	0.105	17.5%
Madanitsa et al, Tanzania, 2023	70/384 (18.2%)	93/387 (24%)			_	1.32 [1.00; 1.74]	0.050	31.4%
Gutman et al, Malawi, unpublished	12/167 (7.2%)	20/182 (11%)				- 1.53 [0.77; 3.03]	0.224	5.1%
Random effects model				\diamond		1.28 [1.10; 1.49]	0.002	100.0%
Prediction interval						-[1.05; 1.55]		
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = 0, J$	v = 0.777							
Test for subgroup differences: $\chi_1^2 = 1.79$, df	$= 1 \ (p = 0.181)$		0.5	1	2			
			Favors	DP Favor	s SP			

Figure S-4. Preterm birth (<37 gestational weeks)

Author Ocument Vers	SP	DP	Diels Detie			Wainht
Author, Country, Year	n/in (%)	n/n (%)	RISK RATIO	RR [95% CI]	p-value	weight
Overall						
Desai et al, Kenya, 2015	15/433 (3.5%)	16/439 (3.6%)		1.05 [0.53; 2.10]	0.886	8.6%
Kakuru et al, Uganda, 2016	8/97 (8.2%)	7/85 (8.2%)		1.00 [0.38; 2.64]	0.998	4.4%
Kajubi et al, Uganda, 2019	21/320 (6.6%)	15/334 (4.5%)		0.68 [0.36; 1.30]	0.249	9.9%
Mlugu et al, Tanzania, 2021	10/410 (2.4%)	4/400 (1%)		0.41 [0.13; 1.30]	0.129	3.1%
Madanitsa et al, Kenya, 2023	20/450 (4.4%)	18/463 (3.9%)		0.87 [0.47; 1.63]	0.674	10.6%
Madanitsa et al, Malawi, 2023	35/418 (8.4%)	30/421 (7.1%)		0.85 [0.53; 1.36]	0.500	18.7%
Madanitsa et al, Tanzania, 2023	26/537 (4.8%)	28/524 (5.3%)		1.10 [0.66; 1.86]	0.710	15.2%
Gutman et al, Malawi, unpublished	44/258 (17.1%)	47/261 (18%)		1.06 [0.73; 1.53]	0.775	29.5%
Random effects model			\diamond	0.93 [0.76; 1.14]	0.473	100.0%
Prediction interval				-[0.72; 1.20]		
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = 0$	0.00; 0.21], <i>p</i> = 0.781					
			0.2 0.5 1 2 5			
			Favors DP Favors SP			

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigravidae			1			
Desai et al. Kenva. 2015	2/150 (1.3%)	8/132 (6.1%)		4.55 [0.98: 21.03]	0.053	5.0%
Kakuru et al, Uganda, 2016	5/35 (14.3%)	4/29 (13.8%)	_	0.97 [0.29; 3.27]	0.955	7.8%
Kajubi et al, Uganda, 2019	10/83 (12%)	5/73 (6.8%)		0.57 [0.20; 1.59]	0.281	11.1%
Mlugu et al, Tanzania, 2021	3/105 (2.9%)	3/95 (3.2%)	_	1.11 [0.23; 5.34]	0.901	4.7%
Madanitsa et al, Kenya, 2023	10/161 (6.2%)	7/155 (4.5%)		0.73 [0.28; 1.86]	0.507	13.2%
Madanitsa et al, Malawi, 2023	13/130 (10%)	11/116 (9.5%)	-+	0.95 [0.44; 2.03]	0.891	20.0%
Madanitsa et al, Tanzania, 2023	9/146 (6.2%)	9/134 (6.7%)		1.09 [0.45; 2.66]	0.851	14.6%
Gutman et al, Malawi, unpublished	16/86 (18.6%)	11/73 (15.1%)		0.81 [0.40; 1.63]	0.556	23.7%
Random effects model			\diamond	0.93 [0.66; 1.30]	0.665	100.0%
Prediction interval			—	-[0.61; 1.42]		
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = < 0$.01, <i>p</i> = 0.588					
Multigravidae						
Desai et al. Kenva. 2015	13/283 (4.6%)	8/307 (2.6%)		0.57 [0.24: 1.35]	0.199	8.9%
Kakuru et al. Uganda, 2016	3/62 (4.8%)	3/56 (5.4%)		1.11 [0.23: 5.26]	0.898	2.7%
Kajubi et al. Uganda, 2019	11/237 (4.6%)	10/261 (3.8%)		0.83 [0.36: 1.91]	0.654	9.5%
Mlugu et al. Tanzania, 2021	7/305 (2.3%)	1/305 (0.3%)		0.14 [0.02: 1.15]	0.068	1.5%
Madanitsa et al. Kenva. 2023	10/289 (3.5%)	11/308 (3.6%)	<u></u>	1.03 [0.45; 2.39]	0.941	9.4%
Madanitsa et al. Malawi. 2023	22/288 (7.6%)	18/303 (5.9%)		0.78 [0.43: 1.42]	0.413	18.4%
Madanitsa et al, Tanzania, 2023	17/388 (4.4%)	19/388 (4.9%)		1.12 [0.59; 2.12]	0.733	16.3%
Gutman et al, Malawi, unpublished	28/170 (16.5%)	36/188 (19.1%)	+	1.16 [0.74; 1.82]	0.510	33.2%
Random effects model	() () () () () () () () () ()	,	$\overline{\mathbf{A}}$	0.93 [0.72; 1.21]	0.592	100.0%
Prediction interval			_	-[0.67; 1.29]		
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = < 0$.01, <i>p</i> = 0.524			- / -		
Test for subgroup differences: $\chi_1^2 = 0.00$, df	= 1 (<i>p</i> = 0.983)		0.1 0.5 1 2 10			
			Favors DP Favors SP			

Figure S-5. Low birthweight

Author, Country, Year	SP n/N (%)	DP n/N (%)	Risk Ratio	BB [95% CI] r	-value Weight
,					
Overall					
Desai et al, Kenya, 2015	19/412 (4.6%)	22/415 (5.3%)		1.15 [0.63; 2.09]	0.648 11.3%
Kakuru et al, Uganda, 2016	12/97 (12.4%)	10/85 (11.8%)		0.95 [0.43; 2.09]	0.900 8.1%
Kajubi et al, Uganda, 2019	21/320 (6.6%)	22/327 (6.7%)		1.03 [0.58; 1.83]	0.933 11.8%
Mlugu et al, Tanzania, 2021	44/410 (10.7%)	22/400 (5.5%) -		0.51 [0.31; 0.84]	0.008 13.8%
Madanitsa et al, Kenya, 2023	19/444 (4.3%)	22/452 (4.9%)		1.14 [0.62; 2.07]	0.674 11.3%
Madanitsa et al, Malawi, 2023	31/407 (7.6%)	50/408 (12.3%)	+	1.61 [1.05; 2.46]	0.029 15.5%
Madanitsa et al, Tanzania, 2023	41/532 (7.7%)	57/523 (10.9%)	• •	1.41 [0.96; 2.07]	0.076 16.8%
Gutman et al, Malawi, unpublished	19/253 (7.5%)	22/255 (8.6%)		1.15 [0.64; 2.07]	0.644 11.5%
Random effects model				1.09 [0.83; 1.43]	0.537 100.0%
Prediction interval				-[0.51; 2.31]	
Heterogeneity: $I^2 = 50\% [0\%; 78\%], \tau^2 = 0$	Heterogeneity: $l^2 = 50\% [0\%; 78\%]$, $\tau^2 = 0.08 [0.00; 0.42]$, $p = 0.049$,	
			0.5 1 2		
			Favors DP Favors SP		

	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI] p-va	ue Weight
Primigravidae					
Desai et al, Kenya, 2015	12/147 (8.2%)	13/126 (10.3%)		1.26 [0.60; 2.67] 0.53	9 14.3%
Kakuru et al, Uganda, 2016	8/35 (22.9%)	4/29 (13.8%)		0.60 [0.20; 1.80] 0.36	6 8.6%
Kajubi et al, Uganda, 2019	11/83 (13.3%)	4/72 (5.6%)		0.42 [0.14; 1.26] 0.12	1 8.5%
Mlugu et al, Tanzania, 2021	14/105 (13.3%)	5/95 (5.3%)		0.39 [0.15; 1.05] 0.06	4 10.0%
Madanitsa et al, Kenya, 2023	8/159 (5%)	11/153 (7.2%)		1.43 [0.59; 3.46] 0.42	8 11.6%
Madanitsa et al, Malawi, 2023	16/127 (12.6%)	18/112 (16.1%)		1.28 [0.68; 2.38] 0.44	4 17.5%
Madanitsa et al, Tanzania, 2023	16/145 (11%)	16/134 (11.9%)		1.08 [0.56; 2.08] 0.81	3 16.7%
Gutman et al, Malawi, unpublished	13/84 (15.5%)	8/72 (11.1%)		0.72 [0.32; 1.63] 0.43	0 12.8%
Random effects model			\diamond	0.92 [0.68; 1.24] 0.57	78 100.0%
Prediction interval				-[0.56; 1.51]	
Heterogeneity: $I^2 = 19\% [0\%; 62\%], \tau^2 = 0.$	02, <i>p</i> = 0.278				
Multigravidae					
Desai et al. Kenva. 2015	7/265 (2.6%)	9/289 (3.1%)		1.18 [0.45: 3.12] 0.74	0 8.9%
Kakuru et al. Uganda, 2016	4/62 (6.5%)	6/56 (10.7%)		1.66 [0.49: 5.58] 0.41	2 6.4%
Kajubi et al. Uganda, 2019	10/237 (4.2%)	18/255 (7.1%)		1.67 [0.79; 3.55] 0.18	0 12.4%
Mlugu et al. Tanzania, 2021	30/305 (9.8%)	17/305 (5.6%)		0.57 [0.32; 1.01] 0.05	2 16.5%
Madanitsa et al. Kenva. 2023	11/285 (3.9%)	11/299 (3.7%)		0.95 [0.42; 2.16] 0.90	9 11.2%
Madanitsa et al. Malawi, 2023	15/280 (5.4%)	32/294 (10.9%)		2.03 [1.13; 3.67] 0.01	9 16.0%
Madanitsa et al, Tanzania, 2023	25/384 (6.5%)	41/387 (10.6%)		1.63 [1.01; 2.62] 0.04	5 19.2%
Gutman et al, Malawi, unpublished	6/167 (3.6%)	14/183 (7.7%)		2.13 [0.84; 5.41] 0.11	2 9.4%
Random effects model			\diamond	1.34 [0.93; 1.92] 0.11	5 100.0%
Prediction interval				-[0.50; 3.57]	
Heterogeneity: $I^2 = 47\% [0\%; 77\%], \tau^2 = 0.$	13, $p = 0.065$			- / -	
Test for subgroup differences: χ_1^2 = 2.45, df	$= 1 \ (p = 0.118)$		0.2 0.5 1 2 5		
			Favors DP Favors SP		

Figure S-6. Neonatal death

	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value Weight
					-
Overall	10/400 (0.00/)	4/445 (0.00()		0.00 [0.11. 1.00]	0.051 01.00/
Desal et al, Kenya, 2015	12/436 (2.8%)	4/445 (0.9%)		0.33 [0.11; 1.00]	0.051 21.3%
Kakuru et al, Uganda, 2016	0/97 (0%)	2/85 (2.4%)	•	5.70 [0.28; 117.12]	0.259 3.3%
Kajubi et al, Uganda, 2019	5/320 (1.6%)	4/334 (1.2%)		0.77 [0.21; 2.83]	0.690 16.3%
Mlugu et al, Tanzania, 2021	0/4/1 (0%)	0/4/8 (0%)	L		0.0%
Madanitsa et al, Kenya, 2023	4/413 (1%)	5/431 (1.2%)		1.20 [0.32; 4.43]	0.787 16.2%
Madanitsa et al, Malawi, 2023	4/399 (1%)	5/404 (1.2%)		1.23 [0.33; 4.56]	0.752 16.2%
Madanitsa et al, Tanzania, 2023	8/418 (1.9%)	2/411 (0.5%)		0.25 [0.05; 1.19]	0.082 11.9%
Gutman et al, Malawi, unpublished	l 4/276 (1.4%)	4/268 (1.5%)		1.03 [0.26; 4.08]	0.967 14.8%
Random effects model			\diamond	0.73 [0.42; 1.26]	0.253 100.0%
Prediction interval	-	_		-[0.30; 1.76]	
Heterogeneity: $I^2 = 14\% [0\%; 75\%], \tau$	² = 0.04 [0.00; 3.0	68], <i>p</i> = 0.325			
		0.0	1 0.1 1 10 10	0	
			Favors DP Favors SP		
	SP	DP			
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value Weight
			1		
Primigravidae			_		
Desai et al, Kenya, 2015	5/150 (3.3%)	2/132 (1.5%)		0.45 [0.09; 2.30]	0.341 27.2%
Kakuru et al, Uganda, 2016	0/35 (0%)	1/29 (3.4%)		- 3.61 [0.15; 85.36]	7.2%
Kajubi et al, Uganda, 2019	1/83 (1.2%)	2/73 (2.7%)		2.27 [0.21; 24.56]	0.499 12.7%
Mlugu et al, Tanzania, 2021	0/126 (0%)	0/115 (0%)			0.0%
Madanitsa et al, Kenya, 2023	3/139 (2.2%)	1/143 (0.7%)		0.32 [0.03; 3.08]	0.326 14.1%
Madanitsa et al, Malawi, 2023	1/123 (0.8%)	1/111 (0.9%)		1.11 [0.07; 17.51]	0.942 9.4%
Madanitsa et al, Tanzania, 2023	4/103 (3.9%)	1/92 (1.1%)		0.28 [0.03; 2.46]	0.251 15.2%
Gutman et al. Malawi, unpublished	3/88 (3.4%)	1/76 (1.3%)		0.39 [0.04: 3.63]	0.405 14.3%
Bandom effects model				0.61 [0.26: 1.42]	0 250 100.0%
Prediction interval				-[0.20: 1.85]	0.200
Heterogeneity: $I^2 = 0\% [0\%: 71\%] + \tau^2$	r = 0, p = 0.724			L	
	= 0, <i>p</i> = 0.721				
Multigravidae					
Desai et al Kenva 2015	7/286 (2.4%)	2/313 (0.6%)		0.26 [0.05 1.25]	0.092 21.2%
Kakuru et al Llganda 2016	0/62 (0%)	1/56 (1.8%)		- 3 32 [0 14 70 83]	5.1%
Kajubi et al Llganda, 2010	1/237 (1 7%)	2/261 (0.8%)		0.45 [0.08 2.46]	0.350 18.2%
Mugu et al Tanzania 2021	4/207 (1.7 /6)	0/262 (0%)	-	0.45 [0.00, 2.40]	0.009 10.278
Medanitas et al Kanya 2022	1/074(0.49/)	0/303(0.76)			
Madaniisa et al, Kenya, 2023	1/2/4 (0.4%)	4/200 (1.4%)		3.01 [0.43, 33.04]	0.231 10.9%
Madanitsa et al, Malawi, 2023	3/2/6 (1.1%)	4/291 (1.4%)		1.26 [0.29; 5.60]	0.757 23.5%
iviadanitsa et al, Tanzania, 2023	4/312 (1.3%)	1/317 (0.3%)		0.25 [0.03; 2.19]	0.209 10.9%
Gutman et al, Malawi, unpublished	d 1/186 (0.5%)	3/192 (1.6%)		2.91 [0.31; 27.69]	0.354 10.2%
Random effects model			\sim	0.85 [0.37; 1.96]	0.697 100.0%
Prediction interval	0			-[0.14; 4.99]	
Heterogeneity: $I^2 = 24\% [0\%; 66\%],$	$t^2 = 0.29, p = 0.2$	48			
			1 1 1 1		
Test for subgroup differences: $\chi_1^2 = 0$.	30, df = 1 (<i>p</i> = 0.	587)	0.1 0.51 2 10		
			Favors DP Favors SP		

Figure S-7. Mean birthweight in grams

	SP	DP			
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI]	o-value Weight
Overall					
Desai et al, Kenya, 2015	412, 3271 (467)	415, 3190 (434)		81 [20; 143]	0.010 13.6%
Kakuru et al, Uganda, 2016	97, 2976 (448)	85, 2964 (450)		12 [-119; 142]	0.860 6.0%
Kajubi et al, Uganda, 2019	320, 3097 (463)	327, 3031 (400)		66 [-1; 132]	0.054 12.8%
Mlugu et al, Tanzania, 2021	410, 2951 (447)	400, 3007 (397)		-56 [-114; 3]	0.061 14.2%
Madanitsa et al, Kenya, 2023	444, 3252 (455)	452, 3153 (446)		- 99 [40; 158]	0.001 14.0%
Madanitsa et al, Malawi, 2023	407, 3044 (479)	408, 2988 (453)		56 [-8; 120]	0.089 13.2%
Madanitsa et al, Tanzania, 2023	532, 3103 (485)	523, 3021 (493)		82 [23; 141]	0.006 14.0%
Gutman et al, Malawi, unpublished	253, 3015 (414)	255, 2973 (408)		42 [-29; 114]	0.249 12.1%
Random effects model				50[13;88]	0.009 100.0%
Prediction interval				- [-62; 162]	
Heterogeneity: $I^2 = 61\% [16\%; 82\%], \tau^2 = 1$	714.00 [112.86; 9143.09	9], <i>p</i> = 0.012			
		-1	50 -50 0 50 100 15	50	
			Favors DP Favors SP		

Author, Country, Year	SP N, Mean (SD)	DP N, Mean (SD)	Mean Difference	MD [95% Cl] p–va	lue Weight
Primigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Mlugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: $l^2 = 42\%$ [0%; 74%], $\tau^2 = 2905$,	147, 3151 (473) 35, 2787 (468) 83, 2877 (449) 105, 2887 (449) 159, 3168 (445) 127, 2913 (497) 145, 2992 (453) 84, 2886 (435) p = 0.100	126, 3040 (463) 29, 2836 (522) 72, 2907 (346) 95, 2962 (355) 153, 3068 (416) 112, 2971 (433) 134, 2905 (436) 72, 2872 (360)		111 [-1; 222] 0.00 -49 [-292; 194] 0.60 -30 [-158; 98] 0.64 -75 [-188; 38] 0.11 101 [5; 196] 0.03 -58 [-177; 61] 0.33 87 [-18; 191] 0.11 13 [-113; 140] 0.83 22 [-35; 79] 0.4 -[-128; 172] 0.4	52 13.9% 91 4.3% 43 11.7% 91 13.7% 39 16.6% 39 12.9% 03 15.0% 36 11.9% 45 100.0%
Multigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Mlugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Kalawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: $l^2 = 51\%$ [0%; 78%], $\tau^2 = 1698$, Test for subgroup differences: $\chi_1^2 = 1.72$, df = 1	265, 3338 (451) 62, 3083 (401) 237, 3174 (443) 305, 2974 (445) 285, 3299 (454) 280, 3103 (460) 384, 3142 (490) 167, 3077 (391) p = 0.044 (p = 0.190)	289, 3255 (405) 56, 3031 (396) 255, 3067 (408) 305, 3021 (409) 299, 3197 (455) 294, 2995 (462) 387, 3059 (506) 183, 3013 (420)	-200 -100 0 100 200 Eavors DP Eavors SP	83 [11; 154] 0.02 52 [-92; 196] 0.4 108 [32; 183] 0.00 -48 [-115; 20] 0.1 102 [28; 176] 0.00 107 [32; 183] 0.00 83 [12; 153] 0.01 65 [-21; 150] 0.1 69 [29; 109] 0.0 -[-44; 182]	23 13.8% 78 6.3% 05 13.2% 70 14.3% 05 13.2% 21 13.9% 38 11.8% 01 100.0%

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-8. Mean gestational age at birth in weeks

	SP	DP			
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI]	p-value Weight
Overall					
Desai et al Kenva 2015	433 39 (1 43)	439 39 (1 4)		_0 00 [_0 19· 0 18]	0.965 17.0%
Kakuru et al Uganda 2016	433, 33 (1.43)	85 20 (2 12)	T _	-0.00[-0.13, 0.10] 0.10[-0.47: 0.67]	0.730 3.8%
Kajubi et al Uganda, 2010	220 20 (1.02)	224 40 (1 6)		0.10[-0.47, 0.07]	0.229 12.1%
Mugu et al. Tenzenia 2001	320, 39(1.0)	334, 40(1.0)			0.015 17.0%
Madapitas et al Kapya 2021	410, 36 (1.35) 4	+00, 39 (1.35)		-0.23 [-0.42, -0.05]	0.015 17.2%
Madanitsa et al, Kenya, 2023	449, 40 (1.76)	461, 40 (1.72)	1	0.15 [-0.08; 0.38]	0.192 14.3%
Madanitsa et al, Malawi, 2023	414, 39 (2.08)	18, 39 (1.88)		-0.02 [-0.29; 0.24]	0.862 11.8%
Madanitsa et al, Tanzania, 2023	536, 40 (1.87)	524, 40 (1.79)		0.09 [-0.13; 0.31]	0.437 14.7%
Gutman et al, Malawi, unpublished	258, 39 (1.99)	261, 38 (1.85)		0.28 [-0.05; 0.60]	0.093 9.3%
Random effects model				0.00 [-0.11; 0.12]	0.940 100.0%
Prediction interval				-[-0.30; 0.31]	
Heterogeneity: $I^2 = 42\% [0\%; 74\%]$.	$c^2 = 0.01 [0.00; 0.09]$	p = 0.097		•	
	L ,,		0.6-0.4-0.2 0 0.2 0.4 0.6		
			Favors DP Favors SP		
	SP	DP			
Author, Country, Year	N, Mean (SD) N, Mean (SD) Mean Difference	MD [95% CI]	p-value Weight
Primigravidae			Г		
Desai et al. Kenva. 2015	151, 39 (1,13	132, 39 (1.62)	·	0.20 [-0.13: 0.52]	0.235 23.5%
Kakuru et al. Uganda, 2016	35, 39 (2,45)	29, 39 (2.57)		- 0.26 [-0.97; 1.50]	0.675 2.0%
Kajubi et al. Uganda, 2019	83, 39 (2.15)	73, 39 (1.65)		-0.11 [-0.72: 0.50]	0.724 7.8%
Mlugu et al. Tanzania 2021	105 38 (1 46	95,39(1.44)		-0.20[-0.60: 0.21]	0.341 16.3%
Madanitsa et al. Kenva, 2023	163, 40 (1.68	155, 40(1.6)		0.18[-0.18: 0.54]	0.322 19.5%
Madanitsa et al. Malawi, 2023	129, 39 (2.2)	116, 39 (1.91)		-0.27 [-0.79: 0.25]	0.308 10.5%
Madanitsa et al. Tanzania, 2023	146, 40 (1.86) 134, 40 (2.02)		0.12 [-0.34: 0.57]	0.616 13.3%
Gutman et al Malawi unpublished	87, 39 (2, 15)	73 39 (1 98)		0.02[-0.62: 0.67]	0.941 7.0%
Bandom effects model	07, 00 (E.10)	70,00 (1.00)	5	0.04 [-0.12: 0.20]	0.617 100.0%
Prediction interval			<u> </u>	-[-0.16: 0.24]	0.017 100.070
Heterogeneity: $l^2 = 0\% [0\%; 68\%]$. $\tau^2 =$	= 0. p = 0.703			[-0.10, 0.24]	
	., .				
Multigravidae	092 20 (1 56	> 200 20 (1 27)		0.09[0.21:0.15]	0 4 9 1 1 7 00/
Desaret al, Kenya, 2015	203, 39 (1.30	56 40 (1.27)			
Kakuru et al, Uganda, 2016	62, 40 (1.3)	56, 40 (1.79)		0.05 [-0.51; 0.61]	0.850 4.1%
Kajubi et al, Uganda, 2019	237, 40 (1.66) 261, 40 (1.58)		-0.12[-0.40; 0.17]	0.427 12.7%
Madapitas et al. Karria, 2021	305, 38 (1.31) 305, 39 (1.33)	- <u>-</u>	-0.23 [-0.44; -0.02]	0.029 19.3%
Madanitsa et al, Kenya, 2023	289, 40 (1.8)	307, 40 (1.77)		0.15 [-0.14; 0.43]	0.316 12.6%
Madanitsa et al, Malawi, 2023	285, 39 (2.01) 301, 39 (1.87)		0.07 [-0.24; 0.39]	0.660 11.0%
Madanitsa et al, Tanzania, 2023	389, 40 (1.88) 389,40 (1.71)		0.06[-0.19; 0.31]	0.634 15.1%
Gutman et al, Malawi, unpublished	170, 39 (1.91) 188, 38 (1.79)		0.35 [-0.03; 0.74]	0.073 8.0%
Handom effects model			Ŷ	-0.00 [-0.13; 0.12]	0.955 100.0%
Prediction interval				-[-0.31; 0.30]	
Heterogeneity: $I^{2} = 33\% [0\%; 70\%], \tau^{2}$	= < 0.1, <i>p</i> = 0.168				
Test for subgroup differences: $\gamma_{1}^{2} = 0.18$	B, df = 1 (p = 0.668)		-1 -0.5 0 0.5 1		
	, , , , , , , , , , , , , , , , , , , ,		Favors DP Favors SP		

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pvrimethamine

Figure S-9. Mean birthweight-for-gestational age z-scores

Author, Country, Year	SP N, Mean (SD)	DP N, Mean (SD)	Mean Difference	MD [95% CI]	p-value Weight
Overall					
Desai et al, Kenya, 2015	412, 0.13 (1.02)	415, -0.07 (0.94)		0.20 [0.07; 0.33]	0.003 13.9%
Kakuru et al, Uganda, 2016	97, -0.59 (0.89)	85, -0.56 (0.82)		-0.03 [-0.28; 0.22]	0.814 6.6%
Kajubi et al, Uganda, 2019	320, -0.35 (0.96)	327, -0.55 (0.92)		0.20 [0.05; 0.34]	0.008 12.9%
Mlugu et al, Tanzania, 2021	410, -0.33 (1.07)	400, -0.28 (1.02)		-0.05 [-0.20; 0.09]	0.458 13.0%
Madanitsa et al, Kenya, 2023	444, -0.1 (0.92)	452, -0.29 (0.9)		0.20 [0.08; 0.32]	0.001 15.3%
Madanitsa et al, Malawi, 2023	406, -0.36 (1.06)	406, -0.51 (1.06)		0.15 [0.00; 0.29]	0.045 12.8%
Madanitsa et al, Tanzania, 2023	532, -0.44 (1.01)	523, -0.65 (1.06)		0.20 [0.08; 0.33]	0.001 14.7%
Gutman et al, Malawi, unpublished	252, -0.2 (0.96)	253, -0.21 (0.99)		0.01 [-0.16; 0.18]	0.937 10.9%
Random effects model Prediction interval			\diamond	0.12 [0.05; 0.20] –[–0.09; 0.33]	0.001 100.0%
Heterogeneity: $I^2 = 51\% [0\%; 78\%], \tau^2$	< 0.01 [0.00; 0.05], p	= 0.045		-	

-0.3-0.2-0.1 0 0.1 0.2 0.3 Favors DP Favors SP

	SP	DP		
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% Cl] p-value Weight
Primigravidae				
Desai et al, Kenya, 2015	147, -0.13 (1.07)	126, -0.31 (0.97)		0.18 [-0.06; 0.42] 0.149 14.5%
Kakuru et al, Uganda, 2016	35, -0.84 (0.87)	29, -0.67 (0.66) -	-	-0.17 [-0.55; 0.22] 0.397 6.8%
Kajubi et al, Uganda, 2019	83, -0.78 (0.89)	72, -0.78 (0.95)		-0.00 [-0.29; 0.29] 0.999 11.0%
Mlugu et al, Tanzania, 2021	105, -0.51 (1.15)	95, -0.36 (0.97)		-0.15 [-0.44; 0.15] 0.328 10.6%
Madanitsa et al, Kenya, 2023	159, -0.3 (0.91)	153, -0.5 (0.95)	· · ·	0.20 [-0.01; 0.40] 0.063 18.4%
Madanitsa et al, Malawi, 2023	127, -0.6 (1.03)	111, -0.59 (1.18)		-0.00 [-0.29; 0.28] 0.974 11.6%
Madanitsa et al, Tanzania, 2023	145, -0.74 (0.92)	134, -0.94 (0.97)		0.20 [-0.02; 0.42] 0.072 16.7%
Gutman et al, Malawi, unpublished	83, -0.55 (1)	71, -0.53 (0.89)		-0.02 [-0.32; 0.28] 0.879 10.3%
Random effects model			\sim	0.07 [-0.03; 0.17] 0.184 100.0%
Prediction interval				-[-0.12; 0.25]
Heterogeneity: $I^2 = 12\% [0\%; 72\%], \tau^2 = 12\% [0\%; 72\%]$	= < 0.01, <i>p</i> = 0.335			
Multigravidae				
Desai et al, Kenya, 2015	265, 0.28 (0.96)	289. 0.04 (0.92)		0.24 [0.09: 0.40] 0.002 14.2%
Kakuru et al, Uganda, 2016	62, -0.45 (0.88)	56, -0.5 (0.89)		0.05 [-0.27; 0.37] 0.750 5.0%
Kajubi et al, Uganda, 2019	237, -0.2 (0.94)	255, -0.48 (0.91)		0.28 [0.12; 0.44] 0.001 13.4%
Mlugu et al, Tanzania, 2021	305, -0.27 (1.03)	305, -0.25 (1.03)		-0.02 [-0.18; 0.14] 0.814 13.4%
Madanitsa et al, Kenya, 2023	285, 0.02 (0.9)	299, -0.19 (0.85)		0.21 [0.06; 0.35] 0.004 15.7%
Madanitsa et al, Malawi, 2023	279, -0.25 (1.06)	293, -0.49 (1)		0.23 [0.07; 0.40] 0.007 12.9%
Madanitsa et al, Tanzania, 2023	384, -0.34 (1.02)	387, -0.55 (1.08)		0.21 [0.06; 0.36] 0.005 15.0%
Gutman et al, Malawi, unpublished	167, -0.03 (0.9)	182, -0.08 (1)		0.05 [-0.15; 0.25] 0.639 10.4%
Random effects model			\diamond	0.17 [0.10; 0.25] < 0.001 100.0%
Prediction interval				-[-0.01; 0.36]
Heterogeneity: $I^2 = 35\% [0\%; 71\%], \tau^2$	= < 0.01, <i>p</i> = 0.152			
Test (an extreme d'#				
rest for subgroup differences: $\chi_1^- = 2.51$, ar = 1 (p = 0.113)		-0.4 -0.2 0 0.2 0.4	
			Favors DP Favors SP	

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-10. Incidence of clinical malaria during pregnancy

	SP	DP		
Author, Country, Year	N, events/PY (IR) N, events/PY (IR)	Incidence Rate Ratio	IRR [95% CI] p-value Weight
Overall				
Desai et al, Kenya, 2015	480, 59/149 (39.53	3) 477, 13/145 (8.96)		0.23 [0.12; 0.41] < 0.001 13.8%
Kakuru et al, Uganda, 2016	103, 49/46 (105.98	3) 89, 15/40 (37.15)	-	0.35 [0.20; 0.63] < 0.001 14.0%
Kajubi et al. Uganda, 2019	356, 73/140 (52.02	2) 364, 3/149 (2.01) -		0.04 [0.01: 0.12] < 0.001 9.8%
Mlugu et al. Tanzania. 2021	478, 14/97 (14,42	478, 2/93 (2,15)		0.15 [0.03: 0.66] 0.012 7.8%
Madanitsa et al. Kenva. 2023	495, 136/155 (87,5	5) 497, 93/170 (54.81)	+	0.69 [0.52: 0.90] 0.006 15.7%
Madanitsa et al. Malawi, 2023	469, 25/151 (16.54	4) 469, 11/152 (7.23)		0.40 [0.19: 0.83] 0.014 12.9%
Madanitsa et al. Tanzania, 2023	597, 96/209 (45.9)	2) 595, 52/212 (24,56)		0.58 [0.41: 0.81] 0.002 15.4%
Gutman et al, Malawi, unpublished	279, 11/97 (11.36) 282, 5/96 (5.21)		0.46 [0.16; 1.32] 0.149 10.5%
Dandam offecto model				
Random effects model			<u> </u>	0.31 [0.18; 0.55] < 0.001 100.0%
Hotorogonoity: $l^2 = 81\%$ [62%/:00%/1 =	² - 0 = 2 [0 1= 2 24] p <	0.001		-[0.05, 2.12]
Heterogeneity: $T = 81\% [62\%; 90\%], t$	= 0.53 [0.15; 3.34], p <	0.001	01 051 2 10	
			Favors DP Favors SP	
	SP	DP		
Author, Country, Year	N, events/PY (IR)	N, events/PY (IR)	Incidence Rate Ratio	IRR [95% CI] p-value Weight
			1	
Primigravidae				
Desai et al, Kenya, 2015	167, 33/52 (63.28)	143, 7/41 (16.93)		0.26 [0.12; 0.60] 0.001 15.4%
Kakuru et al, Uganda, 2016	41, 20/17 (118.7)	31, 8/13 (62.58)		0.53 [0.23; 1.20] 0.126 15.4%
Kajubi et al, Uganda, 2019	95, 46/36 (127.27)	83, 1/32 (3.12) 🛛 🔶		0.02 [0.00; 0.18] < 0.001 4.8%
Mlugu et al, Tanzania, 2021	128, 10/25 (39.53)	115, 1/22 (4.63) –	*	0.12 [0.01; 0.91] 0.041 4.5%
Madanitsa et al, Kenya, 2023	178, 69/53 (129.07)	177, 44/58 (76.21)		0.67 [0.45; 0.98] 0.041 23.6%
Madanitsa et al. Malawi, 2023	151, 13/48 (27.08)	136, 6/43 (13,96)		0.43 [0.15: 1.21] 0.108 12.2%
Madanitsa et al. Tanzania, 2023	164, 37/56 (65,94)	160, 17/55 (30,83)		0.52 [0.29: 0.94] 0.031 19.7%
Gutman et al Malawi unpublisher	95 6/34 (17 46)	79 1/28 (3.62)		0.21 [0.02: 1.72] 0.145 4.3%
Bandom effects model		10, 1120 (0.02)	\bigcirc	0.38 [0.24: 0.61] < 0.001 100.0%
Prediction interval			~	_[0 11 • 1 33]
Hotorogonoity: $I^2 = 56\% [4\%: 90\%]$	$r^{2} = 0.20$ n = 0.024			-[0.11, 1.35]
Here $1000 = 100 \times 10^{-10} = 50 \times 10^{-10} \times 10^{-10}$	t = 0.20, p = 0.024			
Multigravidae				
Desai et al, Kenya, 2015	313, 26/97 (26.77)	334, 6/104 (5.79)		0.22 [0.09; 0.53] 0.001 13.0%
Kakuru et al. Uganda, 2016	62, 29/29 (98.69)	58, 7/28 (25.37)		0.26 [0.11: 0.59] 0.001 14.0%
Kajubi et al. Uganda, 2019	261, 27/104 (25,91)	281, 2/117 (1,71) -		0.07 [0.02: 0.28] < 0.001 7.3%
Mluqu et al Tanzania 2021	350 4/72 (5 57)	363 1/72 (1.4)		0.25 [0.03: 2.24] 0.216 3.7%
Madanites et al Kenva 2023	317 67/102 (65 76)	320 40/112 (43 78)		0.71 [0.49; 1.03] 0.070 21.8%
Madanitsa et al, Neliya, 2023	317, 07/102 (03.70)	221 5/102 (45.76)		0.20 [0.14; 1.12] 0.091 11.09/
Madanitsa et al, Malawi, 2023	310, 12/103 (11.03)	331, 5/109 (4.59)		
Madanitsa et al, Tanzania, 2023	430, 58/152 (38.18)	433, 35/156 (22.48)		0.62 [0.41; 0.95] 0.027 21.0%
Gutman et al, Malawi, unpublished	d 182, 5/62 (8.08)	203, 4/68 (5.86)		0.72[0.19; 2.70] 0.631 8.2%
Random effects model			$\langle \rangle$	0.38 [0.23; 0.63] < 0.001 100.0%
Prediction interval	0			–[0.09; 1.65]
Heterogeneity: $I_{2}^{2} = 63\% [19\%; 83\%],$	$\tau^2 = 0.30, p = 0.009$			7
				-
Test for subgroup differences: $\chi_1^2 = 0$.	00, df = 1 (<i>p</i> = 0.987)	0.01	0.5 1 2	5
			Favors DP Favors	s SP

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; IR = incidence rate (episodes per 100 person-years); IRR = incidence rate ratio; PY = person-years; SP = sulfadoxine-pyrimethamine

Figure S-11. Any evidence of pigment in placental tissue by histopathology

SP

Author, Country, Year	SP n/N (%)	DP n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Author, Country, Year Overall Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Mlugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Kenya, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: $I^2 = 69\%$ [36%; 85%], $\tau^2 =$	119/394 (30.2%) 43/91 (47.3%) 165/285 (57.9%) 10/449 (2.2%) 10/49 (2.2%) 10/4379 (27.4%) 83/356 (23.3%) 6/453 (1.3%) 138/226 (61.1%)	120/403 (29.8%) 26/83 (31.3%) 93/328 (28.4%) 6/472 (1.3%) 73/393 (18.6%) 53/360 (14.7%) 3/444 (0.7%) 88/223 (39.5%)		0.99 [0.80; 1.22] 0.66 [0.45; 0.97] 0.49 [0.40; 0.60] 0.57 [0.21; 1.56] 0.68 [0.52; 0.88] 0.63 [0.46; 0.86] 0.51 [0.13; 2.03] 0.65 [0.53; 0.78] 0.66 [0.55; 0.80] - [0.38; 1.15]	0.896 0.037 < 0.001 0.274 0.004 0.339 < 0.001 < 0.001	17.5% 11.7% 18.0% 3.1% 15.7% 14.0% 1.8% 18.2% 100.0%
			0.2 0.5 1 2 5 Favors DP Favors SP			

DP

Author, Country, Year	n/N (%)	n/N (%)	Risk	Ratio	RR [95% CI]	p-value	Weight
Primigravidae							
Desai et al, Kenya, 2015	67/136 (49.3%)	57/122 (46.7%)	-	+	0.95 [0.73; 1.22]	0.684	16.9%
Kakuru et al, Uganda, 2016	22/32 (68.8%)	19/27 (70.4%)		-	1.02 [0.73; 1.44]	0.893	15.3%
Kajubi et al, Uganda, 2019	58/63 (92.1%)	48/73 (65.8%)			0.71 [0.60; 0.86]	< 0.001	18.2%
Mlugu et al, Tanzania, 2021	2/118 (1.7%)	3/112 (2.7%)	-		1.58 [0.27; 9.28]	0.612	2.2%
Madanitsa et al, Kenya, 2023	52/131 (39.7%)	36/130 (27.7%)	-	-	0.70 [0.49; 0.99]	0.043	15.1%
Madanitsa et al, Malawi, 2023	47/109 (43.1%)	36/96 (37.5%)		F	0.87 [0.62; 1.22]	0.416	15.4%
Madanitsa et al, Tanzania, 2023	1/119 (0.8%)	1/108 (0.9%)		•	- 1.10 [0.07; 17.40]	0.945	1.0%
Gutman et al, Malawi, unpublished	39/71 (54.9%)	32/59 (54.2%)	+	-	0.99 [0.72; 1.35]	0.937	15.8%
Random effects model			\diamond	×	0.85 [0.74; 0.98]	0.028	100.0%
Prediction interval			_	+	-[0.62; 1.17]		
Heterogeneity: $I^2 = 12\% [0\%; 71\%], \tau^2 =$	= 0.01, <i>p</i> = 0.340						
Multigravidae							
Desai et al, Kenya, 2015	52/258 (20.2%)	63/281 (22.4%)	+		1.11 [0.80; 1.54]	0.522	17.6%
Kakuru et al, Uganda, 2016	21/59 (35.6%)	7/56 (12.5%)			0.35 [0.16; 0.76]	0.008	9.0%
Kajubi et al, Uganda, 2019	107/222 (48.2%)	45/255 (17.6%)			0.37 [0.27; 0.49]	< 0.001	18.2%
Mlugu et al, Tanzania, 2021	8/331 (2.4%)	3/360 (0.8%)		+	0.34 [0.09; 1.29]	0.113	4.2%
Madanitsa et al, Kenya, 2023	52/248 (21%)	37/263 (14.1%)		-	0.67 [0.46; 0.99]	0.042	16.3%
Madanitsa et al, Malawi, 2023	36/247 (14.6%)	16/262 (6.1%)			0.42 [0.24; 0.74]	0.002	12.5%
Madanitsa et al, Tanzania, 2023	4/332 (1.2%)	2/334 (0.6%)		<u> </u>	0.50 [0.09; 2.70]	0.418	2.8%
Gutman et al, Malawi, unpublished	99/154 (64.3%)	56/164 (34.1%)			0.53 [0.42; 0.68]	< 0.001	19.4%
Random effects model			\diamond		0.53 [0.38; 0.74]	< 0.001	100.0%
Prediction interval					-[0.19; 1.47]		
Heterogeneity: $I^2 = 76\% [51\%; 88\%], \tau^2$	= 0.14, <i>p</i> < 0.001						
			1				
Test for subgroup differences: $\chi_1^2 = 6.40$,	$df = 1 \ (p = 0.011)$		0.1 0.5	1 2 10			
			Favors DP	Favors SP			

Figure S-12. Any evidence of parasites in placental tissue or blood by histopathology, microscopy, PCR, or RDT

Author Country Year	SP		Dick Datio	DD [05% Cl] a volue Weight
Authol, Country, Tear	TVIN (%)	11/IN (76)		nn [95% Ci] p-value weight
Overall	50/400 (4 40/)	00/440 /5 00/		
Desai et al, Kenya, 2015	59/420 (14%)	23/412 (5.6%))	0.40 [0.25; 0.63] < 0.001 14.4%
Kakuru et al, Uganda, 2016	18/96 (18.8%)	2/84 (2.4%)		0.13 [0.03; 0.53] 0.005 7.0%
Kajubi et al, Uganda, 2019	70/314 (22.3%)	7/330 (2.1%)		0.10[0.04; 0.20] < 0.001 11.9%
Milugu et al, Tanzania, 2021	59/4/8 (12.3%)	17/4/8 (3.6%		0.29[0.17; 0.49] < 0.001 13.9%
Madanitsa et al, Kenya, 2023	34/410 (6.3%)	22/423 (5.2%)		
Madanitsa et al. Tanzania 2023	27/403 (0.7%)	22/412 (0.0%)		
Madaniisa et al, Tanzania, 2023	28/491 (5.7%)	18/4/5 (3.8%))	
Gutman et al, Malawi, unpublished	18/247 (7.3%)	9/249 (3.6%)		0.50 [0.23; 1.08] 0.078 11.7%
Random effects model			\diamond	0.38 [0.23; 0.63] < 0.001 100.0%
Prediction interval				-[0.07; 2.00]
Heterogeneity: $l^2 = 76\%$ [53%; 88%], $\tau^2 =$	0.39 [0.10; 2.35], p	< 0.001		
			0.1 0.5 1 2 10	
			Favors DP Favors SP	
	SP	DP		
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI] p-value Weight
Primigravidae			I	
Desai et al. Kenva. 2015	30/151 (19.9%)	11/126 (8.7%)		0.44 [0.23: 0.84] 0.013 18.2%
Kakuru et al. Uganda, 2016	13/36 (36.1%)	2/28 (7.1%)		0.20 [0.05: 0.81] 0.024 7.8%
Kajubi et al. Uganda, 2019	28/82 (34.1%)	5/74 (6.8%)		0.20 [0.08: 0.49] < 0.001 13.6%
Mlugu et al. Tanzania, 2021	16/128 (12.5%)	6/115 (5.2%)		0.42 [0.17: 1.03] 0.058 13.6%
Madanitsa et al. Kenva. 2023	12/143 (8.4%)	11/144 (7.6%)		0.91 [0.42; 2.00] 0.814 15.6%
Madanitsa et al. Malawi, 2023	9/125 (7.2%)	4/116 (3.4%)		0.48 [0.15; 1.51] 0.210 10.2%
Madanitsa et al, Tanzania, 2023	9/133 (6.8%)	4/114 (3.5%)		0.52 [0.16; 1.64] 0.263 10.2%
Gutman et al, Malawi, unpublished	11/83 (13.3%)	4/66 (6.1%)		0.46 [0.15; 1.37] 0.162 10.8%
Random effects model	,	(<i>i</i>	\diamond	0.43 [0.30; 0.62] < 0.001 100.0%
Prediction interval				-[0.22; 0.87]
Heterogeneity: $I^2 = 9\% [0\%; 71\%], \tau^2 = 0$.05, <i>p</i> = 0.360			-
Multigravidae				
Desai et al Kenva 2015	29/269 (10.8%)	12/286 (4.2%)		0.39 [0.20: 0.75] 0.005 16.5%
Kakuru et al Lloanda 2016	5/60 (8.3%)	0/56 (0%)		
Kajubi et al. Uganda, 2019	42/232 (18 1%)	2/256 (0.8%)		0.04 [0.01; 0.18] < 0.001 7.0%
Mluqu et al. Tanzania 2021	43/350 (12.3%)	11/363 (3%)		0.25 [0.13; 0.47] < 0.001 16.6%
Madanitsa et al Kenya 2023	22/267 (8 2%)	11/279 (3.9%)		0.48 [0.24: 0.97] 0.040 15.5%
Madanitsa et al. Malawi 2023	18/278 (6.5%)	18/294 (6.1%)		0.95 [0.50; 1.78] 0.862 16.8%
Madanitsa et al. Tanzania 2023	18/355 (5.1%)	14/359 (3.9%)	<u>-</u>	0.77 [0.39; 1.52] 0.451 15.9%
Gutman et al Malawi unpublished	7/162 (4.3%)	5/183 (2.7%)		0.63 [0.20; 1.95] 0.426 9.5%
Bandom effects model	11102 (4.070)	0/100 (2.7 /0)	\bigcirc	0.39 [0.21: 0.71] 0.002 100.0%
Prediction interval			<u> </u>	-[0.06: 2.62]
Heterogeneity: $I^2 = 70\%$ [38%; 86%], $\tau^2 =$	0.51, <i>p</i> = 0.002			[0.00, =.0=]
Test for subgroup differences: $\chi_1^2 = 0.08$, c	$df = 1 \ (p = 0.774)$		0.01 0.1 1 10 100	
			Favors DP Favors SP	

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; PCR = polymerase chain reaction; RDT = rapid diagnostic test; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-13. Any evidence of pigment or parasites in placental tissue or blood by histopathology, microscopy, PCR, or RDT

	SP	DP		
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI] p-value Weight
Overall				
Desai et al Kenva 2015	156/419 (37.2%)	137/411 (33.3%)	÷	0 90 [0 74: 1 08] 0 241 15 1%
Kakuru et al Uganda 2016	49/96 (51%)	27/84 (32 1%)		0.63 [0.44: 0.91] 0.014 10.8%
Kajubi et al Llganda, 2010	202/313 (64.5%)	97/328 (29.6%)	·	0.00[0.04, 0.01] = 0.014 = 10.076 0.46[0.38; 0.55] < 0.001 = 15.1%
Mugu et al. Tanzania, 2013	64/478 (13.4%)	21/178 (1 1%)		0.33[0.20; 0.53] < 0.001 8.6%
Madanites et al Konya 2022	107/202 (22 /%)	80/400 (22 2%)		0.55[0.20, 0.55] < 0.001 0.076
Madanitsa et al, Neliya, 2023	105/261 (20.1%)	72/261 (20.2%)		0.09 [0.04, 0.07] 0.002 14.076
Madanitsa et al, Malawi, 2023	24/457(7.4%)	21/447 (4.7%)		0.62 [0.27: 1.07] 0.000 13.4%
Gutman et al Malawi unpublished	147/001 (62.69/)	21/447 (4.7%)		0.03[0.37, 1.07] 0.008 $7.7%$
Gutman et al, Malawi, unpublished	147/231 (03.0%)	94/225 (41.0%)		0.66 [0.55, 0.79] < 0.001 15.2%
Random effects model			\diamond	0.62 [0.51: 0.75] < 0.001 100.0%
Prediction interval				-[0.33: 1.17]
Heterogeneity: $I^2 = 79\%$ [59%; 89%], τ^2 :	= 0.06 [0.01: 0.35], p	< 0.001		[]
5			0.5 1 2	
			Favors DP Favors SP	
	SP	DP		
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI] p-value Weight
Primigravidae			1	
Desai et al, Kenya, 2015	84/150 (56%)	63/126 (50%)	-	0.89 [0.71: 1.12] 0.323 15.5%
Kakuru et al, Uganda, 2016	26/36 (72.2%)	20/28 (71.4%)		0.99 [0.73: 1.35] 0.944 14.1%
Kajubi et al, Uganda, 2019	77/82 (93.9%)	51/73 (69.9%)	= 1	0.74 [0.63; 0.87] < 0.001 16.4%
Mlugu et al. Tanzania, 2021	17/128 (13.3%)	7/115 (6 1%)		0.46 [0.20; 1.07] 0.070 6.3%
Madanitsa et al. Kenva. 2023	59/136 (43.4%)	44/135 (32.6%)		0.75 [0.55; 1.02] 0.070 14.1%
Madanitsa et al. Malawi, 2023	52/111 (46.8%)	38/97 (39.2%)		0.84 [0.61: 1.15] 0.269 14.0%
Madanitsa et al. Tanzania. 2023	10/121 (8.3%)	5/108 (4.6%)		0.56 [0.20: 1.59] 0.276 4.7%
Gutman et al. Malawi, unpublished	48/76 (63.2%)	36/61 (59%)		0.93 [0.71: 1.22] 0.623 14.8%
Random effects model	40/70 (00.270)	00/01 (00/0)		0.82 [0.74; 0.91] < 0.001 100.0%
Prediction interval			Ť	-[0 70: 0 96]
Heterogeneity: $I^2 = 0\% [0\%; 68\%], \tau^2 = 0\%$	< 0.01, <i>p</i> = 0.437			-[0.70, 0.00]
Maria and a s				
Multigravidae	70/000 (00 00()	74/005 (000/)	1	0.07 [0.70, 1.00] 0.001 15.00/
Kekuru et el Llaende 2016	72/269 (26.8%)	74/285 (26%)		0.97 [0.73; 1.28] 0.831 15.2%
Kakulu et al, Uganda, 2010	23/60 (38.3%)	7/56 (12.5%)		0.33 [0.15; 0.70] 0.004 7.4%
Mugu et al. Tanzania, 2019	125/231 (54.1%)	46/255 (18%)		0.33 [0.25; 0.44] < 0.001 15.1%
Madanitas et al Kanya 2021	47/350 (13.4%)	14/363 (3.9%)		0.29 [0.16; 0.51] < 0.001 9.9%
Madanitsa et al, Kenya, 2023	68/256 (26.6%)	45/265 (17%)		0.64 [0.46; 0.89] 0.009 14.2%
Madanitsa et al, Malawi, 2023	53/250 (21.2%)	34/262 (13%)		0.61 [0.41; 0.91] 0.015 13.1%
Madanitsa et al, Tanzania, 2023	22/333 (6.6%)	16/337 (4.7%)		0.72 [0.38; 1.34] 0.301 9.2%
Gutman et al, Malawi, unpublished	99/154 (64.3%)	58/164 (35.4%)		0.55 [0.43; 0.70] < 0.001 15.9%
Random effects model			\diamond	0.53 [0.39; 0.71] < 0.001 100.0%
Prediction interval				-[0.20; 1.41]
Heterogeneity: $I^{-} = 81\% [62\%; 90\%], \tau^{2}$:	= 0.14, <i>p</i> < 0.001			
Tast for subgroup differences: $x^2 = 7.40$	df = 1 (n = 0.007)			
rest for subgroup differences: $\chi_1 = 7.40$,	u = 1 (p = 0.007)		0.2 0.5 1 2 5	
			Favors DP Favors SP	

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; PCR = polymerase chain reaction; RDT = rapid diagnostic test; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-14. Any evidence of peripheral malaria at delivery by microscopy, PCR, or RDT

	SP	DP		
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% Cl] p-value Weight
Querall				
Desai et al Kenva 2015	53/425 (12 5%) 16/425 (3.8%)	-	0 30 [0 18: 0 52] ~ 0 001 15 6%
Kakuru et al Lloanda 2016	25/100 (25%)	2/85 (2.4%)		0.09[0.02; 0.39] = 0.001 + 4.9%
Kajubi et al Llganda, 2010	27/328 (8 2%)	1/3/6 (0.3%)		0.00[0.02, 0.00] = 0.001 = 2.8%
Mugu et al Tanzania 2021	12/178 (8.8%)	10/478 (4%)		0.04 [0.00, 0.20] < 0.001 2.078
Madanitsa et al Kenya 2023	42/470 (0.0%)	20/1/2 (1.5%)		0.48 [0.28; 0.80] 0.005 16.1%
Madanitsa et al, Neliya, 2023	5//12 (12 10/) 20/442 (4.3%)	1.00	0.40 [0.20, 0.00] 0.000 10.178
Madanitaa at al Tanzania 2022	46/500 (09/)	14/409 (2.00/)		0.70[0.47, 1.04] 0.077 19.078
Cutman at al Malauri unnublished	40/509 (9%)	14/400 (2.9%)	1.1	0.52[0.16, 0.57] < 0.001 14.7%
Gutman et al, Malawi, unpublished	17/240 (0.9%)	9/248 (3.6%)		0.53 [0.24; 1.16] 0.109 11.0%
Bandom effects model				0.39 [0.27: 0.55] < 0.001 100.0%
Prediction interval				-[0.15: 1.03]
Heterogeneity: $l^2 = 64\% [24\%; 83\%]$, 1	$r^2 = 0.13 [0.03: 3.63]$	p = 0.007		[0.10, 1.00]
], p = 0.007	0.01 0.1 1 10 10	00
			Favors DP Favors SP	
	SP	DP		
Author, Country, Year	n/N (%)	n/N (%)	Bisk Batio	BB [95% CI] p-value Weight
,, ,				[
Primigravidae				
Desai et al, Kenya, 2015	25/152 (16.4%)	9/129 (7%)		0.42 [0.21; 0.88] 0.020 22.7%
Kakuru et al, Uganda, 2016	12/38 (31.6%)	2/29 (6.9%)		0.22 [0.05; 0.90] 0.035 6.2%
Kajubi et al, Uganda, 2019	14/85 (16.5%)	1/77 (1.3%)		0.08 [0.01; 0.59] 0.013 3.1%
Mlugu et al, Tanzania, 2021	12/128 (9.4%)	6/115 (5.2%)		0.56 [0.22; 1.43] 0.225 13.6%
Madanitsa et al, Kenya, 2023	17/153 (11.1%)	7/149 (4.7%)		0.42 [0.18; 0.99] 0.047 16.7%
Madanitsa et al, Malawi, 2023	17/127 (13.4%)	12/113 (10.6%)		0.79 [0.40; 1.59] 0.513 24.6%
Madanitsa et al, Tanzania, 2023	16/137 (11.7%)	1/119 (0.8%)		0.07 [0.01; 0.53] 0.010 3.1%
Gutman et al, Malawi, unpublished	10/82 (12.2%)	4/66 (6.1%)		0.50 [0.16; 1.51] 0.218 10.0%
Random effects model			\diamond	0.44 [0.31; 0.64] < 0.001 100.0%
Prediction interval			_	-[0.24; 0.81]
Heterogeneity: $I^2 = 30\% [0\%; 69\%], \tau^2$	= 0.02, <i>p</i> = 0.192			
Multigravidae	28/272 (10 2%)	7/206 (2 1%)		0 22 [0 10: 0 52] < 0 001 11 1%
Kakuru et al Uganda, 2016	12/62 (21%)	0/56 (0%)		0.04 [0.00: 0.67]
Kajubi et al Uganda, 2010	12/02 (21/0)	0/260 (0%)		0.04 [0.00, 0.07] = 1.0%
Mugu et al Tanzonia 2001	13/243 (3.3%)	12/262 (2.69/)		0.03 [0.00, 0.30] = - 1.0%
Madanitas et al. Kanya, 2021	30/350 (0.0%)	13/303 (3.0%)	-	0.42 [0.22, 0.79] 0.007 17.7%
Madanitsa et al, Kenya, 2023	24/2/8 (8.0%)	13/293 (4.4%)		0.51[0.27; 0.99] 0.046 $10.7%$
Madanitsa et al, Malawi, 2023	37/280 (12.9%)	25/299 (8.4%)		0.65 [0.40; 1.05] 0.075 29.1%
Cutmon et al. Moleuri, unnublished	29/309 (1.9%)	E 100 (0.7%)		
Gutman et al, Malawi, unpublished	7/162 (4.3%)	5/182 (2.7%)		
nandom enects model			<u> </u>	0.45 [0.33; 0.00] < 0.001 100.0%
Heterogeneity $l^2 = 200(100(+700(1-2$	-0.00 - 0.100		_	-[0.20; 0.70]
Heterogeneity: $I^{-} = 39\% [0\%; 73\%], \tau^{-}$	= 0.02, p = 0.122			
Test for subgroup differences: $\gamma^2 = 0.00$	0. df = 1 ($p = 0.960$)		0.01 0.1 1 10 100	
	,		Favors DP Favors SP	

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; PCR = polymerase chain reaction; RDT = rapid diagnostic test; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-15. Any evidence of severe anaemia (Hb <7 g/dL) during pregnancy

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
0						
Overall Desai et al Kenva 2015	1/303 (0.3%)	1/307 (0.3%)	;_	0 00 [0 06: 15 71]	0 003	3 5%
Kakuru et al Llganda, 2015	0/104 (0%)	0/00 (0.3 %)		0.99 [0.00, 15.71]	0.993	0.0%
Kakulu et al, Uganda, 2010	0/104(0%)	0/90(0%)		0.05 [0.05, 1.15]	0.074	10.0%
Kajubi et al, Oganda, 2019	8/381 (2.1%)	2/388 (0.5%)		0.25 [0.05; 1.15]	0.074	10.5%
Madagitas et al Kagua 0000	3/4/8 (0.6%)	2/4/8 (0.4%)		0.67 [0.11; 3.97]	0.050	8.0%
Madanitsa et al, Kenya, 2023	13/495 (2.6%)	14/497 (2.8%)		1.07 [0.51; 2.26]	0.854	35.8%
Madanitsa et al, Malawi, 2023	8/469 (1.7%)	3/469 (0.6%)		0.38 [0.10; 1.40]	0.146	14.0%
Madanitsa et al, Tanzania, 2023	9/597 (1.5%)	11/595 (1.8%)		1.23 [0.51; 2.94]	0.647	28.1%
Gutman et al, Malawi, unpublished						0.0%
Bandom effects model				0 70 [0 /7 1 33]	0 376	100.0%
Prediction interval				-[0 30 2 11]	0.570	100.078
Hotorogopoity: $l^2 = 2\% [0\%: 75\%] = r^2 = l$	0.05 [0.00 1.00]	n = 0.406		-[0.50, 2.11]		
Therefore the term $t = 2 \sqrt{6} [0 \sqrt{6}, 75 \sqrt{6}], t = 0$	0.03 [0.00, 1.99], /	0 = 0.400	01 05 1 2 10			
			Tavois DF Tavois SF			
	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigravidae			ſ			
Desai et al Kenva 2015	1/105 (1%)	0/91 (0%)		0.38 [0.02. 0.35]		5 5%
Kakuru et al Uganda 2016	0/42 (0%)	0/31 (0%)	-	0.00 [0.02, 9.02]		0.0%
Kajubi et al. Uganda, 2010	5/100 (5%)	0/02 (0%)				6.7%
Mugu et al Tanzania 2021	1/100 (0.9%)	1/115(0.09/)		1 11 [0 07: 17 50]	0 020	7 20/
Madanitas et al Kanya 2022	1/120 (0.0%)	1/115(0.9%)		1 51 [0.07, 17.59]	0.939	7.3%
Madanitsa et al, Kenya, 2023	4/1/0 (2.2%)	0/177 (3.4%)			0.010	35.7%
Madaniisa et al, Malawi, 2023	4/151 (2.6%)	1/136 (0.7%)		0.28 [0.03; 2.45]	0.249	11.7%
Madanitsa et al, Tanzania, 2023	4/164 (2.4%)	5/160 (3.1%)		1.28 [0.35; 4.69]	0.708	33.1%
Gutman et al, Malawi, unpublished					0.939	0.0%
Random effects model			\sim	0.89 [0.42; 1.87]	0.749	100.0%
Prediction interval				-[0.31; 2.55]		
Heterogeneity: $I^{2} = 0\% [0\%; 75\%], \tau^{2} =$	0, <i>p</i> = 0.462					
Multigravidae						
Desai et al Kenva 2015	0/108 (0%)	1/216 (0.5%)		2 75 [0 11:67 13]		3.6%
Kakuru at al Uganda 2016	0/62 (0%)	0/50 (0%)	-	2.75 [0.11, 07.15]		0.0%
Kajubi et al. Uganda, 2010	2/291 (1 19/)	2/205(0.78)		0.64 [0.11 2.77]	0.617	11 5%
Mugu et al Tanzonia 2001	3/201 (1.1 /0)	1/262 (0.2%)		0.04[0.11, 0.77]	0.017	6 49/
Madanitas et al Kanya 2021	2/350 (0.0%)	1/303 (0.3%)		0.46 [0.04, 5.29]	0.551	0.4%
Madaniisa et al, Kenya, 2023	9/317 (2.8%)	8/320 (2.5%)	- 1	0.88 [0.34; 2.25]	0.791	41.5%
Madanitsa et al, Malawi, 2023	4/318 (1.3%)	2/331 (0.6%)	<u>_</u>	0.48 [0.09; 2.60]	0.395	12.8%
Madanitsa et al, Tanzania, 2023	5/430 (1.2%)	5/433 (1.2%)		0.99 [0.29; 3.41]	0.991	24.1%
Gutman et al, Malawi, unpublished					0.551	0.0%
Random effects model			\diamond	0.81 [0.44; 1.48]	0.494	100.0%
Prediction interval				-[0.34; 1.91]		
Heterogeneity: $I^2 = 0\% [0\%; 75\%], \tau^2 =$	0, <i>p</i> = 0.933					
0	1 12 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1					
Test for subgroup differences: $\chi_1^2 = 0.03$	h, df = 1 (p = 0.855)	5)	0.01 0.1 1 10 100			
			Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; g/dL = grams/deciliter; Hb = haemoglobin; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-16. Any evidence of moderate anaemia (Hb <9 g/dL) during pregnancy

Author, Country, Year	SP n/N (%)	DP n/N (%)		Risk Ra	tio		RR [95% CI]	p-value	Weight
Overall									
Desai et al, Kenya, 2015	24/303 (7.9%)	18/307 (5.9%)					0.74 [0.41; 1.34]	0.318	8.1%
Kakuru et al, Uganda, 2016	13/104 (12.5%)	4/90 (4.4%)					0.36 [0.12; 1.05]	0.062	2.8%
Kajubi et al, Uganda, 2019	55/381 (14.4%)	32/388 (8.2%)					0.57 [0.38; 0.86]	0.008	13.6%
Mlugu et al, Tanzania, 2021	81/478 (16.9%)	64/478 (13.4%)					0.79 [0.58; 1.07]	0.127	19.5%
Madanitsa et al, Kenya, 2023	96/495 (19.4%)	94/497 (18.9%)					0.98 [0.76; 1.26]	0.848	22.8%
Madanitsa et al, Malawi, 2023	43/469 (9.2%)	36/469 (7.7%)					0.84 [0.55; 1.28]	0.411	13.1%
Madanitsa et al, Tanzania, 2023	75/597 (12.6%)	81/595 (13.6%)		-	-		1.08 [0.81; 1.45]	0.591	20.1%
Gutman et al, Malawi, unpublished									0.0%
Random effects model				\diamond			0.83 [0.69; 1.00]	0.050	100.0%
Prediction interval							-[0.52; 1.32]		
Heterogeneity: $I^2 = 41\% [0\%; 75\%], \tau^2 =$	= 0.02 [0.00; 0.51], p	= 0.116							
			0.2	0.5 1	2	5			

Favors DP Favors SP

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigravidae						
Desai et al, Kenya, 2015	14/105 (13.3%)	6/91 (6.6%)		0.49 [0.20; 1.23]	0.131	6.6%
Kakuru et al, Uganda, 2016	9/42 (21.4%)	3/31 (9.7%)		0.45 [0.13; 1.53]	0.202	3.8%
Kajubi et al, Uganda, 2019	35/100 (35%)	13/93 (14%)		0.40 [0.23; 0.71]	0.002	14.9%
Mlugu et al, Tanzania, 2021	28/128 (21.9%)	21/115 (18.3%)		0.83 [0.50; 1.39]	0.485	17.9%
Madanitsa et al, Kenya, 2023	34/178 (19.1%)	40/177 (22.6%)		1.18 [0.79; 1.78]	0.418	24.6%
Madanitsa et al, Malawi, 2023	24/151 (15.9%)	16/136 (11.8%)		0.74 [0.41; 1.33]	0.316	14.1%
Madanitsa et al, Tanzania, 2023	22/164 (13.4%)	30/160 (18.8%)		1.40 [0.84; 2.32]	0.194	18.0%
Gutman et al, Malawi, unpublished					0.485	0.0%
Random effects model			\diamond	0.78 [0.54; 1.13]	0.182	100.0%
Prediction interval				-[0.26; 2.33]		
Heterogeneity: $I^2 = 61\% [12\%; 83\%], \tau^2$	= 0.15, <i>p</i> = 0.016					
Multigravidae						
Desai et al, Kenya, 2015	10/198 (5.1%)	12/216 (5.6%)		1.10 [0.49; 2.49]	0.819	6.5%
Kakuru et al, Uganda, 2016	4/62 (6.5%)	1/59 (1.7%) -	· · · · ·	0.26 [0.03; 2.28]	0.226	1.0%
Kajubi et al, Uganda, 2019	20/281 (7.1%)	19/295 (6.4%)		0.90 [0.49; 1.66]	0.747	10.8%
Mlugu et al, Tanzania, 2021	53/350 (15.1%)	43/363 (11.8%)		0.78 [0.54; 1.14]	0.199	22.1%
Madanitsa et al, Kenya, 2023	62/317 (19.6%)	54/320 (16.9%)	-	0.86 [0.62; 1.20]	0.381	25.8%
Madanitsa et al, Malawi, 2023	19/318 (6%)	20/331 (6%)		1.01 [0.55; 1.86]	0.971	10.7%
Madanitsa et al, Tanzania, 2023	53/430 (12.3%)	50/433 (11.5%)	-	0.94 [0.65; 1.35]	0.724	23.0%
Gutman et al, Malawi, unpublished					0.199	0.0%
Random effects model			\$	0.88 [0.74; 1.05]	0.161	100.0%
Prediction interval			-	-[0.70; 1.11]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$	0, <i>p</i> = 0.900		· · · · · · · · · · · · · · · · · · ·			
Test for subgroup differences: $\chi_1^2 = 0.35$,	df = 1 (<i>p</i> = 0.553)		0.1 0.5 1 2 10 Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; g/dL = grams/deciliter; Hb = haemoglobin; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-17. Any evidence of mild anaemia (Hb <11 g/dL) during pregnancy

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Overall						
Desai et al, Kenya, 2015	143/303 (47.2%)	167/307 (54.4%)	+	1.15 [0.99; 1.35]	0.076	10.5%
Kakuru et al, Uganda, 2016	62/104 (59.6%)	50/90 (55.6%) -		0.93 [0.73; 1.19]	0.570	5.6%
Kajubi et al, Uganda, 2019	247/381 (64.8%)	238/388 (61.3%)		0.95 [0.85; 1.05]	0.316	15.7%
Mlugu et al. Tanzania, 2021	309/478 (64.6%)	272/478 (56.9%)		0.88 [0.79: 0.98]	0.015	16.5%
Madanitsa et al. Kenva, 2023	316/495 (63.8%)	336/497 (67.6%)		1.06 [0.97: 1.16]	0.212	18.2%
Madanitsa et al. Malawi, 2023	243/469 (51.8%)	254/469 (54.2%)		1.05 [0.93: 1.18]	0.472	14.1%
Madanitsa et al Tanzania 2023	396/597 (66.3%)	392/595 (65.9%)		0.99[0.92:1.08]	0.870	19.5%
Gutman et al, Malawi, unpublished			T			0.0%
Bandom effects model				1 00 [0 93 1 06]	0 919	100.0%
Prediction interval				_[0 83: 1 19]	0.515	100.070
Heterogonaity: $l^2 = 52\% [0\%: 80\%] r^2$.	< 0.01 [0.00· 0.04] p	- 0.052		-[0.05, 1.15]		
Therefore the transformation $T = 52.76 [0.76, 00.76], t$	< 0.01 [0.00, 0.04], p	- 0.052	0.8 1 1.25			
			Favors DP Favors SP			
	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigravidae	40/105 (40.00/)	44/04 (40 40/)	_	1 10 [0 01 1 10]	0.504	0 40/
Desai et al, Kenya, 2015	46/105 (43.8%)	44/91 (48.4%)		1.10 [0.81; 1.49]	0.524	6.4%
Kakuru et al, Uganda, 2016	36/42 (85.7%)	23/31 (74.2%)		0.87 [0.68; 1.10]	0.005	9.4%
Kajubi et al, Uganda, 2019	83/100 (83%)	66/93 (71%)		0.86 [0.73; 1.00]	0.051	17.7%
Milugu et al, Tanzania, 2021	85/128 (66.4%)	62/115 (53.9%)		0.81 [0.66; 1.00]	0.051	11.8%
Madanitsa et al, Kenya, 2023	123/178 (69.1%)	119/177 (67.2%)		0.97 [0.84; 1.12]	0.705	20.2%
Madanitsa et al, Malawi, 2023	93/151 (61.6%)	82/136 (60.3%)		0.98 [0.81; 1.18]	0.822	14.1%
Madanitsa et al, Tanzania, 2023	115/164 (70.1%)	114/160 (71.2%)		1.02 [0.88; 1.17]	0.824	20.5%
Gutman et al, Malawi, unpublished						0.0%
Random effects model			\sim	0.94 [0.88; 1.01]	0.079	100.0%
Prediction interval				-[0.84; 1.05]		
Heterogeneity: $I^{2} = 6\% [0\%; 73\%], \tau^{2} = 0$	< 0.01, <i>p</i> = 0.380					
Multigravidae						
Desai et al, Kenya, 2015	97/198 (49%)	123/216 (56.9%)		1.16 [0.97; 1.40]	0.108	10.5%
Kakuru et al, Uganda, 2016	26/62 (41.9%)	27/59 (45.8%)		- 1.09 [0.73; 1.63]	0.672	2.8%
Kajubi et al, Uganda, 2019	164/281 (58.4%)	172/295 (58.3%)		1.00 [0.87; 1.15]	0.989	15.3%
Mlugu et al, Tanzania, 2021	224/350 (64%)	210/363 (57.9%)		0.90 [0.80; 1.02]	0.093	18.3%
Madanitsa et al, Kenya, 2023	193/317 (60.9%)	217/320 (67.8%)		1.11 [0.99; 1.25]	0.069	18.6%
Madanitsa et al, Malawi, 2023	150/318 (47.2%)	171/331 (51.7%)		1.10 [0.94; 1.28]	0.254	13.1%
Madanitsa et al, Tanzania, 2023	278/430 (64.7%)	277/433 (64%)		0.99 [0.90; 1.09]	0.835	21.5%
Gutman et al, Malawi, unpublished						0.0%
Random effects model			\Leftrightarrow	1.03 [0.96; 1.11]	0.414	100.0%
Prediction interval				-[0.86; 1.23]		
Heterogeneity: $I_{2}^{2} = 37\% [0\%; 73\%], \tau^{2} =$	< 0.01, p = 0.146					
Test for subgroup differences; $\gamma_4^2 = 3.29$.	$df = 1 \ (p = 0.070)$		0.75 1 1.5			
, , , , , , , , , , , , , , , , , , ,	u/		Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; g/dL = grams/deciliter; Hb = haemoglobin; RR = risk ratio; SP = sulfadoxine-pyrimethamine

Figure S-18. Mean maternal MUAC in cm at delivery

Author, Country, Year	SP N, Mean (SD)	DP N, Mean (SD)	Mean Difference	MD [95% CI]	p-value	Weight
Overall						
Desai et al, Kenya, 2015	477, 27 (2.96)	472, 27 (2.67)		0.02 [-0.37; 0.40]	0.937	9.6%
Kakuru et al, Uganda, 2016						0.0%
Kajubi et al, Uganda, 2019						0.0%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	427, 27 (3.1)	437, 26 (3.03)		0.23 [0.03; 0.43]	0.026	35.4%
Madanitsa et al, Malawi, 2023	413, 26 (2.86)	417, 26 (2.75)		0.11 [-0.14; 0.36]	0.392	22.4%
Madanitsa et al, Tanzania, 2023	505, 27 (3.76)	485, 27 (3.41)		0.31 [0.08; 0.54]	0.009	26.9%
Gutman et al, Malawi, unpublished	240, 26 (2.9)	236, 26 (3.48)		0.18 [-0.32; 0.67]	0.486	5.7%
Random effects model			\diamond	0.20 [0.08; 0.32]	0.001	100.0%
Prediction interval				-[0.01; 0.39]		
Heterogeneity: $I^2 = 0\% [0\%; 79\%], \tau^2 =$	0 [0.00; 0.08], <i>p</i> =	0.685				
			-0.6-0.4-0.2 0 0.2 0.4 0.6			
			Favors DP Favors SP			

Primigravidae			Micall Billerenee	MD [95% CI]	p-value	Weight
FIIIIIuaviuae						
Desai et al. Kenva, 2015	165, 26 (2.34)	140, 26 (2.23)		-0.03 [-0.57; 0.51]	0.913	14.2%
Kakuru et al, Uganda, 2016	/	/				0.0%
Kajubi et al, Uganda, 2019						0.0%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	149, 26 (2.4)	146, 25 (2.54)		0.40 [0.07; 0.74]	0.018	36.7%
Madanitsa et al, Malawi, 2023	127, 25 (2.32)	115, 25 (2.13)		0.32 [-0.09; 0.74]	0.130	23.7%
Madanitsa et al, Tanzania, 2023	134, 26 (3.71)	115, 25 (2.54)		0.60 [0.11; 1.10]	0.017	16.7%
Gutman et al, Malawi, unpublished	82, 26 (2.32)	62, 25 (2.57)		0.89 [0.20; 1.58]	0.011	8.7%
Random effects model			\diamond	0.40 [0.20; 0.60] <	< 0.001	100.0%
Prediction interval				-[0.07; 0.73]		
Heterogeneity: $I^2 = 23\% [0\%; 69\%], \tau^2 =$	< 0.01, <i>p</i> = 0.266					
Multigravidae						
Desai et al, Kenya, 2015	312, 27 (3.15)	332, 27 (2.78)		0.11 [-0.39; 0.61]	0.667	8.5%
Kakuru et al, Uganda, 2016						0.0%
Kajubi et al, Uganda, 2019						0.0%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	278, 27 (3.32)	291, 27 (3.09)		0.13 [-0.12; 0.38]	0.295	33.6%
Madanitsa et al, Malawi, 2023	286, 26 (3.04)	300, 26 (2.86)		0.04 [-0.27; 0.35]	0.793	21.7%
Madanitsa et al, Tanzania, 2023	368, 28 (3.68)	368, 27 (3.47)		0.21 [-0.05; 0.47]	0.118	31.2%
Gutman et al, Malawi, unpublished	156, 26 (3.16)	174, 26 (3.68)		-0.09 [-0.74; 0.56]	0.793	5.0%
Random effects model			\diamond	0.12 [-0.02; 0.27]	0.095	100.0%
Prediction interval				-[-0.11; 0.36]		
Heterogeneity: $I^2 = 0\% [0\%; 79\%], \tau^2 = 0$	0, p = 0.899					
Test for subgroup differences: $\chi_1^2 = 4.70$,	df = 1 (<i>p</i> = 0.030)	-	1.5 -1 -0.5 0 0.5 1	1.5		

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; MUAC = mid-upper arm circumference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-19. Mean maternal weight gain per week in grams

	SP	DP			
Author, Country, Year	N, Mean (SI) N, Mean (SD)	Mean Difference	MD [95% CI] p-	-value Weight
Overall					
Desai et al, Kenya, 2015	416, 290 (325	5) 391, 221 (267)	· · · ·	67 [26; 108]	0.001 11.0%
Kakuru et al, Uganda, 2016	104, 273 (14	1) 90, 262 (184)		8 [-36; 53]	0.713 9.9%
Kajubi et al, Uganda, 2019	365, 233 (215	5) 371, 227 (188)		7 [-22; 36]	0.648 16.3%
Mlugu et al, Tanzania, 2021	354, 409 (308	3) 337, 400 (213)		4 [-34; 42]	0.841 12.0%
Madanitsa et al. Kenva. 2023	457, 331 (202	2) 464, 287 (200)		46 [21: 72] <	0.001 18.2%
Madanitsa et al. Malawi. 2023	431, 311 (443	3) 435, 261 (240)		48 [0: 96]	0.048 9.0%
Madanitsa et al. Tanzania. 2023	573, 303 (284	4) 575, 265 (234)		39 [10: 68]	0.009 16.1%
Gutman et al, Malawi, unpublished	269, 344 (336	6) 273, 292 (304)		- 64 [10; 117]	0.020 7.6%
Pandom offects model				34 [17: 51]	0 001 100 0%
Prediction interval			<u> </u>	_[_10, 77]	0.001 100.076
Hotorogonality: $I^2 = 42\% [0\%: 74\%] = c^2$.	- 242 04 [0 00. 230	0.001 p = 0.009		-[-10, 77]	
Here $1000000000000000000000000000000000000$	= 242.04 [0.00, 230	[0.90], p = 0.098	100 50 0 50 100	h	
)	
	SP	DP	Favois DF Favois SF		
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI] p-	value Weight
Duine investida e			1		
Primigravidae	444 005 (004)	111 010 (071)	_	00 [4 4 40] 0	
Desai et al, Kenya, 2015	144, 285 (304)	111, 216 (271)	_	68 [-4; 140] 0	.063 10.6%
Kakuru et al, Uganda, 2016	42, 270 (146)	31, 224 (135)	-	46 [-20; 111] 0	.174 11.9%
Kajubi et al, Uganda, 2019	96, 213 (156)	85, 201 (253)		11 [-49; 72] 0	.713 13.3%
Mlugu et al, Tanzania, 2021	89, 444 (392)	80, 384 (257)		60 [-41; 161] 0	.243 6.3%
Madanitsa et al, Kenya, 2023	157, 365 (229)	156, 320 (210)		45 [–4; 93] 0	.071 17.0%
Madanitsa et al, Malawi, 2023	138, 279 (206)	123, 281 (233)		-2 [-55; 52] 0	.955 15.4%
Madanitsa et al, Tanzania, 2023	153, 369 (188)	156, 266 (211)		103 [58; 147] < 0	0.001 18.5%
Gutman et al, Malawi, unpublished	91, 293 (374)	78, 253 (209)		39 [-54; 133] 0	.408 7.1%
Random effects model			\diamond	47 [18; 76] 0	.001 100.0%
Prediction interval				-[-26; 120]	
Heterogeneity: $I^2 = 36\% [0\%; 72\%], \tau^2$	= 674.20, <i>p</i> = 0.14	11			
Multigravidae					
Desai et al. Kenva, 2015	272, 293 (337)	280, 222 (266)		70 [20: 121] 0	.006 11.4%
Kakuru et al Uganda 2016	62 274 (139)	59 281 (203)		-7 [-69: 55] 0	829 9.0%
Kajubi et al Lloanda 2019	269 240 (232)	286 235 (164)		5 [-28: 38] 0	772 16.3%
Mugu et al. Tanzania 2021	265, 240 (202)	257 105 (108)		_8 [_/0: 33] 0	707 13.0%
Madanites at al Konva 2022	200, 313 (194)	308 271 (102)		12 [12: 72] 0	006 17 49/
Madanites et al. Malawi 2023	202 225 (510)	311 252 (242)		70 [0.106] 0	028 0 70/
Madanita et al, Malawi, 2023	233, 323 (318)	417 065 (040)		12 [0, 130] 0	402 15.00/
Outrean et al Malauti unnubliste d	417, 278 (308)	417, 205 (242)			.493 15.0%
Guiman et al, Malawi, unpublished	176, 371 (315)	195, 307 (334)		04[-2;130] 0	012 400 60
Handom effects model			\diamond	27[6;49] 0	.012 100.0%
Prediction interval				-[-29; 84]	
Heterogeneity: $I^{c} = 46\% [0\%; 76\%], \tau^{c}$	= 410.20, p = 0.07	/3			
Test for subgroup differences: $v_{i}^{2} = 1.15$	5. df = 1 ($p = 0.283$	3) _1	50 -50 0 50 100 150		
	,	,	Favors DP Favors SP		

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-20. Any evidence of stunting (LAZ <2 SD) from birth to two months of life

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Overall						
Desai et al Kenva 2015	127/361 (35.2%)	142/349 (40 7%)	+ =	1 16 [0 96 1 40]	0 131	20.8%
Kakuru et al. Uganda, 2016	23/94 (24 5%)	18/82 (22%) -		0.90 [0.52; 1.54]	0.694	3.4%
Kajubi et al Uganda 2019	77/304 (25.3%)	110/322 (34.2%)	-	1 35 [1 06: 1 72]	0.034	14.0%
Mugu et al Tanzania 2021	777004 (20.078)	110/022 (04.270)		1.00 [1.00, 1.72]	0.017	0.0%
Madanitsa et al Kenya 2023	13/108 (10 5%)	55/427 (12 0%)		1 22 [0 84 1 78]	0 205	6.7%
Madanitsa et al, Neliya, 2020	102/202 (10.3 /0)	101/200 (40%)		1.22 [0.04, 1.70]	0.235	20.20/
Madanitsa et al, Malawi, 2023	61/406 (15%)	77/406 (109/)		1.02 [0.09, 1.19]	0.740	29.3%
Gutmon et al Malawi unpublished	01/400 (15%)	77/400 (19%)		1.20 [0.93; 1.72]	0.130	9.0%
Guiman et al, Malawi, unpublisheu	71/162 (43.8%)	87/155 (56.1%)		1.28 [1.02; 1.60]	0.030	16.2%
Random effects model				1.16 [1.05: 1.29]	0.004	100.0%
Prediction interval				-[0 95: 1 43]	0.004	100.070
Heterogeneity: $l^2 = 3\% [0\%; 72\%] \tau^2 <$	0 01 [0 00 [.] 0 06] <i>p</i>	= 0.403		[0.00, 1.40]		
	0.01 [0.00, 0.00], p	- 0.100	0.75 1 1.5			
			Favors DP Favors SP			
	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Primigrovidoo			1			
Primigravidae	E1/101 /40 10/)	40/00 (40.00/)		1 00 [0 70, 1 01]	0.007	00.00/
Desai et al, Kenya, 2015 Kelumu et el Unende, 2016	51/121 (42.1%)	46/98 (46.9%)		1.08 [0.73; 1.61]	0.697	22.8%
Kakuru et al, Uganda, 2016	11/35 (31.4%)	9/28 (32.1%)		1.02 [0.42; 2.47]	0.961	4.7%
Kajubi et al, Uganda, 2019	31/77 (40.3%)	34/69 (49.3%)		1.23 [0.76; 2.01]	0.397	15.3%
Mugu et al, Tanzania, 2021			_	4 45 [0 77, 0 70]		0.0%
Madanitsa et al, Kenya, 2023	16/136 (11.8%)	24/142 (16.9%)		- 1.45 [0.77; 2.72]	0.248	9.0%
Madanitsa et al, Malawi, 2023	69/118 (58.5%)	51/109 (46.8%)		0.79 [0.55; 1.13]	0.197	27.6%
Madanitsa et al, Tanzania, 2023	18/98 (18.4%)	18/91 (19.8%)		1.07 [0.56; 2.06]	0.838	8.5%
Gutman et al, Malawi, unpublished	27/49 (55.1%)	25/47 (53.2%)		0.94 [0.55; 1.63]	0.837	12.2%
Random effects model			$\langle \rangle$	1.02 [0.84; 1.23]	0.853	100.0%
Prediction interval				-[0.79; 1.31]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$: 0, <i>p</i> = 0.693					
Multigrovidoo						
Dessi et al Kenva 2015	76/040 (01 70/)	06/051 (20 00/)		1 10 [0 00: 1 61]	0.251	20 00/
Kekuru et el Llaende 2016	10/240 (31.7%)	90/231(30.2%)		0.92 [0.25, 1.01]	0.251	20.0%
Kakuru et al, Uganda, 2016	12/59 (20.3%)	9/54 (10.7%) -			0.003	2.5%
Rajubi et al, Oganda, 2019	46/227 (20.3%)	76/253 (30%)		1.49 [1.03; 2.15]	0.031	14.1%
Miugu et al, Tanzania, 2021			_		0 74 0	0.0%
Madanitsa et al, Kenya, 2023	27/272 (9.9%)	31/285 (10.9%)		1.10 [0.66; 1.84]	0.716	7.1%
Madanitsa et al, Malawi, 2023	114/265 (43%)	139/279 (49.8%)		1.17 [0.92; 1.51]	0.201	30.7%
Madanitsa et al, Tanzania, 2023	43/305 (14.1%)	59/313 (18.8%)		1.31 [0.89; 1.95]	0.170	12.2%
Gutman et al, Malawi, unpublished	44/111 (39.6%)	62/108 (57.4%)		1.44 [0.98; 2.12]	0.063	12.6%
Random effects model			\diamond	1.25 [1.09; 1.43]	0.002	100.0%
Prediction interval				-[1.04; 1.50]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$	0, <i>p</i> = 0.819					
			1 1 1			
Test for subgroup differences: $\chi_1^2 = 2.93$	3, df = 1 ($p = 0.087$)		0.5 1 2			
			Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; LAZ = length-for-age z-score; RR = risk ratio; SD = standard deviation; SP = sulfadoxine-pvrimethamine

Figure S-21. Any evidence of underweight (WAZ <2 SD) from birth to two months of life

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Quarall						
Overali Desai et al. Kenva. 2015	18/363 (5%)	21/349 (6%)		1 21 [0 66: 2 24]	0 536	8 5%
Kakuru et al Llganda 2016	12/94 (12.8%)	5/81 (6 2%)		0.48 [0.18: 1.31]	0.550	3.2%
Kajubi et al Uganda 2019	26/305 (8 5%)	26/322 (8 1%)		0.95 [0.56: 1.50]	0.104	11 7%
Mugu et al Tanzania 2021	20/000 (0.078)	20/022 (0.170)	T	0.35 [0.50, 1.53]	0.000	0.0%
Madanitea et al Kenva 2023	27/408 (6.6%)	46/426 (10.8%)	<u> </u>	1 63 [1 03 2 57]	0.035	15.3%
Madanitsa et al, Neliya, 2023	53/387 (13 7%)	75/301 (10.0%)	1	1 40 [1 01 1 03]	0.000	30.5%
Madanitsa et al. Tanzania. 2023	<i>A1/A07</i> (10.1%)	62/408 (15.2%)		1.40 [1.01, 1.30]	0.041	23.2%
Gutman et al Malawi unnublished	17/162 (10.1%)	16/155 (10.2%)		0.08 [0.52.1.88]	0.029	20.2 /0
Gutthan et al, Malawi, unpublished	17/102 (10.5%)	10/155 (10.5 %)	T	0.30 [0.32, 1.00]	0.900	1.0 /0
Bandom effects model				1 30 [1 08: 1 55]	0 004	100.0%
Prediction interval			Ť	-[1 03: 1 64]	0.001	100.070
Heterogeneity: $l^2 = 22\% [0\%: 65\%] \tau^2$	< 0.01 [0.00.0.66]	n = 0.259		[1.00, 1.04]		
	< 0.01 [0.00, 0.00],	p = 0.200	02 05 1 2 5			
			Favors DP Favors SP			
	SP	DP				
Author Country Vear	n/N (%)	n/N (%)	Bick Batio	BB [95% CI]	n_value	Weight
Author, Country, Tear	11/14 (76)	1/14 (76)	HISK Hallo	nn [95 /8 Cij	p-value	weight
Primigravidae			T			
Desai et al. Kenva. 2015	10/121 (8.3%)	11/98 (11.2%)		1.32 [0.56: 3.11]	0.525	12.5%
Kakuru et al. Uganda, 2016	9/35 (25.7%)	1/27 (3.7%)	i i	0.14 [0.02: 1.14]	0.020	2.1%
Kajubi et al. Uganda, 2019	10/78 (12.8%)	9/69 (13%)		1.03 [0.42; 2.52]	0.956	11.3%
Mlugu et al, Tanzania, 2021	/					0.0%
Madanitsa et al, Kenya, 2023	11/136 (8.1%)	20/142 (14.1%)	+	1.75 [0.84; 3.66]	0.126	16.9%
Madanitsa et al, Malawi, 2023	22/120 (18.3%)	24/109 (22%)		1.18 [0.66; 2.11]	0.566	27.3%
Madanitsa et al, Tanzania, 2023	17/98 (17.3%)	15/91 (16.5%)	- 	0.94 [0.47; 1.89]	0.872	19.0%
Gutman et al. Malawi, unpublished	13/49 (26.5%)	7/47 (14.9%)		0.55 [0.22; 1.38]	0.191	10.8%
Random effects model	(()	\$	1.06 [0.79; 1.44]	0.691	100.0%
Prediction interval			<u> </u>	-[0.72; 1.58]		
Heterogeneity: $I^2 = 24\% [0\%; 66\%], \tau^2$	= < 0.01, <i>p</i> = 0.249					
Multigravidae						
Desai et al, Kenya, 2015	8/242 (3.3%)	10/251 (4%)		1.19 [0.47; 3.02]	0.713	7.2%
Kakuru et al, Uganda, 2016	3/59 (5.1%)	4/54 (7.4%)		1.46 [0.33; 6.52]	0.619	2.8%
Kajubi et al, Uganda, 2019	16/227 (7%)	17/253 (6.7%)	- 	0.96 [0.48; 1.89]	0.899	13.4%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	16/272 (5.9%)	26/284 (9.2%)	-	1.56 [0.84; 2.92]	0.153	16.1%
Madanitsa et al, Malawi, 2023	31/267 (11.6%)	50/280 (17.9%)	-	1.56 [1.00; 2.44]	0.049	31.0%
Madanitsa et al, Tanzania, 2023	23/306 (7.5%)	47/315 (14.9%)		1.96 [1.19; 3.22]	0.007	25.0%
Gutman et al, Malawi, unpublished	4/111 (3.6%)	9/108 (8.3%)		2.30 [0.71; 7.46]	0.150	4.5%
Random effects model			\diamond	1.54 [1.20; 1.98]	0.001	100.0%
Prediction interval			—	-[1.11; 2.14]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$	= 0, <i>p</i> = 0.744					
0			1 1 1 1			
Test for subgroup differences: $\chi_1^2 = 3.44$	4, df = 1 (<i>p</i> = 0.064)		0.1 0.5 1 2 10			
			Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; RR = risk ratio; SD = standard deviation; SP = sulfadoxine-pyrimethamine; WAZ = weight-for-age z-score

Figure S-22. Any evidence of wasting (WLZ <2 SD) from birth to two months of life

	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% CI]	p-value	Weight
Overall						
Desai et al. Kenva. 2015	31/359 (8.6%)	36/344 (10.5%)		- 1.21 [0.77: 1.91]	0.410	6.1%
Kakuru et al. Uganda, 2016	31/94 (33%)	27/81 (33.3%)		1.01 [0.66: 1.54]	0.960	7.2%
Kajubi et al. Uganda, 2019	63/304 (20.7%)	69/322 (21.4%)		1.03 [0.76: 1.40]	0.829	13.9%
Mlugu et al. Tanzania, 2021						0.0%
Madanitsa et al. Kenva, 2023	64/406 (15.8%)	69/425 (16.2%)		1.03 [0.75: 1.41]	0.853	13.2%
Madanitsa et al. Malawi, 2023	119/375 (31.7%)	146/385 (37.9%)		1.20 [0.98: 1.45]	0.075	33.4%
Madanitsa et al. Tanzania, 2023	86/406 (21.2%)	115/407 (28.3%)		1.33 [1.05: 1.70]	0.020	21.6%
Gutman et al. Malawi, unpublished	24/161 (14.9%)	23/152 (15.1%)		1.02 [0.60: 1.72]	0.956	4.6%
		(,)				
Random effects model			\diamond	1.15 [1.03; 1.29]	0.013	100.0%
Prediction interval				-[1.00; 1.34]		
Heterogeneity: $I^{2} = 0\% [0\%; 71\%], \tau^{2} =$	0 [0.00; 0.03], p = 0.	790				
			0.75 1 1.5			
			Favors DP Favors SP			
	SP	DP				
Author, Country, Year	n/N (%)	n/N (%)	Risk Ratio	RR [95% Cl]	p-value	Weight
Primigravidae						
Desai et al. Kenva. 2015	12/120 (10%)	11/95 (11.6%)		- 1.12 [0.50: 2.55]	0.781	7.7%
Kakuru et al. Uganda, 2016	11/35 (31.4%)	9/27 (33.3%)		-1.06[0.44; 2.56]	0.896	6.7%
Kajubi et al. Uganda, 2019	21/77 (27.3%)	25/69 (36.2%)		1 34 [0 75: 2 39]	0.322	15.4%
Mlugu et al. Tanzania, 2021			_			0.0%
Madanitsa et al. Kenva, 2023	25/136 (18.4%)	32/142 (22.5%)		1.23 [0.73: 2.08]	0.428	18.9%
Madanitsa et al. Malawi, 2023	33/115 (28.7%)	38/107 (35.5%)		1.22 [0.77: 1.95]	0.393	23.8%
Madanitsa et al. Tanzania, 2023	27/98 (27.6%)	35/91 (38.5%)		1.39 [0.84: 2.29]	0.199	20.5%
Gutman et al. Malawi, unpublished	10/48 (20.8%)	11/47 (23.4%)		-1.10[0.47; 2.59]	0.828	7.1%
Random effects model	10/10 (2010/0)	(2017/0)		1.25 [0.99: 1.56]	0.058	100.0%
Prediction interval				-[0.92: 1.68]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$	0, <i>p</i> = 0.998			[0.02, 1.00]		
Multigravidae	10/220 (7.0%)	25/240 (10%)		1 25 [0 60: 2 26]	0.467	7 29/
Kakuru et al Llaanda 2016	19/239 (1.9%)	19/54 (22 20/)	1	0.09 [0.52, 1.96]	0.407	6 10/
Kajubi ot al Llganda, 2010	12/227 (19 5%)	10/34 (33.3 %)		0.90 [0.52, 1.60]	0.302	1/ /0/
Mugu et al Tanzania 2021	42/22/ (10.5%)	44/200 (17.4%)		0.94 [0.02, 1.44]	0.707	0.0%
Madanita at al Kanya 2022	20/270 (14 4%)	27/202 (12 10/)		0.01 [0.59:1.42]	0.691	10.0%
Madanitsa et al, Keliya, 2023	96/260 (22 10/)	107/076 (20.00/)		1 10 [0 00: 1 59]	0.001	22.0%
Madanitsa et al. Tanzania 2023	50/200 (33.1%) 50/205 (10.2%)	1077270 (30.0%) 90/214 (25 59/)		1.19 [0.90, 1.30]	0.231	02.0%
Cutmon et al Malauri, unpublished	14/111 (10 G9/)	10/314 (23.5%)		1.30 [0.93, 1.62]	0.125	22.0%
Bandom offects model	14/111 (12.0%)	12/105 (11.4%)		1 11 [0 05, 1 20]	0.788	4.0%
Prodiction interval				[0 00, 1 27]	0.200	100.0%
Heterogeneity: $l^2 = 00/(100/(1710/1))^2$	0 - 0 0 1 5			-[0.90; 1.37]		
Here ogenery; $I = 0\% [0\%; 71\%], \tau =$	0, p = 0.815		r1			
Test for subgroup differences: $\gamma^2 = 0.65$	df = 1 (n = 0.420)		0.5 1 2			
	, 2. , (0 = 0. , 20)		Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; RR = risk ratio; SD = standard deviation; SP = sulfadoxine-pyrimethamine; WLZ = weight-for-length z-score

Figure S-23. Mean length-for-age z-score at two months of life

Author, Country, Year	SP N, Mean (SD)	DP N, Mean (SD)	Mean Difference	MD [95% CI]	p-value	Weight
Overall					-	
Dessi et al Kanva 2015	000 0.04 (1.50)	051 115 (150)		0.01 [0.04, 0.59]	0.007	0.70/
Desar et al, Kenya, 2015	230, -0.84 (1.52)	251, -1.15 (1.53)		- 0.31 [0.04, 0.56]	0.027	9.7%
Kakuru et al, Uganda, 2016	94, -0.38 (1.45)	82, -0.26 (1.41)		-0.12 [-0.55; 0.30]	0.577	4.0%
Kajubi et al, Uganda, 2019	303, -0.68 (1.16)	320, -0.81 (1.15)		0.13 [-0.05; 0.31]	0.151	22.0%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	404, -0.07 (1.21)	419, -0.35 (1.16)		0.28 [0.12; 0.44]	< 0.001	27.9%
Madanitsa et al, Malawi, 2023	366, -0.78 (2.13)	380, -0.85 (1.87)		0.07 [-0.22; 0.36]	0.642	8.8%
Madanitsa et al, Tanzania, 2023	404, -0.36 (1.33)	406, -0.52 (1.31)		0.16 [-0.02; 0.34]	0.090	21.9%
Gutman et al, Malawi, unpublished	154, -1.17 (1.51)	143, -1.36 (1.65)		0.19 [-0.17; 0.55]	0.291	5.6%
Random effects model			\diamond	0.18 [0.10; 0.27]	< 0.001	100.0%
Prediction interval				-[0.07; 0.30]		
Heterogeneity: $l^2 = 0\% [0\%: 71\%] \tau^2$	-0[000:007] $n - 1$	0 529				

Prediction interval Heterogeneity: $l^2 = 0\%$ [0%; 71%], $\tau^2 = 0$ [0.00; 0.07], p = 0.529

-0.4 -0.2 0 0.2 0.4 Favors DP Favors SP

	SP	DP					
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mear	n Difference	MD [95% CI]	p-value	Weight
Primigravidae				1			
Desai et al, Kenya, 2015	75, -0.79 (1.63)	76, -1.34 (1.61)			- 0.55 [0.03; 1.07]	0.038	9.7%
Kakuru et al, Uganda, 2016	35, -0.79 (1.33)	28, -0.73 (1.4)			-0.06 [-0.73; 0.62]	0.866	5.6%
Kajubi et al, Uganda, 2019	76, -0.97 (1.17)	68, -1.1 (1.21)	12	-	0.13 [-0.26; 0.52]	0.513	17.0%
Mlugu et al, Tanzania, 2021							0.0%
Madanitsa et al, Kenya, 2023	135, -0.28 (1.23)	139, -0.45 (1.17)			0.17 [-0.11; 0.46]	0.231	31.9%
Madanitsa et al, Malawi, 2023	111, -1.32 (2.16)	104, -1.08 (1.73)		E	-0.24 [-0.76; 0.29]	0.373	9.4%
Madanitsa et al, Tanzania, 2023	97, -0.68 (1.26)	91, -0.72 (1.14)	-		0.04 [-0.30; 0.39]	0.817	21.7%
Gutman et al, Malawi, unpublished	45, -1.51 (1.79)	44, -1.23 (1.77) -			-0.28 [-1.02; 0.46]	0.452	4.7%
Random effects model				\diamond	0.10 [-0.06; 0.26]	0.222	100.0%
Prediction interval					-[-0.11; 0.31]		
Heterogeneity: $I^2 = 2\% [0\%; 71\%], \tau^2$	= < 0.01, p = 0.410						
Multigravidae							
Desai et al, Kenya, 2015	155, -0.86 (1.47)	175, -1.07 (1.49)			0.20 [-0.12; 0.52]	0.216	9.7%
Kakuru et al, Uganda, 2016	59, -0.13 (1.48)	54, -0.01 (1.37)			-0.12 [-0.65; 0.40]	0.648	3.6%
Kajubi et al, Uganda, 2019	227, -0.58 (1.14)	252, -0.73 (1.12)			0.15 [-0.05; 0.36]	0.140	24.0%
Mlugu et al, Tanzania, 2021	`						0.0%
Madanitsa et al, Kenya, 2023	269, 0.04 (1.18)	280, -0.29 (1.15)			0.33 [0.14; 0.53]	0.001	26.1%
Madanitsa et al, Malawi, 2023	255, -0.55 (2.08)	274, -0.76 (1.92)			0.22 [-0.13; 0.56]	0.216	8.5%
Madanitsa et al, Tanzania, 2023	304, -0.25 (1.34)	313, -0.46 (1.35)		-	0.21 [-0.00; 0.42]	0.054	21.9%
Gutman et al, Malawi, unpublished	107, -1.04 (1.36)	99, -1.42 (1.6)			0.38 [-0.03; 0.78]	0.068	6.1%
Random effects model				\diamond	0.23 [0.13; 0.33]	<0.001	100.0%
Prediction interval				_	-[0.10; 0.36]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2$	= 0, <i>p</i> = 0.689						
		ſ					
Test for subgroup differences: $\chi_1^2 = 1.7$	70, df = 1 (<i>p</i> = 0.193)	-	1 –0.5	0 0.5	1		
			Favors I	DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-24. Mean weight-for-age z-score at two months of life

	SP	DP				
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI]	p-value	Weight
Overall						
Desai et al, Kenya, 2015	234, 0.05 (1.1)	258, 0 (1.08)		0.05 [-0.15; 0.24]	0.630	11.7%
Kakuru et al, Uganda, 2016	94, -0.28 (0.95)	81, -0.18 (0.95)		-0.10 [-0.38; 0.18]	0.487	5.5%
Kajubi et al, Uganda, 2019	303, -0.24 (0.98)	321, -0.24 (0.92)		0.00 [-0.15; 0.15]	0.981	19.6%
Mlugu et al, Tanzania, 2021						0.0%
Madanitsa et al, Kenya, 2023	406, -0.01 (1.1)	423, -0.13 (1.1)		0.12 [-0.03; 0.26]	0.129	19.5%
Madanitsa et al, Malawi, 2023	382, -0.35 (1.19)	388, -0.45 (1.21)		0.10 [-0.07; 0.27]	0.259	15.2%
Madanitsa et al, Tanzania, 2023	404, -0.21 (0.97)	405, -0.38 (1.11)		0.17 [0.03; 0.31]	0.021	21.0%
Gutman et al, Malawi, unpublished	159, -0.24 (1.08)	155, -0.34 (1.09)		0.09 [-0.15; 0.34]	0.440	7.5%
Random effects model Prediction interval			\diamond	0.08 [0.01; 0.15] -[-0.01: 0.17]	0.017	100.0%

Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 = 0 [0.00; 0.02], p = 0.609$

-0.3 -0.1 0 0.1 0.2 0.3 Favors DP Favors SP

Author Country Year	SP N. Mean (SD)	DP N. Mean (SD)	Mean Difference		n_value	Weight
Aution, Country, Tear	N, Mean (50)	N, Mean (5D)	Mean Difference		p-value	weight
Primigravidae						
Desai et al, Kenya, 2015	76, -0.22 (1.08)	78, -0.17 (1.25)		-0.04 [-0.41; 0.33]	0.817	11.2%
Kakuru et al, Uganda, 2016	35, -0.55 (1.11)	27, -0.3 (0.81)		-0.25 [-0.75; 0.25]	0.321	6.2%
Kajubi et al, Uganda, 2019	76, -0.47 (0.97)	69, -0.51 (0.93)		0.04 [-0.27; 0.35]	0.796	16.0%
Mlugu et al, Tanzania, 2021	'					0.0%
Madanitsa et al, Kenya, 2023	135, -0.17 (0.97)	141, -0.33 (1.11)		0.16 [-0.09; 0.40]	0.213	25.4%
Madanitsa et al, Malawi, 2023	118, -0.41 (1.12)	108, -0.58 (1.33)		0.17 [-0.15; 0.49]	0.289	15.0%
Madanitsa et al, Tanzania, 2023	97, -0.48 (1)	90, -0.63 (0.99)		0.15 [-0.14; 0.44]	0.303	18.8%
Gutman et al, Malawi, unpublished	49, -0.48 (1.2)	47, -0.53 (1.07)		0.05 [-0.40; 0.51]	0.817	7.4%
Random effects model			\sim	0.08 [-0.04; 0.21]	0.185	100.0%
Prediction interval				-[-0.08; 0.25]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2 =$	= 0, <i>p</i> = 0.791					
Marthianardalaa						
Multigravidae	150 0 10 (1 00)	100 0 00 (0 00)	_	0 10 [0 10 0 00]	0.070	10 10/
Desal et al, Kenya, 2015	158, 0.18 (1.09)	180, 0.08 (0.99)		0.10 [-0.12; 0.32]	0.379	12.1%
Kakuru et al, Uganda, 2016	59, -0.11 (0.81)	54, -0.12 (1.01)	<u> </u>	0.00 [-0.33; 0.34]	0.993	5.3%
Nurse et al. Tanzania 2019	227, -0.16 (0.98)	252, -0.17 (0.9)		0.01 [-0.16; 0.17]	0.953	21.0%
Madanitas et al Kanya 2022	071 0 07 (1 15)		-			17.00/
Madaniisa et al, Kenya, 2023	271, 0.07 (1.15)	282, -0.02 (1.08)		0.09 [-0.09; 0.28]	0.317	17.3%
Madaniisa et al, Malawi, 2023	264, -0.33 (1.22)	278, -0.39(1.14)		0.06 [-0.13; 0.26]	0.526	15.0%
Cutmon et al Molowi unpublished	304, -0.11 (0.94)	313, -0.31(1.14)		0.20 [0.03; 0.36]	0.019	21.8%
Bandam affasta madal	106, -0.13 (1.02)	106, -0.25 (1.1)		0.12[-0.16; 0.40]	0.400	100.09/
Production interval			\sim	0.09[0.01, 0.17]	0.020	100.0%
Hotorogonoity: $J^2 = 0\% [0\% : 71\%] = c^2$	0 0 - 0 907			-[-0.01; 0.19]		
Hereiogeneity. $T = 0\% [0\%, 71\%], \tau =$	$= 0, \mu = 0.807$					
Test for subgroup differences: $\chi_1^2 = 0.0$	1, df = 1 (p = 0.917)		-0.6 -0.2 0 0.2 0.4 0.6			
			Favors DP Favors SP			

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Figure S-25. Mean weight-for-length z-score at two months of life

	SP	DP				
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI]	p-value	Weight
Overall						
Desai et al, Kenya, 2015	224, 1.13 (1.71)	240, 1.43 (1.8)		-0.30 [-0.61; 0.02]	0.070	9.1%
Kakuru et al, Uganda, 2016	93, -0.29 (1.56)	80, -0.34 (1.33)		0.04 [-0.39; 0.48]	0.844	4.8%
Kajubi et al, Uganda, 2019	304, 0.16 (1.31)	320, 0.29 (1.27)		-0.13 [-0.34; 0.07]	0.196	22.6%
Mlugu et al, Tanzania, 2021	`	`				0.0%
Madanitsa et al, Kenya, 2023	403, 0.17 (1.24)	420, 0.31 (1.4)		-0.14 [-0.32; 0.04]	0.121	28.2%
Madanitsa et al, Malawi, 2023	332, 0.26 (2.37)	348, 0.25 (2.35)		0.01 [-0.34; 0.37]	0.949	7.3%
Madanitsa et al, Tanzania, 2023	401, 0.2 (1.42)	405, 0.17 (1.5)		0.03 [-0.17; 0.23]	0.756	22.6%
Gutman et al, Malawi, unpublished	150, 0.72 (1.76)	144, 0.93 (1.85)		-0.22 [-0.63; 0.20]	0.303	5.4%
	, , , , ,					
Random effects model			\diamond	-0.10 [-0.19; -0.00]	0.044	100.0%
Prediction interval				-[-0.22; 0.03]		
Heterogeneity: $I^2 = 0\% [0\%; 71\%], \tau^2$:	= 0 [0.00; 0.06], <i>p</i> =	= 0.609		- · · ·		
		-	-0.6 -0.4 -0.2 0 0.2 0.4	0.6		
			Favors DP Favors SP			
	SP	DP				
Author, Country, Year	N, Mean (SD)	N, Mean (SD)	Mean Difference	MD [95% CI]	p-value	Weight
Primigravidaa			I			

Primigravidae		
Desai et al, Kenya, 2015 74, 0.75 (1.75) 69, 1.29 (1.6) -0.53 [-1.08; 0.02]	0.058	10.7%
Kakuru et al, Uganda, 2016 35, -0.15 (1.65) 26, -0.12 (1.28) -0.03 [-0.80; 0.73]	0.931	5.6%
Kajubi et al, Uganda, 2019 77, 0.17 (1.41) 68, 0.28 (1.44) -0.11 [-0.57; 0.36]	0.645	15.1%
Mlugu et al, Tanzania, 2021		0.0%
Madanitsa et al, Kenya, 2023 135, 0.19 (1.22) 140, 0.19 (1.39) 0.00 [-0.31; 0.31]	0.995	34.1%
Madanitsa et al, Malawi, 2023 100, 0.73 (2.34) 96, 0.44 (2.3) 0.29 [-0.36; 0.94]	0.377	7.7%
Madanitsa et al, Tanzania, 2023 95, 0.21 (1.32) 90, 0.08 (1.38) 0.13 [-0.26; 0.52]	0.508	21.6%
Gutman et al, Malawi, unpublished 43, 0.98 (1.97) 45, 0.7 (1.81) 0.29 [-0.51; 1.08]	0.480	5.2%
Random effects model	0.918	100.0%
Prediction interval -[-0.25; 0.23]		
Heterogeneity: $J^2 = 0\% [0\%; 71\%], \tau^2 = 0, \rho = 0.479$		
Multigravidae		
Desai et al, Kenya, 2015 150, 1.32 (1.66) 171, 1.48 (1.87) -0.17 [-0.55; 0.22]	0.404	8.5%
Kakuru et al, Uganda, 2016 58, -0.38 (1.52) 54, -0.44 (1.36)	0.814	4.5%
Kajubi et al, Uganda, 2019 227, 0.15 (1.28) 252, 0.3 (1.22) -0.14 [-0.36; 0.08]	0.217	25.7%
Mlugu et al, Tanzania, 2021		0.0%
Madanitsa et al, Kenya, 2023 268, 0.16 (1.26) 280, 0.37 (1.4) -0.22 [-0.44; 0.01]	0.059	25.8%
Madanitsa et al, Malawi, 2023 232, 0.06 (2.36) 250, 0.19 (2.38) -0.13 [-0.55; 0.29]	0.549	7.2%
Madanitsa et al, Tanzania, 2023 303, 0.2 (1.46) 313, 0.19 (1.54) - 0.01 [-0.23; 0.25]	0.924	22.9%
Gutman et al, Malawi, unpublished 105, 0.63 (1.66) 99, 1.04 (1.87) -0.40 [-0.89; 0.08]	0.101	5.5%
Random effects model	0.023	100.0%
Prediction interval -[-0.28; 0.02]		
Heterogeneity: $l^2 = 0\% [0\%; 71\%], \tau^2 = 0, p = 0.715$		
Test for subgroup differences: $\gamma_{4}^{2} = 1.26$, df = 1 (p = 0.261) -1 -0.5 0 0.5 1		
Envero DB Envero SB		

Abbreviations: CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SD = standard deviation; SP = sulfadoxine-pyrimethamine

Appendix 8. Study-specific effect estimates from mediation analyses

Figure S-26. IPTp differences in BWGA z-scores mediated by incidence of clinical malaria during pregnancy



Abbreviations: BWGAz = Birthweight-for-gestational age, CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SP = sulfadoxine-pyrimethamine

Figure S-27. IPTp differences in BWGA z-scores mediated by placental malaria infection defined as any evidence of pigment or parasites detected by histopathology, microscopy, PCR, or RDT

lr	ndirect (Mediated) Effec	t	Dir	ect (Non-mediated) Effec	et	
		A				
IPTp (SP vs D	P)> Placental malaria	BWGA	IPTp (SP vs D	P)> Placental malaria>	BWGA	
Author, Country, Year	Mean Difference	MD [95% CI] Weight	Author, Country, Year	Mean Difference	MD [95% CI]	Weight
Overall			Overall			
Desai et al Kenva 2015	*	_0.00[_0.02: 0.01] 18.0%	Desai et al. Kenva, 2015		0.21 [0.08: 0.35]	14.0%
Kakuru et al Uganda 2016		-0.01 [-0.05; 0.03] 3.0%	Kakuru et al, Uganda, 2016		-0.03 [-0.28; 0.22]	7.1%
Kajubi et al. Uganda 2019	I	-0.10[-0.17:-0.03] 0.9%	Kajubi et al, Uganda, 2019		0.32 [0.16; 0.48]	11.9%
Mlugu et al. Tanzania, 2021		-0.01 [-0.03: 0.02] 6.8%	Mlugu et al, Tanzania, 2021		-0.04 [-0.18; 0.11]	12.9%
Madanitsa et al. Kenva. 2023		-0.02 [-0.04: -0.00] 13.3%	Madanitsa et al, Kenya, 2023		0.22 [0.10; 0.34]	15.2%
Madanitsa et al. Malawi, 2023		-0.01 [-0.03: 0.01] 18.1%	Madanitsa et al, Malawi, 2023		0.16 [0.02; 0.31]	13.0%
Madanitsa et al. Tanzania. 2023	3	-0.01 [-0.02; 0.01] 33.4%	Madanitsa et al, Tanzania, 2023		0.20 [0.08; 0.32]	14.7%
Gutman et al, Malawi, unpublish	ned 🚽	-0.02 [-0.05; 0.00] 6.5%	Gutman et al, Malawi, unpublished		0.06 [-0.11; 0.22]	11.3%
Random effects model	•	-0.01 [-0.02: -0.00] 100.0%	Random effects model	\diamond	0.15 [0.07; 0.23]	100.0%
Prediction interval	_	-[-0.02; 0.00]	Prediction interval		-[-0.09; 0.39]	
Heterogeneity: I ² = 21% [0%; 63%	p = 0.261	•	Heterogeneity: $I^2 = 57\%$ [5%; 80%], p	0 = 0.023		
-	-0.15 -0.05 0 0.05 0.1 0.1	5		-0.4 -0.2 0 0.2 0.4		
	Favors DP Favors SP			Favors DP Favors SP		
Author, Country, Year	Mean Difference	MD [95% CI] Weight	Author, Country, Year	Mean Difference	MD [95% CI]	Weight
Primigravidae			Primigravidae	T		
Desai et al, Kenya, 2015	+	-0.00 [-0.04; 0.03] 25.8%	Desai et al, Kenya, 2015		0.17 [-0.08; 0.42]	14.7%
Kakuru et al, Uganda, 2016		-0.10 [-0.29; 0.08] 1.3%	Kakuru et al, Uganda, 2016		-0.11 [-0.49; 0.26]	7.1%
Kajubi et al, Uganda, 2019		-0.13 [-0.25; -0.02] 3.4%	Kajubi et al, Uganda, 2019		0.13 [-0.19; 0.45]	9.7%
Mlugu et al, Tanzania, 2021		-0.04 [-0.11; 0.04] 7.4%	Mlugu et al, Tanzania, 2021		-0.13 [-0.43; 0.17]	10.6%
Madanitsa et al, Kenya, 2023		-0.02 [-0.06; 0.03] 18.1%	Madanitsa et al, Kenya, 2023		0.21 [-0.00; 0.42]	18.7%
Madanitsa et al, Malawi, 2023		-0.01 [-0.06; 0.04] 16.0%	Madanitsa et al, Malawi, 2023		-0.02 [-0.30; 0.27]	11.9%
Madanitsa et al, Tanzania, 2023	3	-0.02 [-0.06; 0.03] 21.6%	Madanitsa et al, Tanzania, 2023	-	0.21 [-0.02; 0.44]	16.8%
Gutman et al, Malawi, unpublis	hed 🛛 🔳	0.02 [-0.06; 0.10] 6.4%	Gutman et al, Malawi, unpublishe	d	0.02 [-0.29; 0.32]	10.4%
Random effects model	\diamond	-0.02 [-0.03; 0.00] 100.0%	Random effects model	\diamond	0.10 [0.00; 0.19]	100.0%
Prediction interval	-	-[-0.04; 0.01]	Prediction interval		-[-0.02; 0.22]	
Heterogeneity: / ² = 0% [0%; 68%]	, <i>p</i> = 0.489		Heterogeneity: $I^{2} = 0\% [0\%; 68\%], p$	= 0.456		
Multigravidae			Multigravidae			
Desai et al, Kenya, 2015	+	-0.01 [-0.04; 0.01] 18.2%	Desai et al, Kenya, 2015		0.24 [0.08; 0.40]	14.3%
Kakuru et al, Uganda, 2016		0.01 [-0.07; 0.09] 2.7%	Kakuru et al, Uganda, 2016		0.05 [-0.28; 0.39]	4.6%
Kajubi et al, Uganda, 2019		-0.08 [-0.16; 0.00] 2.8%	Kajubi et al, Uganda, 2019		0.37 [0.20; 0.55]	12.5%
Mlugu et al, Tanzania, 2021	–	-0.03 [-0.06; 0.00] 15.4%	Mlugu et al, Tanzania, 2021		0.01 [-0.16; 0.17]	13.9%
Madanitsa et al, Kenya, 2023	T	0.00 [-0.02; 0.02] 23.8%	Madanitsa et al, Kenya, 2023		0.20 [0.05; 0.34]	16.5%
Madanitsa et al, Malawi, 2023	-	0.02 [-0.00; 0.05] 19.3%	Madanitsa et al, Malawi, 2023		0.22 [0.05; 0.38]	13.5%
Madanitsa et al, Tanzania, 2023	3	0.02 [-0.02; 0.06] 10.2%	Madanitsa et al, Tanzania, 2023		0.17 [0.02; 0.33]	14.9%
Gutman et al, Malawi, unpublis	hed 1	-0.01 [-0.06; 0.04] 7.4%	Gutman et al, Malawi, unpublishe	d The second sec	0.06 [-0.15; 0.27]	9.8%
Handom effects model	Ŷ	-0.00 [-0.02; 0.01] 100.0%	Handom effects model	\diamond	0.18 [0.10; 0.26]	100.0%
Prediction interval		-[-0.04; 0.03]	Prediction interval	- 0.100	-[-0.02; 0.38]	
Heterogeneity: /~ = 40% [0%; 74%	$p_{j}, p = 0.110$		Heterogeneity: $I^{-} = 38\% [0\%; 73\%],$	p = 0.128		
	-0.2 -0.1 0 0.1 0.2			-0.4 -0.2 0 0.2 0.4		
	Favors DP Favors SP			Favors DP Favors SP		
1			11			

Abbreviations: BWGAz = birthweight-for-gestational age z-score; CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; SP = sulfadoxine-pyrimethamine

Indirect (Mediated	Effect	Direc	t (Non-mediated) Effe	ect	
IPTp (SP vs DP)	→ BWGA	IPTD (SP vs	DP)> GWG> BV	VGA	
Author, Country, Year Mean Differer	ce MD [95% CI] Weight	Author, Country, Year	Mean Difference	MD [95% CI]	Weight
OverallDesai et al, Kenya, 2015Kakuru et al, Uganda, 2016Kajubi et al, Uganda, 2019Miugu et al, Tanzania, 2021Madanitsa et al, Kenya, 2023Madanitsa et al, Kanya, 2023Madanitsa et al, Tanzania, 2023Gutman et al, Malawi, unpublishedRandom effects modelPrediction intervalHeterogeneity: $l^2 = 65\%$ [26%; 84%], $p = 0.005$	- 0.02 [0.00; 0.05] 15.2% 0.00 [-0.04; 0.05] 8.1% -0.00 [-0.03; 0.03] 12.5% -0.01 [-0.03; 0.01] 15.8% 0.06 [0.03; 0.09] 13.2% 0.06 [0.02; 0.10] 10.0% - 0.04 [0.01; 0.07] 13.0% 0.02 [-0.01; 0.05] 12.2% 0.02 [0.00; 0.04] 100.0% -[-0.03; 0.08]	Overall Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Miugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: / ² = 32% [0%; 70%], ^{[,p}	=0.172	0.18 [0.05; 0.31] -0.03 [-0.28; 0.23] -0.20 [0.06; 0.34] -0.03 [-0.18; 0.11] 0.13 [0.02; 0.26] 0.12 [-0.03; 0.26] 0.17 [0.04; 0.29] -0.00 [-0.17; 0.16] 0.11 [0.05; 0.17] -[-0.03; 0.25]	14.5% 4.9% 13.0% 12.3% 16.7% 12.9% 15.3% 10.3% 100.0%
Favors DP Favo	rs SP	-0.3	-0.2-0.1 0 0.1 0.2 0.3 Favors DP Favors SP		
Author, Country, Year Mean Differen	e MD [95% CI] Weight	Author, Country, Year	Mean Difference	MD [95% CI]	Weight
Primigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Mlugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Kenya, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: I ² = 51% [0%; 78%], p = 0.044 Multigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Muterogeneity: de Jarcareire 2021	-0.01 [-0.06; 0.04] 27.1% -0.04 [-0.16; 0.08] 5.0% 0.04 [-0.04; 0.11] 11.2% -0.02 [-0.09; 0.04] 15.6% 0.03 [-0.05; 0.11] 10.3% -0.06 [-0.00; 0.13] 14.8% -0.06 [-0.00; 0.13] 14.8% -0.03 [-0.12; 0.05] 9.8% 0.02 [-0.02; 0.06] 100.0% -[-0.09; 0.12] -0.02 [-0.00; 0.05] 18.9% 0.02 [-0.02; 0.06] 12.7% 0.04 [-0.07; 0.15] 1.9% 0.02 [-0.02; 0.06] 12.7%	Primigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2019 Mlugu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Kanya, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: $l^2 = 0\%$ [0%; 68%], $p =$ Multigravidae Desai et al, Kenya, 2015 Kakuru et al, Uganda, 2016 Kajubi et al, Uganda, 2016 Kajubi et al, Uganda, 2019		0.12 [-0.12; 0.36] -0.10 [-0.45; 0.24] -0.01 [-0.31; 0.28] -0.14 [-0.46; 0.17] 0.15 [-0.06; 0.35] 0.04 [-0.20; 0.29] 0.02 [-0.29; 0.34] 0.04 [-0.06; 0.13] -[-0.08; 0.16] 0.13 [-0.04; 0.31] 0.07 [-0.28; 0.42] 0.26 [0.10; 0.43]	16.2% 8.0% 10.9% 9.6% 21.1% 9.1% 15.6% 9.5% 100.0%
Midgu et al, Tanzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: $I^2 = 20\%$ [0%; 63%], $p = 0.268$ -0.2 - 0.1 0 0. Favors DP Favor	-0.01 [-0.03; 0.02] 17.7% 0.04 [0.01; 0.07] 17.7% - 0.08 [0.02; 0.13] 5.9% 0.02 [-0.01; 0.06] 13.7% 0.02 [-0.02; 0.06] 11.6% 0.02 [0.01; 0.04] 100.0% -[-0.01; 0.05]	Miugu et al, Ianzania, 2021 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublished Random effects model Prediction interval Heterogeneity: / ² = 13% [0%; 55%], p -0.4	= 0.330 4 -0.2 0 0.2 0.4 Favors DP Favors SP	-0.02 [-0.18; 0.15] 0.16 [0.02; 0.30] 0.17 [0.01; 0.33] 0.18 [0.03; 0.32] -0.00 [-0.20; 0.20] 0.13 [0.07; 0.20] -[0.01; 0.25]	13.2% 17.7% 14.2% 16.6% 9.2% 100.0%

Figure S-28. IPTp differences in BWGA z-scores mediated by gestational weight gain

Abbreviations: BWGAz = Birthweight-for-gestational age, CI = confidence interval; DP = dihydroartemisinin-piperaquine; GWG = Gestational weight gain; MD = mean difference; SP = sulfadoxine-pyrimethamine

Figure S-29. IPTp differences in BWGA z-scores mediated by MUAC

Inc	direct (Mediated) Effe	ct	Direc	et (Non-mediated) Ef	fect
	DP) \longrightarrow MUAC \longrightarrow B	ŴGA	IPTp (SP vs	_{DP)} > MUAC> E	BWGA
Author, Country, Year	Mean Difference	MD [95% CI] Weight	Author, Country, Year	Mean Difference	MD [95% CI] Weight
Overall Desai et al, Kenya, 2015 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublishe Random effects model Prediction interval Heterogeneity: <i>I</i> ² = 0% [0%; 79%], <i>µ</i>	d = 0.976 .02 -0.01 0 0.01 0.02 Favors DP Favors SP	0.001 [-0.022; 0.025] 9.3% 0.006 [-0.011; 0.022] 20.3% -0.002 [-0.025; 0.021] 9.9% 0.002 [-0.008; 0.013] 46.5% 0.007 [-0.013; 0.026] 14.0% 0.003 [-0.004; 0.010] 100.0% -[-0.009; 0.015]	OverallDesai et al, Kenya, 2015Madanitsa et al, Kenya, 2023Madanitsa et al, Malawi, 2023Madanitsa et al, Tanzania, 2023Gutman et al, Malawi, unpublishedRandom effects modelPrediction intervalHeterogeneity: $I^2 = 10\%$ [0%; 81%], $\overline{p} = -0.3$	= 0.349 3-0.2 -0.1 0 0.1 0.2 Favors DP Favors SP	- 0.18 [0.06; 0.29] 24.6% - 0.19 [0.07; 0.31] 24.8% - 0.18 [0.03; 0.32] 15.8% - 0.20 [0.08; 0.32] 22.4% -0.00 [-0.17; 0.16] 12.3% 0.16 [0.11; 0.22] 100.0% -[0.07; 0.26] 0.3
Author, Country, Year	Mean Difference	MD [95% Cl] Weight	Author, Country, Year	Mean Difference	MD [95% CI] Weight
Primigravidae Desai et al, Kenya, 2015 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublishe Random effects model Prediction interval Heterogeneity: $I^2 = 0\%$ [0%; 79%], μ	d = 0.452	-0.005 [-0.087; 0.077] 8.0% 0.001 [-0.036; 0.037] 40.4% - 0.040 [-0.030; 0.111] 10.8% 0.039 [-0.008; 0.086] 24.5% -0.021 [-0.079; 0.036] 16.4% 0.010 [-0.013; 0.033] 100.0% -[-0.027; 0.048]	PrimigravidaeDesai et al, Kenya, 2015Madanitsa et al, Kenya, 2023Madanitsa et al, Malawi, 2023Madanitsa et al, Tanzania, 2023Gutman et al, Malawi, unpublishedRandom effects modelPrediction intervalHeterogeneity: $J^2 = 0\%$ [0%; 79%], $p = 0$.815	0.153 [-0.062; 0.369] 25.5% 0.182 [-0.024; 0.388] 28.0% 0.019 [-0.302; 0.339] 11.5% 0.163 [-0.067; 0.394] 22.3% -0.003 [-0.309; 0.303] 12.7% 0.128 [0.019; 0.237] 100.0% -[-0.049; 0.305]
Multigravidae Desai et al, Kenya, 2015 Madanitsa et al, Kenya, 2023 Madanitsa et al, Malawi, 2023 Madanitsa et al, Tanzania, 2023 Gutman et al, Malawi, unpublishe Random effects model Prediction interval Heterogeneity: <i>I</i> ² = 0% [0%; 79%], <u>f</u> -0.	d = 0.727 1 -0.05 0 0.05 0.1 Favors DP Favors SP	-0.009 [-0.036; 0.017] 10.2% 0.003 [-0.011; 0.016] 38.1% 0.004 [-0.024; 0.031] 9.7% 0.001 [-0.014; 0.017] 30.8% 0.017 [-0.008; 0.042] 11.2% 0.003 [-0.006; 0.011] 100.0% -[-0.011; 0.016]	MultigravidaeDesai et al, Kenya, 2015Madanitsa et al, Kenya, 2023Madanitsa et al, Malawi, 2023Madanitsa et al, Tanzania, 2023Gutman et al, Malawi, unpublishedRandom effects modelPrediction intervalHeterogeneity: $I^2 = 0\% [0\%; 79\%], p = 0$ -0.4	.599 -0.2 0 0.2 0.4 Favors DP Favors SP	0.192 [0.051; 0.334] 24.1% 0.184 [0.043; 0.325] 24.4% - 0.253 [0.083; 0.424] 16.7% 0.199 [0.051; 0.346] 22.5% 0.038 [-0.161; 0.237] 12.3% 0.183 [0.113; 0.253] 100.0% -[0.070; 0.296] 4

Abbreviations: BWGAz = Birthweight-for-gestational age, CI = confidence interval; DP = dihydroartemisinin-piperaquine; MD = mean difference; MUAC = midupper arm circumference; SP = sulfadoxine-pyrimethamine

Appendix 9. Results for excluded Okoro et al, Nigeria (2023) trial

Table S-9. Table 1 Participant characteristics

Enrolmont obstactoristics	Total	IPTp-SP	IPTp-DP
	N=197	N=91	N=106
Maternal age in years, mean (SD)	27.4 (6.0)	27.7 (6.3)	27.0 (5.8)
Gestational age in weeks, mean (SD)	17·5 (1·6)	17·7 (1·6)	17·3 (1·5)
Gravidity categories, n/N (%)			
Primigravidae	68/197 (35%)	30/91(33%)	38/106 (36%)
Secundigravidae	25/197 (13%)	11/91 (12%)	14/106 (13%)
Multigravidae (3+)	104/194 (53%)	50/91 (55%)	54/106 (51%)
Weight in kg, mean (SD)	65.0 (15.6)	66.1 (14.9)	64.0 (16.1)
Height in cm, mean (SD)	158·7 (7·8)	159.0 (6.7)	158·3 (8·6)
Maternal MUAC in cm, mean (SD)			
Highest level of schooling completed, n/N	(%)		
None			
Primary			
Secondary			
Higher			
Wealth index tertiles, n/N (%)			
Lowest tertile			
Middle tertile			
Highest tertile			
Slept under a bed net last night, n/N (%)			
Microscopy positivity, n/N (%)	82/196 (42%)	41/91 (48%)	39/105 (37%)
PCR/LAMP positivity, n/N (%)			

Table S-9. Description of study characteristics and outcomes collected

Study Information	Okoro et al ²²
Study Details	
Source	PACTR202002644579177
Study site(s)	Tertiary hospital in Maiduguri, Nigeria
Prevalence of PfDHPS 540E mutation, %*	0%
Prevalence of PfDHPS 581G mutation, %*	0%
Number of Participants Randomized (Among Singleton Pregnancies)	197
Sulfadoxine-Pyrimethamine	91
Dihydroartemisinin-Piperaquine	106
IPTp dosing regimen	3-course IPTp given at 16-20, 28, and 36 weeks
Number of IPTp doses, median (IQR)	2 (2-3)
Microscopy positivity at enrolment, %	42%
Birth outcomes	
Foetal Loss	Available (nne observed)
Small-for-Gestational Age	Infant sex not collected
Preterm Delivery	Available [†]
Low Birthweight	Available
Neonatal Death	Available (none observed)
Continuous Birth Outcomes	
Mean Birthweight	Available
Mean Gestational Age at Delivery	Available [†]
Mean Birthweight-for-Gestational Age Z-scores	Infant sex not collected
Malaria Outcomes	
Incidence of Clinical Malaria Episodes in Pregnancy	Not collected
Any Evidence of Pigment Only in Placental Tissue by Histopathology	Available
Any Evidence of Parasites in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Available; Testing of placental blood for parasitemia not done
Any Evidence of Parasites or Pigment in Placental Tissue or Blood by Histopathology, PCR, Microscopy, or RDT	Available; Testing of placental blood for parasitemia not done
Any Evidence of Parasites in Maternal Peripheral Blood at Delivery by RDT, Microscopy, or PCR	Available; Testing by microscopy only
Maternal Outcomes	
Any Evidence of Severe Anaemia (Hb <7 g/dl) During Pregnancy	Not collected

Study Information	Okoro et al ²²
Any Evidence of Moderate Anaemia (Hb <9 g/dl) During Pregnancy	Not collected
Any Evidence of Mild Anaemia (Hb <11 g/dl) During Pregnancy	Not collected
MUAC at Delivery	Not collected
Maternal weight gain per week [‡]	Not collected
Infant Outcomes	
Any Evidence of Stunting (LAZ <2 SD) from Birth to 2 Months of Life	Not collected
Any Evidence of Underweight (WAZ <2 SD) from Birth to 2 Months of Life	Not collected
Any Evidence of Wasting (WLZ <2 SD) from Birth to 2 Months of Life	Not collected
Mean LAZ at 2 Months of Life	Not collected
Mean WAZ at 2 Months of Life	Not collected
Mean WLZ at 2 Months of Life	Not collected

Abbreviations: ANC = antenatal care visit; Hb = haemoglobin; IQR = interquartile range; LAZ = length-for-age z-score; MUAC = mid-upper arm circumference; WAZ = weight-for-age z-score; WLZ = weight-for-length z-score

* Prevalence of polymorphisms were taken from another study from a neighboring site.²³

† Gestational age dating not confirmed by ultrasound

‡ Maternal weight gain per week calculated using the following formula:

 $Weight_{last ANC visit before delivery} - Weight_{enrollment}$

of weeks between enrollment and last ANC visit

Figure S-30. Birth outcomes

Results from Okoro et al, 2023 tria

Binary	Birth	Outcomes
		outcomes

	Prevaler	nce, n/N (%)		DP:SP Summary	Estimate	gravidity
Birth Outcomes	DP	SP		RR [95% CI]	p-value	Pinteraction
Any composite adverse pregnancy outcome	_∋ 9/106 (8·5%)	12/91 (13·2%)		0.64 [0.28, 1.46]	0.29	0.83
(foetal loss, preterm birth, SGA, LBW, neonatal death)	2/38 (5·3%)	2/30 (6.7%)	•	0.79 [0.12, 5.28]	0.81	
	7/68 (10·3%)	10/61 16·4%)		0.63 [0.25, 1.55]	0.31	
Eastal loss	0/106 (0%)	0/91 (0%)				
(miscarriage, abortion, or	0/38 (0%)	0/30 (0%)				
stillbirth)	0/68 (0%)	0/61 (0%)				
Small-for-gestational age						
(<10 th percentile for birthweight-for-gestational age) ¹						
Distance Dista	4/106 (3·8%)	5/91 (5·5%)	•	0.69 [0.19, 2.48]	0.57	
Preterm Birth (<37 gestational weeks)	0/38 (0%)	0/30 (0%)				
	4/68 (5.9%)	5/61 (8·2%)	•	0.72 [0.20, 2.55]	0.61	
	8/106 (7·5%)	12/91 (13·2%)	-	0.57 [0.24, 1.34]	0.20	0.72
Low Birthweight	2/38 (5·3%)	2/30 (6.7%)	•	0.79 [0.12, 5.28]	0.81	
(<2000 grams)	6/68 (8.8%)	10/61 (16·4%)	-	0.54 [0.21, 1.39]	0.20	
Neonatal Death	0/106 (0%)	0/91 (0%)				
(death within the first 28 days of life)	0/38 (0%)	0/30 (0%)				
	0/68 (0%)	0/61 (0%)				
			0·2 0·5 1·0 1·5 2·0 2 DP Better ↔ SP Better	5 3.0		

Continuous Birth Outcomes²

	N, N	/lean (SD)		SP:DP Summary	/ Estimate	gravidity
Outcome	DP	SP		MD [95% CI]	p-value	Pinteraction
Mean newborn birthweight in grams	106, 3078 (502) 38 (3137 (447) 68, 3045 (531)	91, 3012 (589) 30, 3080 (381) 61, 2978 (668)	-200 -100 0 100	-66 [-218, 86] -57 [-258, 143] -66 [-274, 141]	0·40 0·58 0·53	0.96
Mean gestational age at birth in weeks	106, 39 (1·6) 38, 39 (1·4) 68, 39 (1·7)	91, 39 (1·4) 30, 39 (0·9) 61, 39 (1·6)	-1·0 -0·5 0 0·5 1· DP Better ↔ SP Better	-0·08 [-0·51, 0·34] 0·09 [-0·48, 0·66] -0·11 [-0·67, 0·46] 0	0·51 0·75 0·71	0.66
		- Overall	🔶 Primigravidae 🔸 Multigravida	le		

Abbreviations: Cl=confidence interval; DP=dihydroartemisinin-piperaquine; MD=mean difference; RR = relative risk ratio; SD=standard deviation; SP=sulfadoxine-pyrimethamine ¹ Did not collect infant sex variable used to determine birthweight percentiles for gestational age ² Birthweight-for-gestational age z-scores missing due to unknown infant sex

Figure S-31. Malaria Outcomes

	Prevalen	ce, n/N (%)	DP:SP Summ	ary Estimate	aravidity
Malaria Outcomes	DP	SP	RR [95% CI]	p-value	Pinteraction
Incidence of clinical malaria					
episodes during pregnancy			-		
	35/75 (49·3%)	28/71 (39·4%)	1.25 [0.87, 1.81] 0.23	0.038
Any evidence of pigment only	16/27 (59·3%)	6/24 (25%)	2·37 [1·11, 5·07] 0.026	
histopathology	21/48 (43.8%)	22/47 (46·8%)	0.93 [0.60, 1.45] 0.77	
Any evidence of parasites in	31/106 (29·2%)	20/91 (22%)	1.33 [0.82, 2.17] 0.25	0.82
placental tissue or blood by histopathology, PCR, microscopy, or RDT	11/38 (28.9%)	6/30 (20%)	1.45 [0.61, 3.46] 0·41	
	20/68 (29.4%)	14/61 (23%)	1.28 [0.71, 2.31] 0.41	
Any evidence of parasites or pigment in placental tissue or blood by histopathology, PCR, microscopy, or RDT	68/106 (64·2%)	48/91 (52.7%)		j] 0·11	0.053
	27/38 (71.1%)	12/30 (40%)	1.78 [1.10, 2.88	3] 0.020	
	41/68 (60·3%)	36/61 (59%)	1.02 [0.77, 1.36	i] 0·88	
Any evidence of parasites	81/106 (76·4%)	61/91 (67%)	1.14 [0.95, 1.36	·] 0·15	0.087
in maternal peripheral	27/38 (71.1%)	23/30 (76.7%)		·] 0·60	
microscopy, or PCR	54/68 (79.4%)	38/61 (62.3%)	1.27 [1.01, 1.60	0.038	
			·2 0·5 1·0 1·5 2·0 2·5 3·0 DP Better ↔ SP Better		

Results from Okoro et al, 2023 trial²²

Abbreviations: Cl=confidence interval; DP=dihydroartemisinin-piperaquine; PCR=polymerase chain reaction; RDT=rapid diagnostic test; RR=relative risk ratio; SP=sulfadoxine-pyrimethamine ¹ Outcome not collected

Appendix 10. Appendix References

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