

# Short birth interval predicts the risk of preterm birth among pregnant women in Sub-Saharan Africa: A systematic review and meta-analysis

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## Research article

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## Abstract

**Background:** World health organization recommends that women wait at least 2 years after a live birth to reduce the risk of adverse birth outcomes, like preterm birth, in the subsequent pregnancy. However, studies have reported inconsistent finding regarding short birth interval as risk factor for preterm birth. Therefore, the aim of this systematic review and meta-analysis is to summarize and estimate the pooled effect of short birth interval on preterm birth among pregnant women with previous live birth.

**Methods:** The search strategy aimed to find both published and unpublished studies. The search was conducted from MEDLINE/PubMed, EMBASE, CINAHL, Web of science, MedNar, Google, Google scholar and African Journals online (AJOL). Observational studies which reported the association between short birth interval and preterm birth were included. The methodological quality of selected papers was assessed by two independent individuals prior to their inclusion in the review using standardized Joanna Briggs Institute (JBI) quality assessment tools. The analysis was done using RevMan software. A random effect meta-analysis was used to estimate the pooled effect with a 95% confidence interval. Forest plot was used to visualize the presence of heterogeneity. Funnel plot was used to check for publication bias.

**Results:** From a total of 234 published and unpublished studies identified, 10 studies that were conducted from 2015 to 2019 in Sub-Saharan African countries were included in the analysis. The meta-analysis result showed that Short birth interval had significant effect on preterm birth. The odds of having preterm birth was 2.21 times higher (OR = 2.21, 95% CI = 1.53, 3.21) among pregnant women with short (less than 2 years) birth interval compared to their counter parts. The sub-group analysis showed that the case-control studies showed statistically significant association between short birth interval and preterm birth, but not the cohort studies.

**Conclusion:** Based on our review findings we may recommend that health planner or clinical practitioners should counsel or educate women, considering the health and economic consequence of premature birth, to increase birth interval to at least two years.

## Background

Preterm birth (infant born before 37 completed weeks of gestation) remains a major contributor to infant mortality and morbidity including neurodevelopmental delay and childhood disability among survivors (1). Of the estimated 12.9 million preterm births worldwide approximately 85% occur in Africa and Asia. As a result of this, preterm birth is the major contributor for neonatal morbidity and mortality in those developing countries (2). Globally, of the estimated 4 million neonatal deaths, preterm and low-birth-weight babies represent more than a fifth(3). Studies have indicated that preterm births are associated with previous premature delivery, birth interval (the length of time between pregnancies), preeclampsia or eclampsia, premature membrane rupture, fewer antenatal care visit, multiple pregnancies, low income, less educated, maternal advanced age and conceived with assisted reproductive technology (4, 5).

Prematurity is the leading cause of neonatal death worldwide, with most deaths occurring in low- and middle-income countries (LMICs) of Asian and Sub-Saharan African countries; therefore, preventing premature birth among population of LMICs might help to address disparities(6).

Preterm birth becomes a public health priority to prevent because of its contribution to infant and childhood morbidity and mortality (7). Preterm infants are particularly vulnerable to complications due to impaired respiration, difficulty in feeding, poor body temperature regulation and high risk of infection (8, 9). Evidence has shown that birth interval between pregnancies has been identified as a potentially modifiable risk factor for adverse birth outcome (10).

The world health organization (WHO) recommends that women wait at least 2 years after a live birth to reduce the risk of adverse birth outcomes in the subsequent pregnancy(11). However, studies have reported inconsistent finding regarding short birth interval as risk factor for preterm birth. Studies conducted in Turkey and China revealed that pregnancy interval of two years or shorter does not increase the risk of preterm birth (12, 13).

In the sustainable development goals (SDG) era, countries are advised to prioritize and enhance efforts to scale up proven life-saving interventions based on their child cause-of death composition to achieve the SDG child survival targets (14). The research question in our review is: "Does short birth interval predict the risk of preterm birth in pregnant women?". Before we initiated this review study, we checked and ruled out that there was no ongoing or recently published review on the topic in Cochrane and Joanna Briggs Institute (JBI) libraries, and other online journals. Therefore, aim of our review was to summarize and pool estimates reported from studies about relationship between birth interval and preterm birth in pregnant women with a previous alive birth.

## Methods

### Protocol and registration

The review protocol was published on PROSPERO and can be accessed through [www.crd.york.ac.uk/prospero/display\\_record.dhp?ID=CRD42019147146](http://www.crd.york.ac.uk/prospero/display_record.dhp?ID=CRD42019147146). The Cochrane RevMan software was used to write this report and to do the necessary analysis.

### Search methods for identification of studies

Our search strategy aimed to find both published and unpublished studies. We followed a three-step search strategy. An initial limited search of MEDLINE/PubMed, EMBASE, CINAHL, Web of science, Cochrane library and JBI library was undertaken followed by an analysis of the text words contained in the title and abstract, and of the index terms used to describe articles. A second search using all the identified keywords and index terms was then undertaken across all included databases and grey literature sources. Thirdly, the reference lists of all identified studies retrieved for critical appraisal were searched for additional studies. The search for unpublished studies included: Google, MedNar, Google scholar, African Journals online, and conference proceedings.

Studies published in the English language, and conducted in Sub-Sahara African countries, were included. Initial keywords used were: short birth interval or short birth spacing; preterm or premature birth; pregnant women.

Comprehensive literature search was done three times at least 2 months apart. The last search was done on January 31/2020. The search was mainly done using the following terms or phrases: The following search strategies, used for PubMed, were modified for the various databases using the two important Boolean operators (OR, AND) (table 1).

**Table 1:** Search strategies used for PubMed and other various databases for the current systematic review and meta-analysis, January 31/2020.

	Population	Intervention or Exposure	Outcome
	<b>Pregnant women</b>	<b>Short birth interval</b>	<b>Preterm birth</b>
Search terms: Indexed or key words	"pregnant women"[MeSH Terms]	"birth interval"[MeSH Terms]	"premature birth"[MeSH Terms]
	OR	OR	OR
	"pregnant women"[Title/Abstract]	"inter pregnancy interval"[Title/Abstract]	AND "premature birth"[Title/Abstract]
	OR	AND OR	OR
	"pregnant woman"[Title/Abstract]	"pregnancy spacing"[Title/Abstract]	OR
		OR	"preterm birth"[Title/Abstract]
		"pregnancy interval"[Title/Abstract]	OR
		OR	"preterm infant"[Title/Abstract]
		"birth spacing"[Title/Abstract]	OR
		OR	"premature infant"[Title/Abstract]
		"short birth interval"[Title/Abstract]	OR
		OR	"preterm delivery"[Title/Abstract]
		"short birth spacing"[Title/Abstract]	
		OR	
		"short inter pregnancy interval"[Title/Abstract]	
		OR	
		"short pregnancy interval"[Title/Abstract]	

### Types of study included

Our review considered prospective and retrospective cohort studies, case control studies and analytical cross-sectional studies examining the association between short birth intervals and preterm births.

### Condition or domain being studied

Preterm birth, defined as being born alive before 37 completed weeks of gestational age.

### Participants/population

Multiparous women for whom there is information on the length of the birth interval between two consecutive births in sub-Saharan African countries.

### Intervention(s), exposure(s)

Short birth intervals as a predictor for the risk of preterm birth in pregnant women.

Birth interval: defined as the time elapsed between the date of birth of the preceding infant and the date of birth of the current consecutive infant/sibling. Short birth interval: defined as less than 24 months (< 24 months) between two consecutive births.

### Comparator(s)/control

Optimal birth interval (the time elapsed between two consecutive births is two or more years).

## Context

Our review considered only studies conducted in sub-Saharan African countries (15).

**Main outcome(s):** Preterm birth.

## Timing and effect measures

We extracted information on raw data for shorter birth intervals and preterm birth from included studies.

## Study selection, quality assessment and data extraction

We used EndNote version X8 reference management software to combine database search results and to remove duplicate articles. The studies retrieved from the searches were screened for relevance based on title and abstract, and those identified as being potentially eligible were fully assessed against the inclusion/exclusion criteria. The papers selected for retrieval were assessed by two independent reviewers for risk of bias or methodological validity prior to their inclusion in the review using **standardized Joanna Briggs Institute (JBI) quality assessment tools** for analytical cross-sectional, case control and cohort studies and there was 90% observed agreement between assessors. Disagreements between assessors were resolved through discussion. Reasons for exclusion of the studies was explained and recorded. PRISMA flow diagram was used to show the process of selection and inclusion of the studies (16). Data were extracted from the papers selected for inclusion in the review using data extraction tool which was prepared using Microsoft excel sheet. The data extraction tool included: data on birth interval (shorter and optimal), primary author name, publication year, study design, study setting, sample size and outcome measures (preterm birth and term birth).

## Strategy for data synthesis

Data from the included studies were summarized in a table. All analyses were conducted using RevMan 5.3 software. A random-effects meta-analysis was performed to compute pooled estimates of short birth interval effects on preterm birth with a 95% confidence interval. The magnitude of heterogeneity was estimated using the  $I^2$  statistic, and heterogeneity was considered significant at a P-value of less than 0.1. Heterogeneity was further investigated using subgroup analyses, and, in addition, sensitivity analyses was carried out to determine the impact of study quality on the results.

Publication bias was assessed by visual inspection of funnel plot of proportion against its standard error, for plot symmetry.

## Analysis of subgroups or subsets

To investigate heterogeneity, subgroup analyses was carried out for study setting (Ethiopia, Kenya, Tanzania and Ghana) and study design type (cohort, case-control and cross-sectional). In addition, sensitivity analyses were carried out to investigate the influence of single studies on the overall estimate obtained.

# Results

## Selection and identification of studies

A total of 234 published and unpublished studies were identified that were conducted from 2015 to 2019 in Sub-Saharan African countries. Of the identified studies, 57 duplicate studies were removed and 126 studies were excluded after reviewing the title and abstracts due to non-relevant title for the current review. The full text of 51 studies were assessed for eligibility and for the report of exposure and outcome of interest. Of these, 8 studies were excluded due to not reported exposure of interest, and 33 studies were excluded due to they failed to meet eligibility criteria, like different exposure definition and outcome, and settings. The quality of included studies was assessed using the Joanna Briggs Institute quality assessment tool for observational studies(17). All of the ten studies scored greater than 5 out of 8-11 criteria and rated them as good quality. Of the three cross-sectional studies, two studies scored 5 and the other scored 6 out of eight criteria, and five of the case-control studies scored 10 out of ten criteria, and both of the cohort studies scored 10 and 11 out of eleven criteria (figure 1).

## Included study Characteristics

A total of 10 studies that assessed the association of short birth interval with preterm birth in Sub-Saharan African countries were included in this review. Five of the included studies were conducted in Ethiopia (18-22), two in Tanzania (23, 24), two in Kenya(25, 26), and one in Ghana (27). Of the ten studies two were cohort study(20, 24), five case-control (18, 21-23, 27) and three cross-sectional (19, 25, 26). In this systematic review and meta-analysis, a total of 19938 women with preterm birth were included. The sample size ranged from 145 (minimum) in study conducted in Ethiopia (21) and 17,030 (maximum) in study conducted in Tanzania (24) (table 2).

**Table 2:** Characteristics of included studies in the current systematic review and met-analysis from 2015-2019.

Study No	Study ID	Study location	Study design	sample size	Number < 2 yrs. BI with outcome	Number >=2 yrs. BI with outcome	Total number of < 2 yrs. BI	Total number of >= 2 yrs. BI	1	Abaraya 2018 (18)	Ethiopia	Case control	656	105
2	Bekele 2015(19)	Ethiopia	Cross sectional	278	19	19	81	197						
3	Brhane 2019(20)	Ethiopia	Cohort study	460	39	9	152	308						
4	Fanaka 2016(23)	Tanzania	Case control	465	72	165	106	359						
5	Mahande 2016(24)	Tanzania	Cohort study	17,030	416	1291	3309	13721						
6	Okube 2017(26)	Kenya	Cross sectional	327	6	24	14	133						
7	Teklay 2018(21)	Ethiopia	Case control	145	3	43	8	137						
8	Wagura 2018(25)	Kenya	Cross sectional	163	2	33	16	147						
9	Woday 2019(22)	Ethiopia	Case control	206	26	51	49	157						
10	Aseidu 2019(27)	Ghana	Case control	388	63	67	174	214						

### Effect of short birth interval on preterm birth among pregnant women

From this meta-analysis we may conclude that the ten studies had significant heterogeneity ( $I^2 = 82\%$ ,  $P$  value  $< 0.00001$ ) in estimating the real value of short birth interval on preterm birth. So, we used the random effect meta-analysis model to estimate the appropriate average value of short birth interval on preterm birth. The meta-analysis result showed that Short birth interval had significant effect on preterm birth. The odds of having preterm birth was 2.21 times higher ( $OR = 2.21$ ,  $95\% CI = 1.53, 3.21$ ) among women who had history of short (less than 2 years) birth interval compared to women with optimal or higher birth interval (figure 2).

### Publication Bias assessment

The risk of publication bias was assessed using funnel plots. The funnel plot seems a symmetry (figure 3).

### Sub-group analysis by study settings

To further assess the source of heterogeneity, we conducted sub-group analysis by study location. The analysis showed that studies conducted in Kenya did not show statistically significant association between short birth interval and preterm birth. Studies conducted in Tanzania showed weaker association between short birth interval and preterm birth compared to studies conducted in Ethiopia. The odds of having preterm birth among pregnant women with short birth interval was 3.13 and 1.78 times higher compared to pregnant women with longer birth interval in the Ethiopia and Tanzania studies with odds ratio of 3.13 ( $95\%CI: 1.71, 5.76$ ) and 1.78 ( $95\% CI: 1.01, 3.14$ ) respectively (figure 4).

### Sub-group analysis by study design

In addition, we conducted sub-group analysis by the type of study design. The analysis showed that the cohort and cross-sectional studies did not show statistically significant association between short birth interval and preterm birth, but the case-control studies showed statistically significant association between short birth interval and preterm birth. The odds of having preterm birth was approximately two times higher among pregnant women with short birth interval compared to pregnant women with longer birth interval in the case-control studies with odds ratio of 1.96 ( $95\%CI: 1.45, 2.65$ ) (figure 5).

### Sensitivity analysis

We conducted sensitivity analysis to investigate the influence of single studies on overall estimate obtained ( $OR = 2.21$ ;  $95\%CI: 1.53, 3.21$ ). In our sensitivity analysis the overall estimate odds ratio 2.21 decreased to 1.70 ( $OR = 1.70$ ;  $95\%CI: 1.28, 2.27$ ) when two of the cross-sectional and one of cohort studies, which scored less during methodological quality assessment, were removed from the primary meta-analysis (figure 6).

## Discussion

The world health organization (WHO) recommended at least 24 months interval between a live birth and next pregnancy in order to reduce the risk of adverse maternal, perinatal and infant outcomes(28).

The current meta-analysis showed that short birth interval is significantly associated with higher risk of preterm birth. The odds of having preterm birth among pregnant women was approximately two times higher among women with short birth interval compared to pregnant women with longer birth interval. The finding in the current review was consistent with a systematic review study which revealed that short intervals between a live birth and next pregnancy were

associated with neonatal and perinatal mortality, preterm delivery and low birth weight. The possible explanation could be women with short birth interval may have risk of maternal nutrition depletion, folate depletion, cervical insufficiency, incomplete healing of uterine scar and abnormal remodeling of endometrial blood vessels, anemia and increasing the risks of certain other factors(29).

The current review also revealed that short birth interval was statistically significant associated with preterm birth in case control studies and in studies conducted in Ethiopia, but short birth interval was not associated with preterm birth in cross sectional and cohort studies. The possible explanation could be the sample inadequacy in some of studies like in cross sectional and in one of cohort studies, and variability in gestational age estimation and variability in study participant selection either from urban only or rural and urban, and difference in controlling confounder factors, data sources and minimizing recall bias in the studies.

Some of the strength of our systematic review and meta-analysis are comprehensive search of published and unpublished literatures through major databases, critical appraisal of the included studies using standardized tools and application of appropriate meta-analysis model to pool the estimate. However, lack of literatures from majority of sub-Saharan African countries, sample inadequacy in some of included studies and not addressing the potential confounders might affect the generalizability of our finding for all sub-Saharan Africa countries pregnant women population.

## Conclusion

From current review findings we concluded that short birth interval was statistically significantly associated with preterm birth; however, the association of short birth interval and preterm birth varies among the type of design used and the location of the study conducted.

Based on our review findings we may recommend that health planner or clinical practitioners should counsel or educate women to increase birth interval to at least 2 years considering the health and economic consequence of premature birth. More over quality longitudinal studies are beneficial to further explore the effect of short birth interval on preterm birth in particular, and neonatal and perinatal outcome in general so as to come up with a high-quality evidence for decision making.

## List Of Abbreviations

LMICs: Low-and Middle-Income Countries; WHO: World Health Organization; SDG: Sustainable Development Goals; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; JBI: Joana Briggs Institute.

## Declarations

### Ethics approval and consent to participate

Not applicable.

### Consent for publication

Not applicable.

### Availability of data and materials

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

### Funding

No source of funding.

### Authors' contributions

SM conceived the study, developed the methods, did literature search and meta-analysis and wrote the first draft of the manuscript. EG, DB, CG, AW and MA supervised, reviewed and edited the report. All authors read and approved the final manuscript.

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## Figures

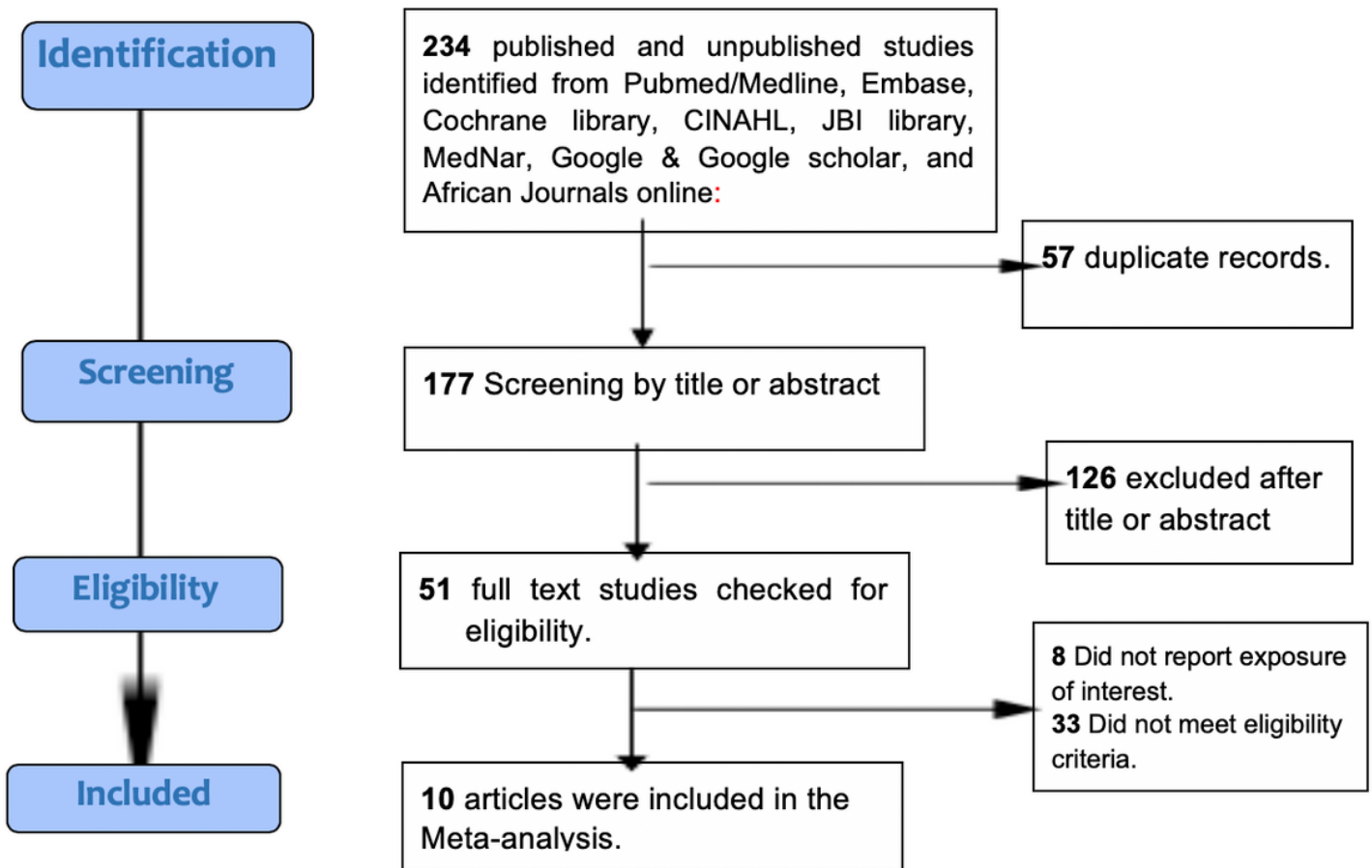


Figure 1

The PRISMA flow diagram of the search and study inclusion process.

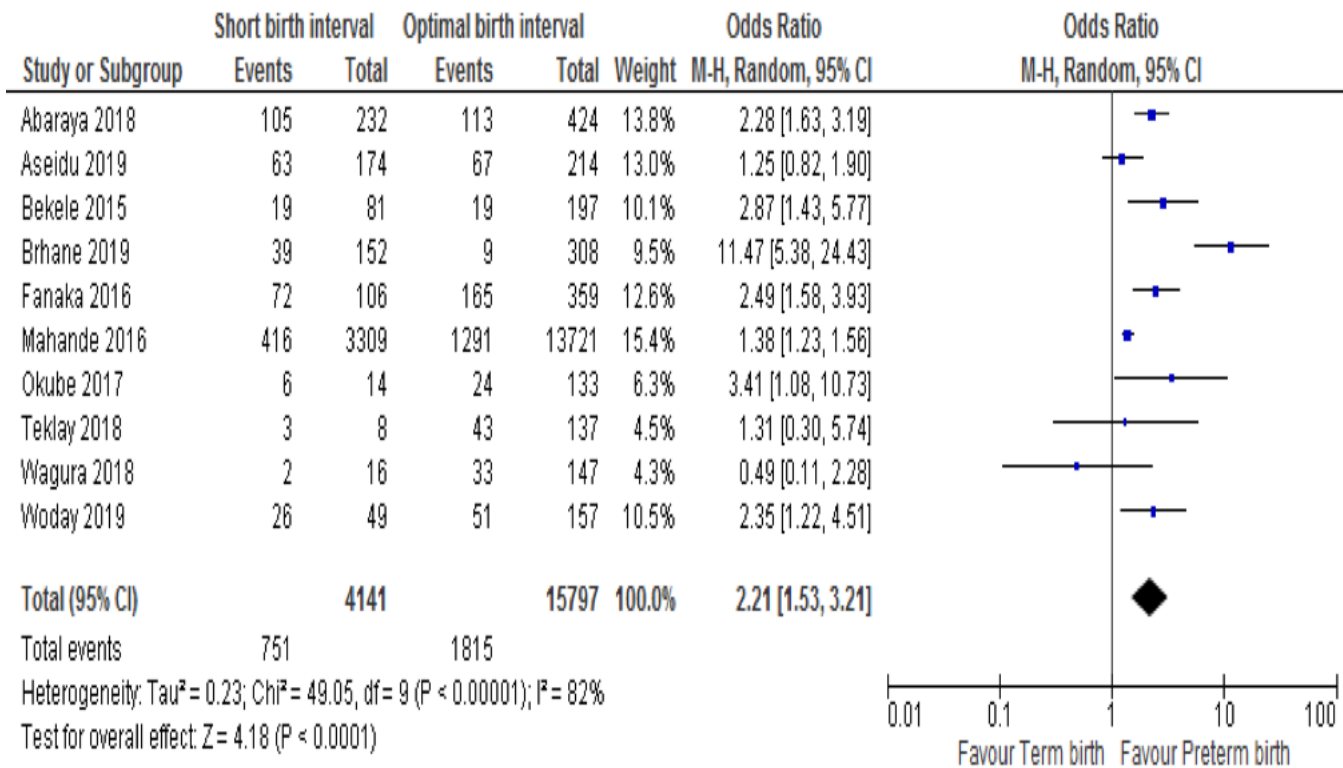




Figure 2

Forest plot of the pooled effect of short birth interval on preterm birth among pregnant women in Sub-Saharan African countries from 2015-2019.

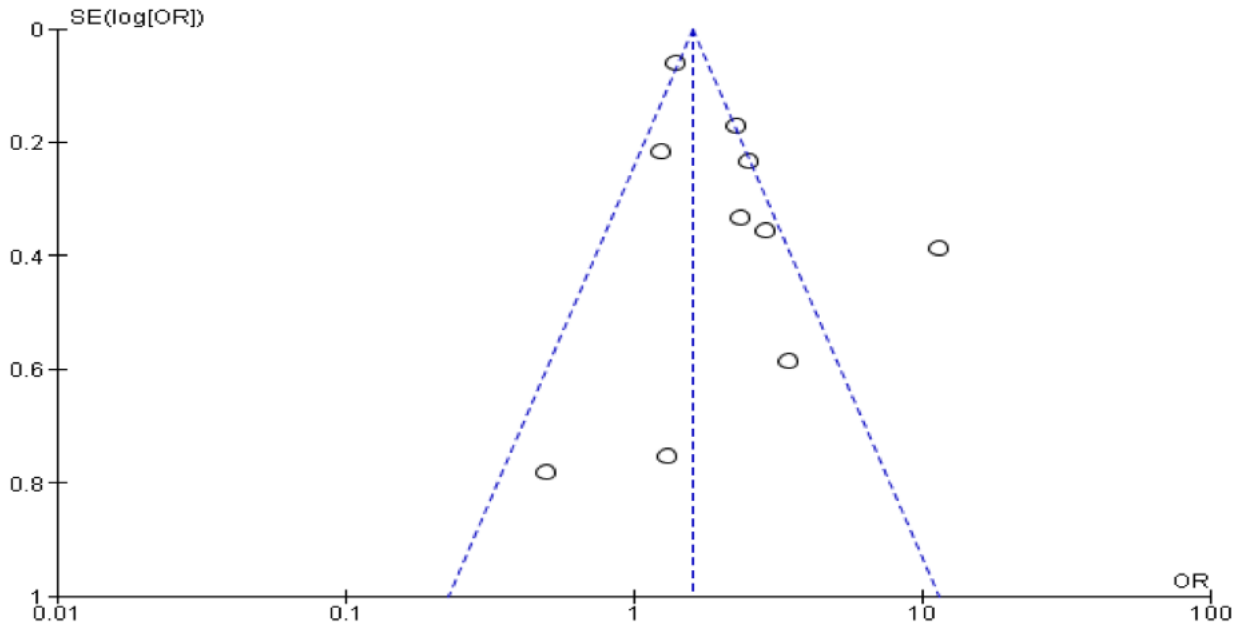


Figure 3

Funnel plot of publication bias of effect of short birth interval on preterm birth among pregnant women in sub-Saharan countries from 2015-2019.

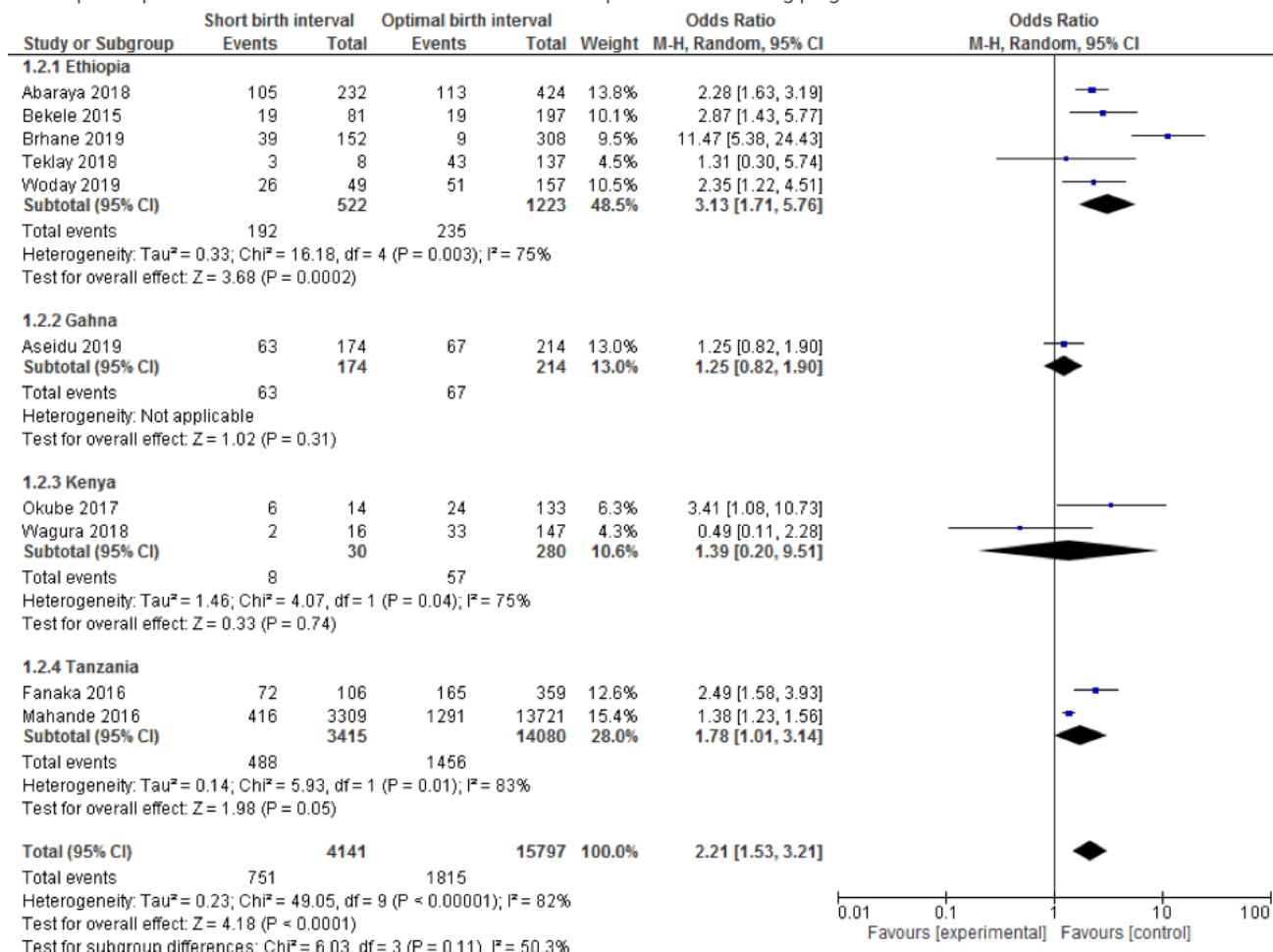


Figure 4

Sub-group analysis of the effect of short birth interval on preterm birth among pregnant women by study country from 2015-2019.

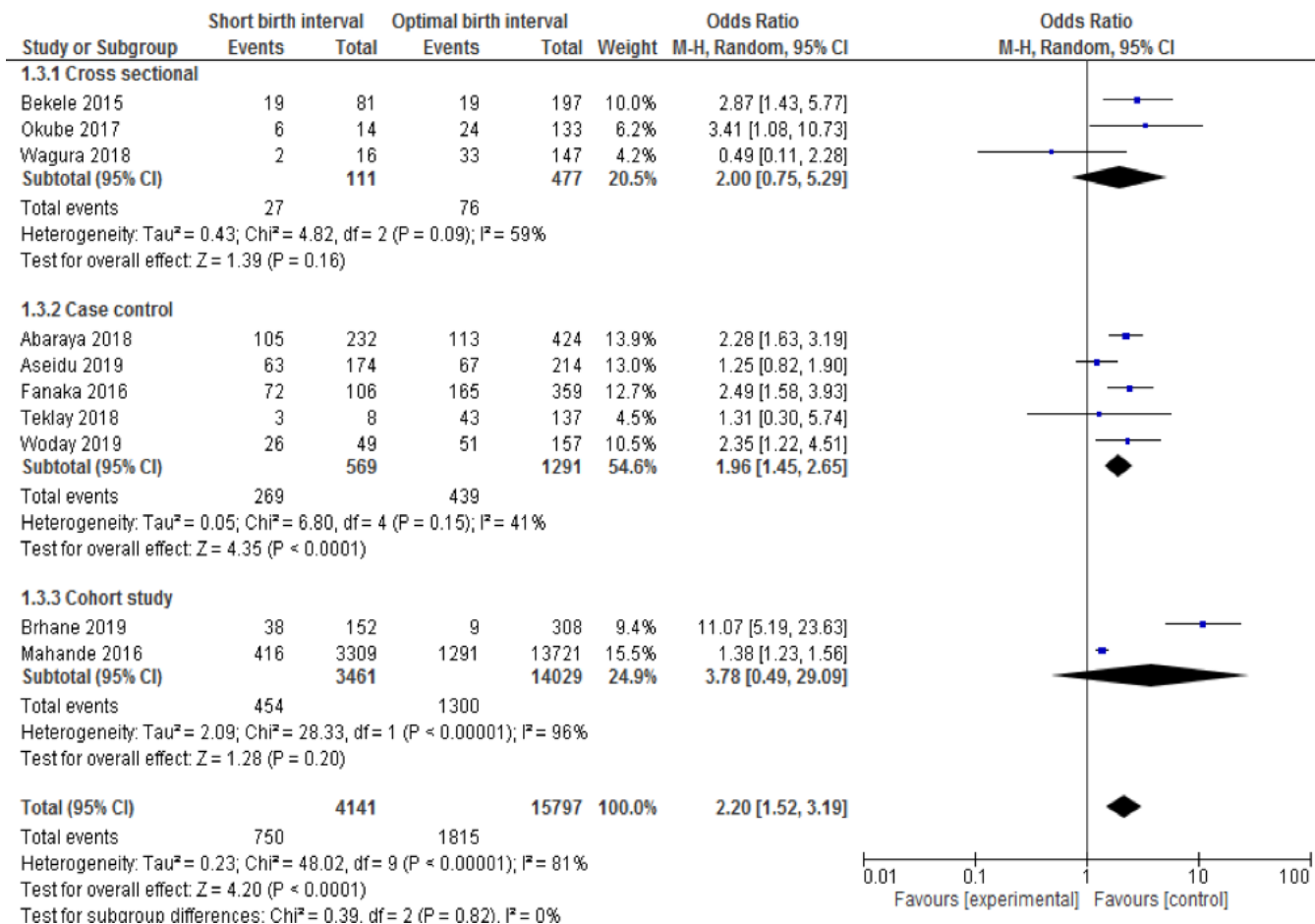


Figure 5

Sub-group analysis of the effect of short birth interval on preterm birth among pregnant women by study design from 2015-2019.

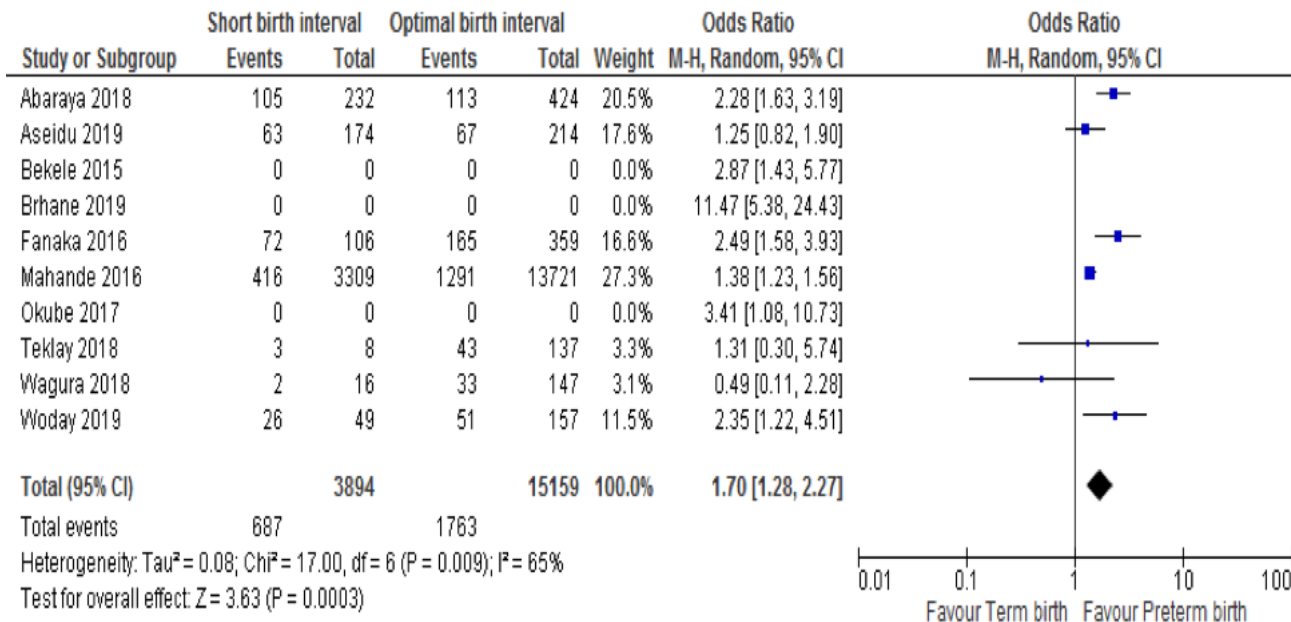


Figure 6

Sensitivity analysis of two cross sectional and one cohort studies influence on overall estimate of effect of short birth interval on preterm birth among pregnant women from 2015-2019.