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The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia

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Abstract

Objective To assess the effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia.

Design A nationally representative cross-sectional survey.

Setting This study used data from the Ethiopia Demographic and Health Survey (EDHS) 2016.

Participants A total of 8,448 women who had at least two live births during the five years preceding the survey were included in the analysis.

Outcome measures Neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months) were the outcome variables.

Methods Weighted logistic regression analysis based on inverse probability of treatment weights (IPTW) was used to estimate exposure effects adjusted for potential confounders.

Results The adjusted odds of neonatal mortality were about 50% higher among women with short birth interval (AOR=1.53, 95% CI= 1.13, 2.09) than those without. The odds of infant mortality were nearly two-fold higher (AOR=1.94, 95% CI= 1.39, 2.70) among women with short birth interval. The odds of under-five child mortality were also about two-fold higher (AOR=2.02, 95% CI= 1.48, 2.74) higher among women with short birth interval.

Conclusion Short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions targeting short birth interval are warranted to reduce neonatal, infant, and under-five mortality.

Introduction

Short birth interval, defined as a birth-to-birth interval of less than 33 months,[1] is a key public health problem with an estimated prevalence of 45.8% in Ethiopia.[2] Previous studies[2-4] have revealed the multifactorial nature of short birth interval, its spatial variation, and socioeconomic inequality in Ethiopia. Only about one-third of women in Ethiopia use modern contraceptives, which can prevent short birth interval.[5] Literature has also shown the effects of short birth interval may include, but are not limited to, preterm birth,[6 7] low birth weight,[6 7] small size for gestational age,[6] congenital anomalies,[8 9] autism,[10] miscarriage, preeclampsia, and premature rupture of membranes.[11 12]

Neonatal, infant, and under-five mortality are defined as the death of a child within 28 days of birth, before the age of 1 year, and before five years, respectively.[5] These mortality outcomes are regarded as a highly sensitive (proxy) measure of population health, a country's poverty and socioeconomic development status, and the availability and quality of health services and medical technology.[13 14]

The Sustainable Development Goal (SDG) 3.2 states that all countries should aim to reduce the neonatal mortality rate (NMR) to 12 deaths per 1000 live births or fewer, and reduce under-five mortality to 25 deaths per 1000 live births or fewer, by 2030.[15] The Growth and Transformation Plan of Ethiopia (GTPE) II also targets reductions in neonatal, infant, and under-five mortality rates, from 28 per 1000 live births, 44 per 1000 live births, and 64 per 1000 live births in 2014/15 to 10, 20, and 30 per 1000 live births by 2019/20, respectively.[16] However, the 2016 Ethiopia Demographic and Health Survey (EDHS) report revealed that the neonatal, infant, and under-five mortality rates in Ethiopia were 29, 48, and 67 deaths per 1,000 live births, respectively: still much higher than GTPE targets.[5 16]

Literature from Ethiopia has shown that neonatal, infant, and under-five mortality are associated with maternal education,[17 18] lack of antenatal care,[19] home delivery,[20] preterm birth,[19 21] low birth weight,[20 21] multiple births,[17 19 22 23] sex of the child,[17 19 22-25] wealth status,[26 27] place of residence,[20 23 24] source of drinking water,[27] and lack of access to improved toilet facility.[28]

Although previous studies[17-19 23 24 27-31] have suggested birth interval as one factor influencing neonatal, infant, under-five mortality, these studies have several limitations. A key limitation is that these studies[17-19 23 24 27-31] did not use the World Health Organization (WHO) recommended[1] definition of short birth interval. Understanding the impact of short birth interval on neonatal, infant, and under-five mortality, using the WHO definition,[1] is necessary for the formulation of valid, consistent policies and health planning strategies and interventions to improve child health outcomes. Second, women who were not eligible to provide birth interval information (i.e., those who had given birth only once) were included in the analysis of some studies.[19 24 28] This may result in underestimation or obscuration of the true effect of birth interval on child mortality. Third, even among studies using the same definition of short birth interval, findings have been inconsistent.[19 24] One of the studies using national data[19] did not control for a range of potential confounders including maternal education, wealth status, number of children, and region of residence, even though these data were available in the datasets used for analysis. In addition, various studies did not consider short birth interval as a potential predictor of neonatal,[21 25 26 32-35] infant,[18 36 37] and under-five mortality[38-41] in their studies.

Generally, the effect of short birth interval, as per the most recent WHO recommendation,[1] on neonatal, infant, and under-five mortality has not been investigated in Ethiopia. Evidence regarding the effect of short birth interval is required for informed decision making by policy makers and health program planners. This paper aimed to assess the effect of short birth interval on neonatal, infant, and under-five mortality using the most recent WHO definition and adjusting for a comprehensive set of potential confounders.

Methods

Study design

This analysis used data from the Ethiopia Demographic and Health Survey (EDHS) 2016. The EDHS is a nationally representative cross-sectional study conducted in nine geographical regions (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations Nationalities and Peoples (SNNP), Gambela, and Harari) and two administrative cities (Addis Ababa and Dire Dawa). A two-stage, stratified, clustered random sampling design was employed to collect data from women who gave birth within the five years preceding the survey. Further descriptions of the sampling procedure for the EDHS are presented elsewhere.[5] A total of 8,448 women who had at least two live births during the five years preceding the 2016 survey were included in the analysis. When women had more than two births in the five years preceding the survey, the birth interval between the most recent index child and the immediately preceding child was considered for all the study participants.

Variables

Outcome variables

The outcome variables in the current study were neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months).[5 42] These outcomes were coded as binary variables (1/0).

Treatment/exposure variable

Short birth interval was the treatment variable and was defined as a birth-to-birth interval of less than 33 months as per the WHO definition.[1] Women's birth interval data were collected by extracting the dates of birth of their biological children from children's birth/immunization certificates, and/or requesting children's dates of birth from participating mothers. Further information regarding birth interval data collection is annexed (Supplementary Material I) and a detailed description is provided elsewhere.[2 3 43]

Control variables

After reviewing relevant literature,[2 17-20 22-24 27 28 38 44 45] Direct Acyclic Graphs (DAGs) were constructed using DAGitty 3.0[46] to identify confounders for the association between short birth interval and child mortality. Adjustment for such confounders is necessary to estimate the unbiased effect of SBI on neonatal, infant, and under-five mortality (figure 1). Identified confounders were maternal age at the birth of the index child, maternal education, maternal occupation, husband's education, husband's occupation, household wealth status, the total number of the preceding child, place of residence (urban/rural), administrative regions, access to media, and decision making autonomy. A list of all variables considered in the DAG is provided in Supplementary Material II.

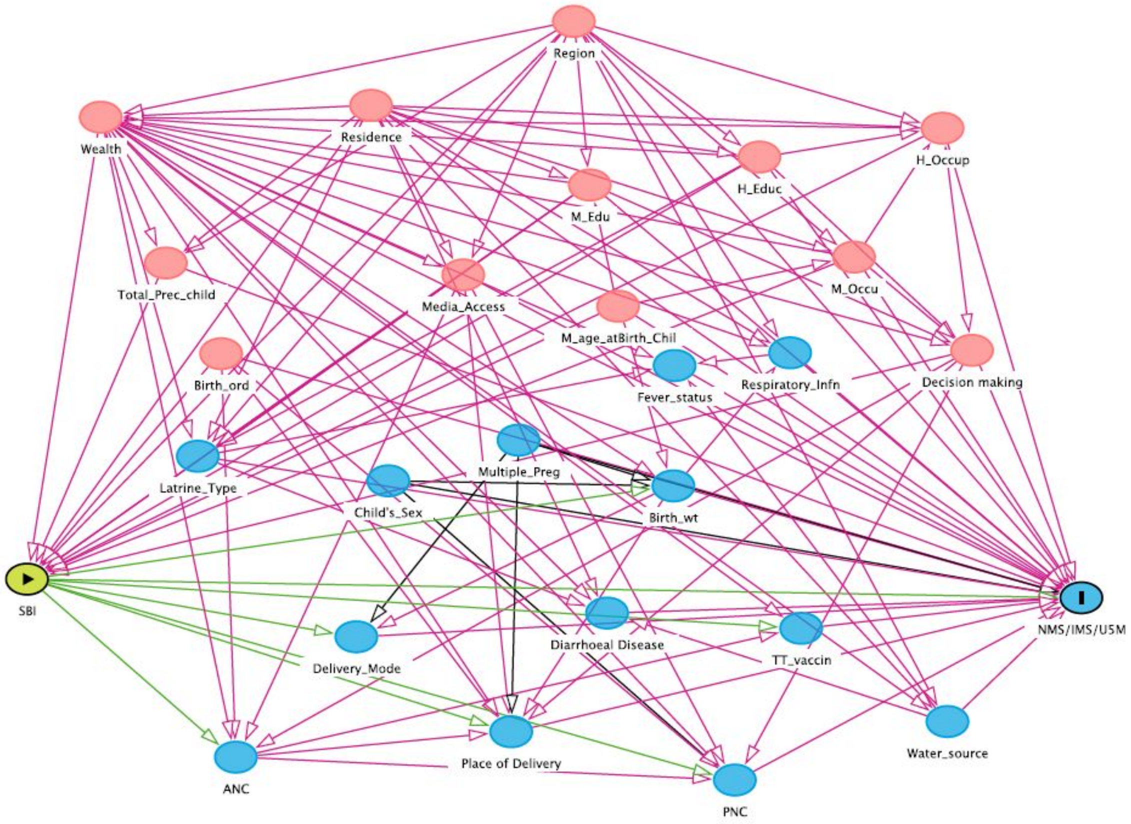

Figure 1 Direct Acyclic Graph (DAG) used to select controlling variables

A yellowish-green circle with a triangle at its centre indicates the main treatment/exposure variable, a blue circle with a vertical bar at its centre indicates the outcome variable, light red circles indicate ancestors of exposure and outcome (i.e., confounders). Blue circles indicate the ancestors of the outcome variable. Green lines indicate a causal pathway. Red lines indicate open paths by which confounding may occur; this confounding can be removed by adjusting for one or several variables on the pathway.

M_age_atBirth_chil= Maternal age at birth of the index child; M_Edu= Maternal education; M_Occu= Maternal Occupation; H_Educ= Husband education; Birth_wt=Birth weight; Respiratory_infn= respiratory infection; Multiple_preg= Multiple pregnancy; ANC=Antenatal care; PNC=Postnatal care; TT=Tetanus toxoid vaccination status; SBI= Short birth interval; NM=Neonatal mortality; IM=Infant mortality; U5M=Under-five mortal

Data analyses

Given the outcomes were relatively infrequent, the unbiased effect of short birth interval on each outcome was estimated using propensity scores (PS) with stabilized inverse probability of treatment weighting (IPTW). A propensity score is defined as the probability of treatment assignment given observed baseline covariates (described in Supplementary Material II).[47] Propensity scores are used to estimate treatment effects on outcomes using observational data when confounding bias due to non-random treatment assignment is likely.[48] Inverse probability of treatment weighting weights the entire study sample by the inverse of the propensity score;[49] a differential amount of information is used from each participant, depending on their conditional probability of receiving treatment. This means observations are less likely to be lost than when using matching for confounder adjustment.[50 51] Propensity scores are a robust alternative to covariate adjustment when the outcome variable is rare, resulting in data sparsity and estimation issues in multivariable models.[51] In this study, the weighted prevalence of the outcome variables of neonatal, infant, and under-five mortality were 2.9% (95% CI: 2.39, 3.61) 4.8% (95% CI: 4.11, 5.58), and 5.5% (95% CI: 4.73, 6.44), respectively.

The analysis procedure was as follows. First, the propensity score was estimated using a logistic regression model in which treatment assignment (short birth interval vs. non-short birth interval) was regressed on the 11 covariates identified using the DAG. The balance of measured covariates/confounders was then assessed across treatment groups (i.e., women with short birth interval) and comparison groups (i.e., women with non-short birth interval) before and after weighting, by computing standardized differences.[51 52] For a continuous covariate, the standardized difference[52 53] is defined as:

$$d = \frac{(\bar{x}_{treatment} - \bar{x}_{control})}{\sqrt{\frac{s^2_{treatment} + s^2_{control}}{2}}}$$

where $\bar{x}_{treatment}$ and $\bar{x}_{control}$ denote the sample mean of the covariate in treated and untreated subjects, respectively and $s^2_{treatment}$ and $s^2_{control}$ denote the corresponding sample variances of the covariate. The standardized difference[52 53] for a dichotomous variable is given as:

$$d = \frac{(\hat{p}_{treatment} - \hat{p}_{control})}{\sqrt{\frac{\hat{p}_{treatment}(1-\hat{p}_{treatment}) \quad + \quad \hat{p}_{control}(1-\hat{p}_{control})}{2}}}$$

where $\hat{p}_{treatment}$ and $\hat{p}_{control}$ denote the prevalence of the dichotomous variable in treated and untreated subjects, respectively.

A standard difference less than 0.1 has been suggested as indicating a negligible difference in the mean or prevalence of a covariate between treatment and control groups and was used here.[52] In addition, kernel densities were plotted to graphically demonstrate the propensity score balance in the treatment group (i.e., women with short birth interval) and control groups (women with non-short birth interval). Balance in propensity scores was considered to be achieved when the kernel density line for the treatment group and control group lay closer together.[54] The inverse probability of treatment weights was then calculated as 1/PS for those exposed to short birth interval and 1/ (1 − PS) for those who were not. The sample was then reweighted by the IPTW and the balance of the covariates checked in the reweighted sample.[48 55] Stabilization of weights was made to preserve the sample size of the original data, reduce the effect of weights of either treated subjects with low propensity scores or untreated subjects with high propensity scores, and provides appropriate improve the estimation of variance estimates and confidence intervals for the treatment effect.[56] Since the EDHS employed a two-stage, stratified, clustered random sampling, which is a complex sampling procedure, sampling weights were also used to adjust for the non-proportional allocation of sample participants to different regions, including urban and rural areas, and consider the possible differences in response rates.[5] Finally, a weighted logistic regression was fit to estimate the effect of the treatment (short birth interval) on the outcome variables (neonatal, infant, and under-five mortality). Estimation of the treatment effect on outcome variables in the final model used the grand weight, which was formed as the product of the survey weight and the stabilized weight. Literature has shown that combining a propensity score method and survey weighting is necessary to estimate unbiased treatment effects which are generalizable to the original survey target population.[57] The treatment effect on the outcome variables was expressed as adjusted odds ratios (AORs) with a 95% confidence interval (CI). Statistical analysis was performed using Stata version 14 statistical software *(StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. 2015)*. Figure 2 presents a schematic summary of the overall analysis procedure.

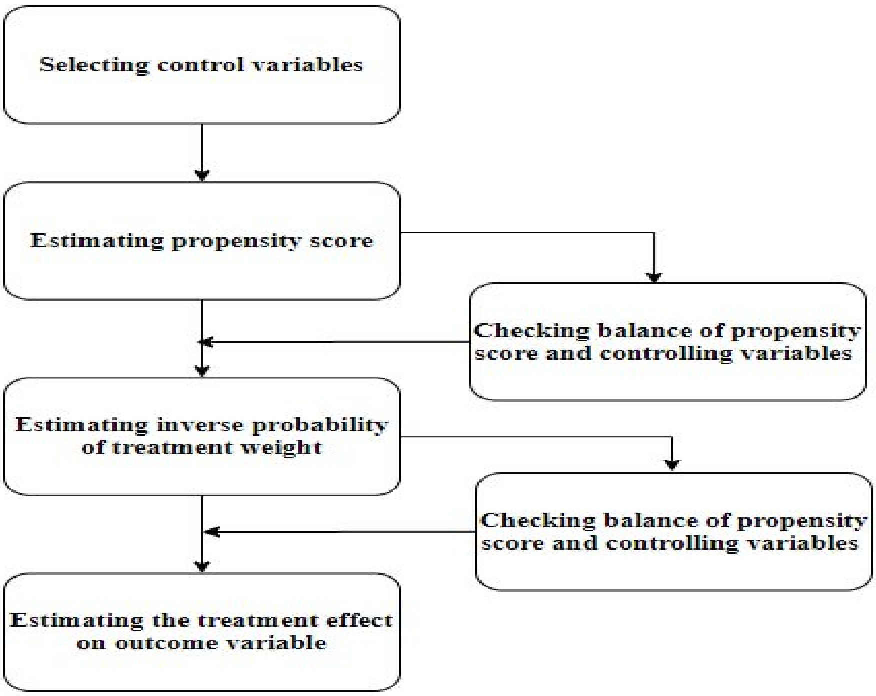

Figure 2 Schematic presentation of the overall steps followed in the analysis

Patient and public involvement

Patients and/or the general public were not involved in the design, or conduct, or drafting of this secondary analysis.

Results

Respondents' characteristics

Table 1 illustrates the baseline characteristics of the study participants.

The occurrence of neonatal mortality differed with maternal age at birth, with mortality rates being higher among mothers aged ≥35 ($p=0.021$). Neonatal mortality was also higher in rural than in urban areas ($p=0.004$). Similarly, infant mortality and under-five mortality were somewhat higher in rural areas ($p<0.001$). Under-five mortality was higher among uneducated mothers ($p=0.027$) and in mothers without access to mass media ($p=0.043$). Mortality at all ages was higher among infants with at least five siblings ($p<0.0001$). Both infant and under-five mortality had slightly higher rates among wealthier families, although numbers were small.

Table 1 The weighted distribution of neonatal, infant, and under-five child mortality by background characteristics, EDHS 2016

Variable	Neonatal Mortality		P-value	Infant Mortality		P-value	Under-five Mortality		P-value
	No (%)	Yes (%)		No (%)	Yes (%)		No (%)	Yes (%)	
Maternal age at the birth of the index child (in years)									
≤19	291 (3.2)	17 (5.8)	0.021	283 (3.1)	25 (6.5)	0.065	280 (3.1)	28 (6.0)	0.068
20-24	1950 (23.4)	52 (18.8)		1896 (23.2)	106 (23.7)		1877 (23.3)	125 (23.0)	
25-29	2587 (30.8)	67 (26.0)		2536 (30.8)	118 (27.6)		2516 (30.8)	138 (27.4)	
30-34	1836 (22.7)	59 (22.6)		1802 (22.9)	93 (21.0)		1781 (22.7)	114 (22.9)	
≥35	1533 (19.9)	56 (26.8)		1515 (20.0)	74 (21.2)		1500 (20.1)	89 (20.7)	
Maternal education									
Uneducated	5890 (73.9)	182 (75.0)	0.859	5759 (73.8)	313 (75.9)	0.157	5694 (73.9)	378 (75.5)	0.027
Primary	1744 (22.0)	54 (19.7)		1715 (22.0)	83 (20.8)		1704 (22.0)	94 (21.1)	
Secondary+	563 (4.1)	15 (5.3)		558 (4.2)	20 (3.3)		556 (4.1)	22 (3.4)	
Maternal occupation									
Not employed	5935 (72.9)	178 (74.6)	0.604	5807 (72.9)	306 (73.2)	0.575	5747 (72.9)	366 (73.6)	0.376
Employed	2267 (27.1)	73 (25.4)		2225 (27.1)	110 (26.8)		2207 (27.1)	128 (26.4)	
Husband education									
Uneducated	4186 (49.9)	145 (53.2)	0.092	4104 (50.0)	227 (50.1)	0.346	4057 (50.0)	274 (49.0)	0.154
Primary	2482 (37.3)	69 (34.6)		2437 (37.3)	114 (36.2)		2416 (37.3)	135 (37.1)	
Secondary+	1529 (12.8)	37 (12.2)		1491 (12.7)	75 (13.7)		1481 (12.7)	85 (13.9)	
Husband occupation									
Not employed	873 (7.7)	22 (6.6)	0.339	846 (7.6)	49 (7.7)	0.421	838 (7.6)	57 (7.4)	0.482
Employed	7324 (92.3)	229 (93.4)		7186 (92.4)	367 (92.3)		7116 (92.4)	437 (92.6)	
Wealth									
Poorest	3238 (25.4)	109 (15.6)	0.248	3163 (25.3)	184 (21.5)	0.015	3118 (25.3)	229 (22.2)	<0.001
Poorer	1430 (23.4)	48 (22.5)		1400 (23.4)	78 (22.2)		1390 (23.5)	88 (21.3)	
Middle	1167 (21.1)	36 (22.8)		1147 (21.3)	56 (20.0)		1136 (21.2)	67 (20.7)	
Richer	1025 (17.8)	30 (24.8)		1000 (17.7)	55 (23.3)		993 (17.6)	62 (23.7)	
Richest	1337 (12.3)	28 (14.3)		1322 (12.3)	43 (13.0)		1317 (12.3)	48 (12.1)	

Total number of preceding child									
≤2	2627 (31.0)	57 (27.0)	<0.001	2591 (31.0)	93 (27.1)	<0.001	2575 (31.1)	109 (26.4)	<0.001
3-4	2561 (30.6)	77 (22.0)		2505 (30.7)	133 (23.6)		2482 (30.7)	156 (24.6)	
≥5	3009 (38.4)	117 (50.9)		2936 (38.2)	190 (49.3)		2897 (38.2)	229 (49.0)	
Residence									
Urban	1264 (8.8)	22 (12.0)	0.004	1251 (8.9)	35 (8.7)	<0.001	1248 (9.0)	38 (7.7)	<0.001
Rural	6933 (91.2)	229 (88.0)		6781 (91.1)	381 (91.3)		6706 (91.0)	456 (92.3)	
Region									
Tigray	765 (6.0)	23 (6.1)	0.516	762 (6.1)	26 (4.1)	0.145	752 (6.1)	36 (5.3)	0.039
Afar	808 (1.0)	20 (0.7)		779 (1.0)	49 (1.2)		762 (1.0)	66 (1.4)	
Amhara	774 (18.7)	26 (22.2)		765 (18.8)	35 (17.9)		761 (18.9)	39 (17.2)	
Oromia	1270 (44.7)	37 (45.5)		1245 (44.6)	62 (47.9)		1235 (44.6)	72 (47.1)	
Somali	1231(5.0)	52 (6.3)		1210 (4.9)	73 (5.4)		1203 (4.9)	80 (5.1)	
Benishangul-Gumuz	711 (1.1)	24 (1.0)		690 (1.1)	45 (1.3)		682 (1.1)	53 (1.4)	
SNNPR***	1021 (21.2)	23 (16.0)		995 (21.1)	49 (20.4)		987 (21.1)	57 (20.9)	
Gambella,	541 (0.2)	16 (0.2)		531 (0.2)	26 (0.2)		522 (0.2)	35 (0.2)	
Harari	443 (0.2)	13 (0.2)		429 (0.2)	27 (0.2)		427 (0.2)	29 (0.2)	
Addis Ababa	246 (1.5)	6 (1.2)		245 (1.5)	7 (1.0)		245 (1.5)	7 (0.8)	
Dire Dawa	387 (0.4)	11 (0.4)		381(0.4)	17 (0.4)		378 (0.4)	20 (0.4)	
Access to mass media									
Yes	1408 (15.8)	36 (23.2)	0.240	1383 (15.9)	61 (20.2)	0.177	1376 (15.9)	68 (19.0)	0.043
No	6789 (84.2)	215 (76.8)		6649 (84.1)	355 (79.8)		6578 (84.1)	426 (81.0)	
Decision making autonomy									
Yes	6014 (77.7)	179 (74.9)	0.469	5898 (77.8)	295 (73.8)	0.258	5848	345	0.072
No	2183 (22.3)	72 (25.1)		2134 (22.2)	121 (26.2)		2106	149	

***SNNPR= Southern Nations, Nationalities, and Peoples' Region; EDHS= Ethiopia Demographic and Health Survey

Balance diagnostics

Propensity score balance

Figure 3 presents the density plot of women in the treatment group (dashed lines) and control group (solid lines) before and after weighting. It reveals that an adequate balance of the propensity score distribution between the treatment groups after weighting (Figure 3).

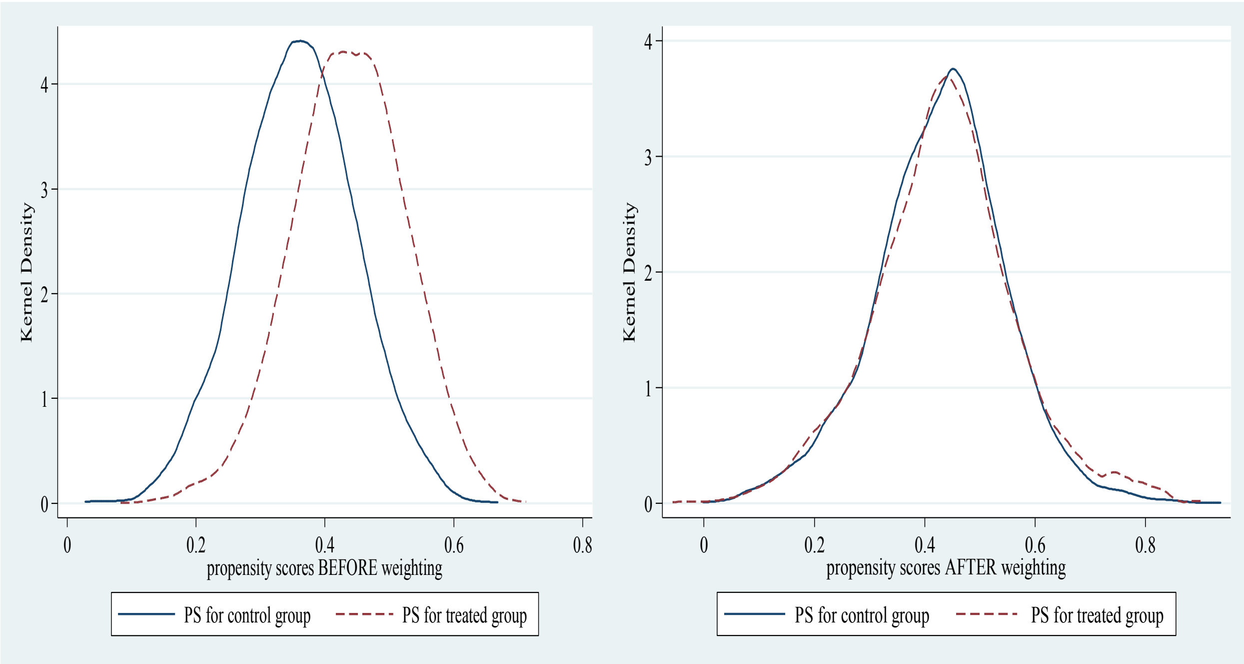

Figure 3 Balance of propensity scores before and after weighting across treatment and comparison groups

PS= propensity score

Covariate balance

After weighting adjustment, standardized differences of covariates were all less than 0.1 (10%), showing comparability between women with and without short birth interval (Supplementary Material III).

Treatment effect estimation

Table 2 presents the estimated effects of short birth interval on neonatal, infant, and under-five mortality. The adjusted estimated odds of neonatal mortality were 53% higher among women who experienced short birth interval (AOR=1.53, 95% CI= 1.13, 2.09) than those who did not. Similarly, the odds of infant mortality were 94% higher (AOR=1.94, 95% CI= 1.39, 2.70) among women who experienced short birth interval compared with women who did not. The odds of under-five child mortality were two times (AOR=2.02, 95% CI= 1.48, 2.74) higher among women who were exposed to short birth interval compared with women who were not.

Table 2 The effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia, EDHS 2016

Treatment variable	**Neonatal mortality**		AOR (95% CI)
	No (%)*	Yes (%)*	
Short birth interval			
No	4166 (54.5)	95 (46.1)	Ref
Yes	4031 (45.5)	156 (53.9)	1.53 (1.13, 2.09)
	Infant mortality		
Short birth interval	No (%)	Yes (%)	
No	4126 (54.9)	135 (40.5)	Ref
Yes	3906 (45.1)	281 (59.5)	1.94 (1.39, 2.70)
	Under-Five mortality		
Short Birth interval	No (%)	Yes (%)	
No	4099 (55.1)	162 (39.3)	Ref
Yes	3855 (44.9)	332 (60.7)	2.02 (1.48, 2.74)

EDHS= Ethiopia Demographic and Health Survey; AOR= Adjusted Odds Ratio; CI= Confidence Interval; Ref= reference group; (%)*=percentage are weighted

Discussion

To our knowledge, this study provides the first comprehensive assessment of the effect of short birth interval on neonatal, infant, and under-five mortality using the WHO recommendation to define short birth interval and applying rigorous analytical techniques to adjust for potential confounders. This study provides evidence that short birth interval is associated with neonatal, infant, and under-five mortality in Ethiopia. These findings will help policy makers and program planners formulate targeted interventions to increase birth intervals and contribute to achieving the GTPE and SDGs target of reducing neonatal, infant, and under-five mortality. [16 15]

In this current study, short birth interval was found to be associated with higher odds of neonatal mortality. This finding is consistent with evidence from the previous studies[22 24 58-61] which have shown a higher risk of neonatal mortality among women with a short birth interval. However, the definition of short birth interval (i.e., <33 months) used in the current study was in line with the WHO definition and longer than those used in previous studies (i.e., ranges from <18 to 24 months). Short birth interval could result in adverse neonatal child health outcomes, such as death, by causing maternal nutritional depletion, specifically folate depletion.[62 63] The maternal nutritional depletion hypothesis states that a short birth-to-pregnancy/birth interval worsens the mother's nutritional status because of inadequate time to recover from the physiological stresses of the subsequent pregnancy.[64] This may compromise maternal nutritional status and ability to support fetal growth, which could result in fetal malnutrition and increased risk of infection and death during childhood.[62] Women with short birth interval may also be less likely to attend postnatal care, which is vital for early detection and treatment of neonatal and maternal health problems. Evidence has shown that the majority of mothers and newborns in low- and middle-income countries do not receive optimal postnatal care[65], yet close to half of the newborn deaths occurred within the first 24 hours after birth, a critical time where mothers and their babies should get their first postnatal care.[66]

Our study found that infant mortality was 94% higher among women who experienced short birth interval compared with women who did not. Our finding was consistent with evidence from Ethiopia,[17 31] Kenya,[67 68] Nepal,[69] and Iran[70] although the cut-off point for short birth interval in the current study was longer than the previous studies. The abovementioned previous studies also documented that the risk of infant mortality was higher among women who experienced short birth interval compared with women who did not. One of the possible reasons for the effect of short birth interval on infant mortality could be low maternal motivation to breastfeed (for example, if the pregnancy was unintended).[71] Maternal perception of being undernourished due to a short birth interval may also influence her infant feeding choices, such as the duration and intensity of breastfeeding and supplemental feeding of the infant. This could in turn affect infants' nutritional status, their resistance to infection, and may expose them to death.[71-74] The abovementioned links between short birth interval and neonatal mortality also apply to infant mortality.

Short birth interval doubled the odds of under-five mortality compared with non-short birth interval. Despite not using the WHO recommendation[1] of less than 33 months to define short birth interval, the existing literature[23 29 58 59 75] also supported our finding. The likely mechanism through which short birth interval affects under-five mortality could be competition between closely spaced siblings for limited household resources, maternal attention, and cross-infection.[71] Moreover, children born within a short birth interval may not receive their vaccination at all or complete their booster series, which is one of the risk factors that exposed children to the infectious disease and its associated death.[76-78] Women with short birth interval could be burdened with caring for highly dependent children[72] and other domestic activities. As a result, they may lack the time and motivation to take children to the health facility for vaccination and other services.

The results of this study need to be interpreted within the limitations of the observational study design. Due to the cross-sectional nature of the study, temporal associations between short birth interval and neonatal, infant, and under-five mortality may not be established.

One of the strengths of the current study was its use of data from a nationally representative survey with a large sample size. In addition, this study used robust statistical methods to estimate the unbiased effect of the treatment group (short birth interval) on the outcome variables (neonatal, infant, and under-five mortality), by using causal diagrams to identify confounders a priori. The application of DAGs,[79-81] a graphical tool used to identify confounding variables by specifying causal paths among treatment/exposure, outcome, and other causally related variables was another strength of this study.

Conclusion

This study provides evidence that short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions aiming to reduce neonatal, infant, and under-five mortality in Ethiopia should target the prevention of short birth interval. These could be achieved through creating awareness on the optimum birth interval and the negative impacts of shorter birth intervals on the health of children. Further expanding the availability and accessibility of family planning services also help women achieve optimum birth interval. Birth interval counseling as per the WHO recommendation should be integrated into the maternal and child health services as part of the child survival intervention.

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Contributors

All authors (DMS, CC, EGH, and DL) contributed to the design of the study and the interpretation of data. DM performed the data analysis and drafted the manuscript. All authors (DMS, CC, EGH, and DL) read, critically revised, and approved the final manuscript.

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The authors declare that they have no competing interests.

Ethics approval

The 2016 EDHS was approved by the National Research Ethics Review Committee of Ethiopia (NRERC) and ICF Macro International. Permission from The DHS Program was obtained to use the 2016 EDHS data for further analysis. This analysis was also approved by The University of Newcastle Human Research Ethics Committee (H-2018-0332).

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Data availability statement

The dataset is available from The DHS Program repository at the following link: https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0.

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Supplemental Material I

Women's birth interval data were collected through extracting the date of birth of their biological children data from children's birth /immunization certificate, and/or asking information regarding their children's date of birth from the women. Mothers were asked to confirm the accuracy of the information before documenting children's date of birth from children's birth/immunization certificates. This crosschecking was performed to avoid errors, since in some cases the documented birth date may represent the date when the birth was recorded, rather than the actual birth date. In the absence of children's birth certificates, information regarding children's date of birth was obtained from their mothers. Birth interval was computed in months. Further information regarding birth interval data collection can be found elsewhere

Supplemental Material II

Table 1 Variables included in Direct Acyclic Graph

Category	**Variables**	**Definition**
Maternal background characteristics	Age at first marriage	The age of the woman at their first marriage, which was considered as a continuous variable
	Age at birth of the index Neonate/Infant/child	The age of the woman during the time she gave birth to the index neonate, which was considered as a continuous variable
	Educational level	Maximum educational level (1= Uneducated, 2=Primary and 3=Secondary+ (or Educated and Uneducated)
	Employment status	Employed/not employed based on women's response to the question "have you been employed in the last 12 months" (1=Not Employed; 2=Employed))
	Place of residence	The place where the women live (1=Urban; 2=Rural)
	Region	Region of residence where women live (1=Tigray, 2=Afar, 3=Amhara, 4=Oromia, 5=Somali, 6=Benishangul-Gumuz, 7=SNNPR*, 8=Gambella, 9=Harari, 10=Addis Ababa, 11=Dire Dawa) *SNNPR= Southern Nations, Nationalities, and Peoples' Region
	Number of living children	Total number of living children the women had ever had
	Decision making autonomy	Coded as 'yes' if she reported being involved in all decisions regarding her own health care, major household purchases and visits to her family or relatives (1=Yes, 2=No).
Husband background characteristics	Husband's education	Maximum educational level of the husband (1= Uneducated, 2= Primary and 3= Secondary+)
	Husband's occupation	
Household characteristics	Access to media	1=Access to media, 2= Not have access to media
	Wealth index	The wealth index provided with the dataset was used. DHS program provides a composite index of household amenities based on the principal component analysis (PCA) and classified the population into

		quintiles: (1st quintile (Poorest); 2nd quintile; 3rd quintile; 4th quintile and 5th quintile (Richest). A quintile is used as a measure of its relative socioeconomic level (i.e., 1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest)
Maternal health status and healthcare-related variables	Antenatal care	Women's antenatal care utilization categorized as no visit, at least one visit, ≥ four visits
	Delivery care	Delivery assisted by physician, nurse, midwife, health officer, and health extension worker; categorized as Yes/No
	Postnatal care	Women received check-up at least once within 48 hours after delivery by a skilled provider; categorized as Yes/No
	TT immunization	Women received at least two doses of the immunization during pregnancy (1=Yes, 2=No)
Neonatal, infant and child characteristics	Sex	1=Male, 2=Female
	Type of birth	1=Singleton, 2 = Multiple
	Birth weight	Based on mother's report that the birth weight was in one of the following categories (below average, average, above average)
	Mode of delivery	Weather the delivery was assisted by caesarean delivery or not (1= Non-Caesarean section, 2=Caesarean section)
	Total children born before the index child	The total children born the index child was considered as a continuous variable Total number children born before the index child was considered as a continuous variable. This was done after checking for the linearity assumption with the log-odds of short birth interval, which is a binary response variable. Multicollinearity was also checked among the exposure variables using the variance inflation factor (VIF). If the values of VIF were lower than 10, then the collinearity problem was considered to be unlikely. The VIF for birth order was 18.15 and for the total number of children born before the index child was 16.26, which indicates the presence of collinearity. Therefore, we removed

		the variable birth order from the model and the VIF became less than 3 for each variable included in the model.
	Birth order	Birth order is the order number of the births from first to last. Twins are given the same birth order, but the birth order of a child born after twins will be the total number of births preceding plus one.
	Diarrhoeal Disease	1= Yes, 2=No
	Fever	1=Yes, 2=No
	Respiratory infection	1=Yes, 2=No
Environmental factors	Source of water	1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well).
	Latrine facility	1 = Improved (access to flush toilet, ventilated improved pit latrine, traditional pit latrine with a slab, or composting toilet and does not share this facility with other households), 2=unimproved.

Supplemental Material III

Table 2 Standardized difference before and after weighting the propensity score

Variable	**Standardized difference**	
	Before weighting	After weighting
Maternal age at the birth of the index child (in years)*	-0.384	0.016
Maternal education		
Uneducated	0.203	0.000
Primary	-0.130	-0.008
Maternal occupation		
Not employed	0.143	0.004
Husband education		
Uneducated	0.153	0.007
Primary	-0.056	0.005
Husband occupation		
Not employed	0.156	0.006
Wealth		
Poorest	0.334	-0.009
Poorer	-0.017	0.011
Middle	-0.069	0.007
Richer	-0.082	-0.002
Total number of preceding child*	0.211	-0.010
Residence		
Urban	-0.225	-0.007
Region		
Tigray	-0.209	0.004
Afar	0.198	0.005
Amhara	-0.286	0.013
Oromia	0.024	0.002
Somali	0.409	-0.005
Benishangul-Gumuz	0.013	-0.007
SNNPR**	-0.057	-0.003
Gambella,	-0.109	-0.005
Harari	-0.002	-0.010
Addis Ababa	-0.170	0.015
Access to mass media		
Yes	-0.194	-0.002
Decision making autonomy		
No	0.069	-0.015

*Maternal age at the birth of the index child (in years) and total number of the preceding child were considered as continuous variables; **SNNPR= Southern Nations, Nationalities, and Peoples' Region

Interpretation of the standardized difference

When the standardized difference is <0.1, it indicates a negligible difference in the mean or prevalence of a covariate between treatment and control groups. Therefore, the standardized difference after weighting shows the balance in covariates between the treatment and control group.

STROBE 2007 (v4) Statement—Checklist of items for the study

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3 & 4
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	5
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	*8*
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8, 9, and 10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8, 9, &10
		(*e*) Describe any sensitivity analyses	8 & 9
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11, 12, & 13
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, 12, &13
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15 & 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	16 & 17
Generalisability	21	Discuss the generalisability (external validity) of the study results	17 &18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia: a nationally representative observational study using inverse probability of treatment weighting

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The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia: a nationally representative observational study using inverse probability of treatment weighting

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Abstract

Objective To assess the effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia.

Design A nationally representative cross-sectional survey.

Setting This study used data from the Ethiopia Demographic and Health Survey (EDHS) 2016.

Participants A total of 8,448 women who had at least two live births during the five years preceding the survey were included in the analysis.

Outcome measures Neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months) were the outcome variables.

Methods Weighted logistic regression analysis based on inverse probability of treatment weights (IPTW) was used to estimate exposure effects adjusted for potential confounders.

Results The adjusted odds of neonatal mortality were about 85% higher among women with short birth interval (AOR=1.85, 95% CI= 1.19, 2.89) than those without. The odds of infant mortality were two-fold higher (AOR=2.16, 95% CI= 1.49, 3.11) among women with short birth interval. The odds of under-five child mortality were also about two times higher (AOR=2.26, 95% CI= 1.60, 3.17) higher among women with short birth interval.

Conclusion Short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions targeting short birth interval are warranted to reduce neonatal, infant, and under-five mortality.

Strengths and limitations of this study

- The application of IPTW mimics a randomized clinical trial by matching two comparison groups using a conditional probability of receiving exposure (short birth interval in this case) given a set of covariates.
- The study has also additional strengths, such as using data from a nationally representative survey with large sample size.
- The application of DAGs, a graphical tool used to identify minimum adjustment sets, which defined the set of explanatory variables for the propensity scores model was another strength of this study.
- Due to the cross-sectional nature of the study, temporal associations between short birth interval and neonatal, infant, and under-five mortality may not be established.
- The second limitation of our study could be associated with the nonrandomized design of the study. Propensity scores based analysis, IPTW, cannot account for unknown confounders in the same way that a randomised trial can. As a result, the effect of residual confounders may not be avoided.

Introduction

Short birth interval, defined as a birth-to-birth interval of less than 33 months,[1] is a key public health problem with an estimated prevalence of 45.8% in Ethiopia.[2] Previous studies[2-4] have revealed the multifactorial nature of short birth interval, its spatial variation, and socioeconomic inequality in Ethiopia. Only about one-third of women in Ethiopia use modern contraceptives, which can prevent short birth interval.[5] Literature has also shown the effects of short birth interval may include, but are not limited to, preterm birth,[6 7] low birth weight,[6 7] small size for gestational age,[6] congenital anomalies,[8 9] autism,[10] miscarriage, preeclampsia, and premature rupture of membranes.[11 12]

Neonatal, infant, and under-five mortality are defined as the death of a child within 28 days of birth, before the age of 1 year, and before five years, respectively.[5] These mortality outcomes are regarded as a highly sensitive (proxy) measure of population health, a country's poverty and socioeconomic development status, and the availability and quality of health services and medical technology.[13 14]

The Sustainable Development Goal (SDG) 3.2 states that all countries should aim to reduce the neonatal mortality rate (NMR) to 12 deaths per 1000 live births or fewer, and reduce under-five mortality to 25 deaths per 1000 live births or fewer, by 2030.[15] The Growth and Transformation Plan of Ethiopia (GTPE) II also targets reductions in neonatal, infant, and under-five mortality rates, from 28 per 1000 live births, 44 per 1000 live births, and 64 per 1000 live births in 2014/15 to 10, 20, and 30 per 1000 live births by 2019/20, respectively.[16] However, the 2019 Ethiopia Mini Demographic and Health Survey (EMDHS) report revealed that the neonatal, infant, and under-five mortality rates in Ethiopia were 30, 43, and 55 deaths per 1,000 live births, respectively: still much higher than GTPE targets.[16 17]

Literature from Ethiopia has shown that neonatal, infant, and under-five mortality are associated with maternal education,[18 19] lack of antenatal care,[20] home delivery,[21] preterm birth,[20 22] low birth weight,[21 22] multiple births,[18 20 23 24] sex of the child,[18 20 23-26] wealth status,[27 28] place of residence,[21 24 25] sources of drinking water,[28] and lack of access to an improved toilet facility.[29]

Although previous studies[18-20 24 25 28-32] have suggested birth interval as one factor influencing neonatal, infant, under-five mortality, these studies have several limitations. A key limitation is that these studies[18-20 24 25 28-32] did not use the World Health Organization (WHO) recommended[1] definition of short birth interval. Understanding the impact of short birth interval on neonatal, infant, and under-five mortality, using the WHO definition,[1] is necessary for the formulation of valid, consistent policies and health planning strategies and interventions to improve child health outcomes. Second, women who were not eligible to provide birth interval information (i.e., those who had given birth only once) were included in the analysis of some studies.[20 25 29] This may result in underestimation or obscuration of the true effect of birth interval on child mortality. Third, even among studies using the same definition of short birth interval, findings have been inconsistent.[20 25] One of the studies using national data[20] did not control for a range of potential confounders including maternal education, wealth status, number of children, and region of residence, even though these data were available in the datasets used for analysis. Similarly, another previous study[30] that used national data did not condition on maternal occupation, husband education, husband occupation, the total number of preceding child, regions, access to mass media, and women's decision making autonomy. In addition, various studies did not consider short birth interval as a potential predictor of neonatal,[22 26 27 33-36] infant,[19 37 38] and under-five mortality[39-42] in their studies.

Generally, the effect of short birth interval, as per the most recent WHO recommendation,[1] on neonatal, infant, and under-five mortality has not been investigated in Ethiopia. Evidence regarding the effect of short birth interval is required for informed decision making by policy makers and health program planners. This paper aimed to assess the effect of short birth interval on neonatal, infant, and under-five mortality using the most recent WHO definition and adjusting for a comprehensive set of potential confounders.

Methods

Study design and study area

This analysis used data from the Ethiopia Demographic and Health Survey (EDHS) 2016. The EDHS is a nationally representative cross-sectional study conducted in nine geographical regions (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations Nationalities and Peoples (SNNP), Gambela, and Harari) and two administrative cities (Addis Ababa and Dire Dawa). A two-stage, stratified, clustered random sampling design was employed to collect data from women who gave birth within the five years preceding the survey. Further descriptions of the sampling procedure for the EDHS are presented elsewhere.[5] A total of 8,448 women who had at least two live births during the five years preceding the 2016 survey were included in the analysis. When women had more than two births in the five years preceding the survey, the birth interval between the most recent index child and the immediately preceding child was considered for all the study participants.

Variables

Outcome variables

The outcome variables in the current study were neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months).[5 43] These outcomes were coded as binary variables (1/0).

Treatment/exposure variable

Short birth interval was the treatment variable and was defined as a birth-to-birth interval of less than 33 months as per the WHO definition.[1] A preceding birth interval, the amount of time between the birth of the child under study (index child) and the immediately preceding birth, was considered in this study. Women's birth interval data were collected through extracting the date of birth of their biological children data from children's birth /immunization certificate, and/or asking information regarding their children's date of birth from the women. Mothers were asked to confirm the accuracy of the information before documenting children's date of birth from children's birth/immunization certificates. This crosschecking was performed to avoid errors, since in some cases the documented birth date may represent the date when the birth was recorded, rather than the actual birth date. In the absence of children's birth certificates, information regarding children's date of birth was obtained from their mothers. Further information regarding birth interval data collection is provided elsewhere.[2 3 44]

Control variables

After reviewing relevant literature,[2 18-21 23-25 28 29 39 45 46] Direct Acyclic Graphs (DAGs) were constructed using DAGitty 3.0[47] to identify confounders for the association between short birth interval and neonatal, infant, and under-five child mortality. Adjustment for such confounders is necessary to estimate the unbiased effect of SBI on neonatal, infant, and under-five mortality (figure 1). DAG is a formal system of mapping variables and the direction of causal relationships among them.[48 49] This graphical representation of causal effects among variables helps understand whether bias is potentially reduced or increased when conditioning on covariates. Moreover, it illustrates covariates that lie in the causal pathway between the treatment and outcomes, which should not be included in the analysis as a confounder. These variables are indicated by green lines in Figure 1. This is because a propensity score that includes covariates affected by the treatment (i.e., variables on the causal pathway between treatment and outcome) obscures part of the treatment effect that one is trying to estimate.[50] Identified confounders were maternal age at the birth of the index child, maternal education, maternal occupation, husband's education, husband's occupation, household wealth status, survival status of the preceding child, the total number of the preceding child, place of residence (urban/rural), regions, access to media, and decision making autonomy. A list of all variables considered in the DAG is provided in Supplementary Material I.

A yellowish-green circle with a triangle at its centre indicates the main treatment/exposure variable, a blue circle with a vertical bar at its centre indicates the outcome variable, light red circles indicate ancestors of exposure and outcome (i.e., confounders). Blue circles indicate the ancestors of the outcome variable. Green lines indicate a causal pathway. Red lines indicate open paths by which confounding may occur; this confounding can be removed by adjusting for one or several variables on the pathway.

M_age_atBirth_chil= Maternal age at birth of the index child; M_Edu= Maternal education; M_Occu= Maternal Occupation; H_Educ= Husband education; H_Occup= Husband occupation; Birth_wt=Birth weight; Total_Prec_child=Total number of preceding child; Respiratory_infn= respiratory infection; Prev_Chi_Survival=Previous child survival; Multiple_preg= Multiple pregnancy; ANC=Antenatal care; PNC=Postnatal care; TT_vaccin=Tetanus toxoid vaccination status; SBI= Short birth interval; NM=Neonatal mortality; IM=Infant mortality; U5M=Under-five mortal

Data analyses

Participants' characteristics were described using frequency with percent. P-values were calculated using Pearson's chi-squared test. Given that the outcomes (i.e., neonatal, infant, and under-five mortality) were relatively infrequent, the unbiased effect of short birth interval on each outcome was estimated using propensity scores (PS) with a stabilized method of inverse probability of treatment weighting (IPTW). A previous study[51] has shown that IPTW with stabilized weights preserves the sample size of the original data, provides an appropriate estimation of the variance of the main effect, and maintains an appropriate type I error rate. The other methods, such as IPTW with normalized weight and greedy algorithm with 1:1 matching methods, are discussed elsewhere.[52-54] A propensity score is defined as the probability of treatment assignment given observed baseline covariates (described in Supplementary Material II).[54] Propensity scores are used to estimate treatment effects on outcomes using observational data when confounding bias due to non-random treatment assignment is likely.[50] Inverse probability of treatment weighting weights the entire study sample by the inverse of the propensity score;[55] a differential amount of information is used from each participant, depending on their conditional probability of receiving treatment. This means observations are less likely to be lost than when using matching for confounder adjustment.[56 57] Propensity scores are a robust alternative to covariate adjustment when the outcome variable is rare, resulting in data sparsity and estimation issues in multivariable models.[57] In this study, the weighted prevalence of the outcome variables of neonatal, infant, and under-five mortality were 2.9% (95% CI: 2.39, 3.61), 4.8% (95% CI: 4.11, 5.58), and 5.5% (95% CI: 4.73, 6.44), respectively.

The analysis procedure was as follows. First, the propensity score was estimated using a logistic regression model in which treatment assignment (short birth interval vs. non-short birth interval) was regressed on the 11 covariates identified using the DAG. The balance of measured covariates/confounders was then assessed across treatment groups (i.e., women with short birth interval) and comparison groups (i.e., women with non-short birth interval) before and after weighting, by computing standardized differences (Supplementary Material II).[57 58] For a continuous covariate, the standardized difference[58 59] is defined as:

$$d = \frac{(\bar{x}_{treatment} - \bar{x}_{control})}{\sqrt{\frac{s^2_{treatment} + s^2_{control}}{2}}}$$

198 where $\bar{x}_{treatment}$ and $\bar{x}_{control}$ denote the sample mean of the covariate in treated and untreated 199 subjects, respectively and $s^2_{treatment}$ and $s^2_{control}$ denote the corresponding sample variances of 200 the covariate. The standardized difference[58 59] for a dichotomous variable is given as:

$$d = \frac{(\hat{p}_{treatment} - \hat{p}_{control})}{\sqrt{\frac{\hat{p}_{treatment}(1-\hat{p}_{treatment}) + \hat{p}_{control}(1-\hat{p}_{control})}{2}}}$$

201 where $\hat{p}_{treatment}$ and $\hat{p}_{control}$ denote the prevalence of the dichotomous variable in treated 202 and untreated subjects, respectively.

203 A standard difference less than 0.1 has been suggested as indicating a negligible difference in 204 the mean or prevalence of a covariate between treatment and control groups and was used 205 here.[58] In addition, kernel densities were plotted to graphically demonstrate the propensity 206 score balance in the treatment group (i.e., women with short birth interval) and control groups 207 (women with non-short birth interval). Balance in propensity scores was considered to be 208 achieved when the kernel density line for the treatment group and control group lay closer 209 together.[60] The inverse probability of treatment weights was then calculated as 1/PS for those 210 exposed to short birth interval and $1/(1-\text{PS})$ for those who were not. The sample was then 211 reweighted by the IPTW and the balance of the covariates checked in the reweighted 212 sample.[50 61] Stabilization of weights was made to preserve the sample size of the original 213 data, reduce the effect of weights of either treated subjects with low propensity scores or 214 untreated subjects with high propensity scores, and provides appropriate improve the 215 estimation of variance estimates and confidence intervals for the treatment effect.[51] Since 216 the EDHS employed a two-stage, stratified, clustered random sampling, which is a complex 217 sampling procedure, sampling weights were also used to adjust for the non-proportional

allocation of sample participants to different regions, including urban and rural areas, and consider the possible differences in response rates.[5] Finally, a weighted logistic regression was fit to estimate the effect of the treatment (short birth interval) on each outcome variable (neonatal, infant, and under-five mortality). Estimation of the treatment effect on outcome variables in the final model used the grand weight, which was formed as the product of the survey weight and the stabilized weight. Literature has shown that combining a propensity score method and survey weighting is necessary to estimate unbiased treatment effects which are generalizable to the original survey target population.[62] The treatment effect on the outcome variables was expressed as adjusted odds ratios (AORs) with a 95% confidence interval (CI). Statistical analysis was performed using Stata version 14 statistical software *(StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. 2015)*. Figure 2 presents a schematic summary of the overall analysis procedure.

Patient and public involvement

Patients and/or the general public were not involved in the design, or conduct, or drafting of this secondary analysis.

Results

Respondents' characteristics

Table 1 illustrates the baseline characteristics of the study participants. The occurrence of neonatal mortality differed with maternal age at birth, with mortality rates being higher among mothers aged ≥35 (p=0.021). Neonatal mortality was also higher in rural than in urban areas (p=0.004). Similarly, infant mortality and under-five mortality were somewhat higher in rural areas (p<0.001). Under-five mortality was higher among uneducated mothers (p=0.027) and in mothers without access to mass media (p=0.043). Mortality at all ages was higher among infants with at least five siblings (p<0.0001). Both infant and under-five mortality were slightly higher among women from the richer household

243 **Table 1** The weighted distribution of neonatal, infant, and under-five child mortality by background characteristics, EDHS 2016

Variable	Neonatal Mortality		P-value	Infant Mortality		P-value	Under-five Mortality		P-value
	No (%)	Yes (%)		No (%)	Yes (%)		No (%)	Yes (%)	
Maternal age at the birth of the index child (in years)									
≤19	291 (3.2)	17 (5.8)	0.021	283 (3.1)	25 (6.5)	0.065	280 (3.1)	28 (6.0)	0.068
20-24	1950 (23.4)	52 (18.8)		1896 (23.2)	106 (23.7)		1877 (23.3)	125 (23.0)	
25-29	2587 (30.8)	67 (26.0)		2536 (30.8)	118 (27.6)		2516 (30.8)	138 (27.4)	
30-34	1836 (22.7)	59 (22.6)		1802 (22.9)	93 (21.0)		1781 (22.7)	114 (22.9)	
≥35	1533 (19.9)	56 (26.8)		1515 (20.0)	74 (21.2)		1500 (20.1)	89 (20.7)	
Maternal education									
Uneducated	5890 (73.9)	182 (75.0)	0.859	5759 (73.8)	313 (75.9)	0.157	5694 (73.9)	378 (75.5)	0.027
Primary	1744 (22.0)	54 (19.7)		1715 (22.0)	83 (20.8)		1704 (22.0)	94 (21.1)	
Secondary+	563 (4.1)	15 (5.3)		558 (4.2)	20 (3.3)		556 (4.1)	22 (3.4)	
Maternal occupation									
Not employed	5935 (72.9)	178 (74.6)	0.604	5807 (72.9)	306 (73.2)	0.575	5747 (72.9)	366 (73.6)	0.376
Employed	2267 (27.1)	73 (25.4)		2225 (27.1)	110 (26.8)		2207 (27.1)	128 (26.4)	
Husband education									
Uneducated	4186 (49.9)	145 (53.2)	0.092	4104 (50.0)	227 (50.1)	0.346	4057 (50.0)	274 (49.0)	0.154
Primary	2482 (37.3)	69 (34.6)		2437 (37.3)	114 (36.2)		2416 (37.3)	135 (37.1)	
Secondary+	1529 (12.8)	37 (12.2)		1491 (12.7)	75 (13.7)		1481 (12.7)	85 (13.9)	
Husband occupation									
Not employed	873 (7.7)	22 (6.6)	0.339	846 (7.6)	49 (7.7)	0.421	838 (7.6)	57 (7.4)	0.482
Employed	7324 (92.3)	229 (93.4)		7186 (92.4)	367 (92.3)		7116 (92.4)	437 (92.6)	
Wealth									
Poorest	3238 (25.4)	109 (15.6)	0.248	3163 (25.3)	184 (21.5)	0.015	3118 (25.3)	229 (22.2)	<0.001
Poorer	1430 (23.4)	48 (22.5)		1400 (23.4)	78 (22.2)		1390 (23.5)	88 (21.3)	
Middle	1167 (21.1)	36 (22.8)		1147 (21.3)	56 (20.0)		1136 (21.2)	67 (20.7)	
Richer	1025 (17.8)	30 (24.8)		1000 (17.7)	55 (23.3)		993 (17.6)	62 (23.7)	
Richest	1337 (12.3)	28 (14.3)		1322 (12.3)	43 (13.0)		1317 (12.3)	48 (12.1)	

Total number of preceding child									
≤2	2627 (31.0)	57 (27.0)	<0.001	2591 (31.0)	93 (27.1)	<0.001	2575 (31.1)	109 (26.4)	<0.001
3-4	2561 (30.6)	77 (22.0)		2505 (30.7)	133 (23.6)		2482 (30.7)	156 (24.6)	
≥5	3009 (38.4)	117 (50.9)		2936 (38.2)	190 (49.3)		2897 (38.2)	229 (49.0)	
Residence									
Urban	1264 (8.8)	22 (12.0)	0.004	1251 (8.9)	35 (8.7)	<0.001	1248 (9.0)	38 (7.7)	<0.001
Rural	6933 (91.2)	229 (88.0)		6781 (91.1)	381 (91.3)		6706 (91.0)	456 (92.3)	
Region									
Tigray	765 (6.0)	23 (6.1)	0.516	762 (6.1)	26 (4.1)	0.145	752 (6.1)	36 (5.3)	0.039
Afar	808 (1.0)	20 (0.7)		779 (1.0)	49 (1.2)		762 (1.0)	66 (1.4)	
Amhara	774 (18.7)	26 (22.2)		765 (18.8)	35 (17.9)		761 (18.9)	39 (17.2)	
Oromia	1270 (44.7)	37 (45.5)		1245 (44.6)	62 (47.9)		1235 (44.6)	72 (47.1)	
Somali	1231(5.0)	52 (6.3)		1210 (4.9)	73 (5.4)		1203 (4.9)	80 (5.1)	
Benishangul-Gumuz	711 (1.1)	24 (1.0)		690 (1.1)	45 (1.3)		682 (1.1)	53 (1.4)	
SNNPR***	1021 (21.2)	23 (16.0)		995 (21.1)	49 (20.4)		987 (21.1)	57 (20.9)	
Gambella,	541 (0.2)	16 (0.2)		531 (0.2)	26 (0.2)		522 (0.2)	35 (0.2)	
Harari	443 (0.2)	13 (0.2)		429 (0.2)	27 (0.2)		427 (0.2)	29 (0.2)	
Addis Ababa	246 (1.5)	6 (1.2)		245 (1.5)	7 (1.0)		245 (1.5)	7 (0.8)	
Dire Dawa	387 (0.4)	11 (0.4)		381(0.4)	17 (0.4)		378 (0.4)	20 (0.4)	
Access to mass media									
Yes	1408 (15.8)	36 (23.2)	0.240	1383 (15.9)	61 (20.2)	0.177	1376 (15.9)	68 (19.0)	0.043
No	6789 (84.2)	215 (76.8)		6649 (84.1)	355 (79.8)		6578 (84.1)	426 (81.0)	
Decision making autonomy									
Yes	6014 (77.7)	179 (74.9)	0.469	5898 (77.8)	295 (73.8)	0.258	5848	345	0.072
No	2183 (22.3)	72 (25.1)		2134 (22.2)	121 (26.2)		2106	149	

***SNNPR= Southern Nations, Nationalities, and Peoples' Region; EDHS= Ethiopia Demographic and Health Survey

Balance diagnostics

Propensity score balance

Figure 3 presents the density plot of women in the treatment group (dashed lines) and control group (solid lines) before and after weighting. It reveals that an adequate balance of the propensity score distribution between the treatment groups after weighting (Figure 3).

Covariate balance

After weighting adjustment, standardized differences of covariates were all less than 0.1 (10%), showing comparability between women with and without short birth interval (Supplementary Material II).

Treatment effect estimation

The prevalence of short birth interval in Ethiopia was 45.8% (95% CI: 42.91–48.62). Table 2 presents the estimated effects of short birth interval on neonatal, infant, and under-five mortality. The adjusted estimated odds of neonatal mortality were 85% higher among women who experienced short birth interval (AOR=1.85, 95% CI=1.19, 2.89) than those who did not. Similarly, the odds of infant mortality were two times higher (AOR=2.16, 95% CI=1.49, 3.11) among women who experienced short birth interval compared with women who did not. The odds of under-five child mortality were two times (AOR=2.26, 95% CI= 1.60, 3.17) higher among women who were exposed to short birth interval compared with women who were not.

Table 2 The effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia, EDHS 2016

Treatment variable	**Neonatal mortality**		AOR (95% CI)
	No (%)*	Yes (%)*	
Short birth interval			
No	4166 (54.5)	95 (46.1)	Ref
Yes	4031 (45.5)	156 (53.9)	1.85 (1.19, 2.89)
	Infant mortality		
Short birth interval	No (%)	Yes (%)	
No	4126 (54.9)	135 (40.5)	Ref
Yes	3906 (45.1)	281 (59.5)	2.16 (1.49, 3.11)
	Under-Five mortality		
Short Birth interval	No (%)	Yes (%)	
No	4099 (55.1)	162 (39.3)	Ref
Yes	3855 (44.9)	332 (60.7)	2.26 (1.60, 3.17)

EDHS= Ethiopia Demographic and Health Survey; AOR= Adjusted Odds Ratio; CI= Confidence Interval; Ref= reference group; (%)*=percentage are weighted

Discussion

To our knowledge, this study provides the first comprehensive assessment of the effect of short birth interval on neonatal, infant, and under-five mortality using the WHO recommendation to define short birth interval and applying rigorous analytical techniques to adjust for potential confounders. This study provides evidence that short birth interval is associated with neonatal, infant, and under-five mortality in Ethiopia. These findings will help policy makers and program planners formulate targeted interventions to increase birth intervals and contribute to achieving the GTPE and SDGs target of reducing neonatal, infant, and under-five mortality. [16 15]

In this current study, short birth interval was found to be associated with higher odds of neonatal mortality. This finding is consistent with evidence from the previous studies[23 25 63-66] which have shown a higher risk of neonatal mortality among women with a short birth interval. However, the definition of short birth interval (i.e., <33 months) used in the current study was in line with the WHO definition and longer than those used in previous studies (i.e., ranges from <18 to 24 months). Short birth interval could result in adverse neonatal child health outcomes, such as death, by causing maternal nutritional depletion, specifically folate depletion.[67 68] The maternal nutritional depletion hypothesis states that a short birth-to-pregnancy/birth interval worsens the mother's nutritional status because of inadequate time to recover from the physiological stresses of the subsequent pregnancy.[69] This may compromise maternal nutritional status and ability to support fetal growth, which could result in fetal malnutrition and increased risk of infection and death during childhood.[67] Women with short birth interval may also be less likely to attend postnatal care, which is vital for early detection and treatment of neonatal and maternal health problems. Evidence has shown that the majority of mothers and newborns in low- and middle-income countries do not receive optimal postnatal care[70], yet close to half of the newborn deaths occurred within the first 24 hours after birth, a critical time where mothers and their babies should get their first postnatal care.[71]

Our study found that infant mortality was two times higher among women who experienced short birth interval compared with women who did not. Our finding was consistent with evidence from Ethiopia,[18 32] Kenya,[72 73] Nepal,[74] and Iran[75] although the cut-off point for short birth interval in the current study was longer than the previous studies. The abovementioned previous studies also documented that the risk of infant mortality was higher among women who experienced short birth interval compared with women who did not. One of the possible reasons for the effect of short birth interval on infant mortality could be low maternal motivation to breastfeed (for example, if the pregnancy was unintended).[76] Maternal perception of being undernourished due to a short birth interval may also influence her infant feeding choices, such as the duration and intensity of breastfeeding and supplemental feeding of the infant. This could in turn affect infants' nutritional status, their resistance to infection, and may expose them to death.[76-79] The abovementioned links between short birth interval and neonatal mortality also apply to infant mortality.

Short birth interval doubled the odds of under-five mortality compared with non-short birth interval. Despite not using the WHO recommendation[1] of less than 33 months to define short birth interval, the existing literature[24 30 63 64 80] also supported our finding. The likely mechanism through which short birth interval affects under-five mortality could be competition between closely spaced siblings for limited household resources, maternal attention, and cross-infection.[76] Moreover, children born within a short birth interval may not receive their vaccination at all or complete their booster series, which is one of the risk factors that exposed children to the infectious disease and its associated death.[81-83] Women with short birth interval could be burdened with caring for highly dependent children[77] and other domestic activities. As a result, they may lack the time and motivation to take children to the health facility for vaccination and other services.

The results of this study need to be interpreted within the limitations of the observational study design. Due to the cross-sectional nature of the study, temporal associations between short birth interval and neonatal, infant, and under-five mortality may not be established. The second limitation of our study could be associated with the nonrandomized design of the study. Propensity scores based analysis, IPTW, cannot account for unknown confounders in the same way that a randomised trial can. As a result, the effect of residual confounders may not be avoided. However, the application of IPTW mimics a randomized clinical trial by matching two comparison groups using a conditional probability of receiving exposure (short birth interval in this case) given a set of covariates. The study has also additional strengths, such as using data from a nationally representative survey with large sample size. The application of DAGs,[48 49 84] a graphical tool used to identify minimum adjustment sets, which defined the set of explanatory variables for the propensity scores model was another strength of this study.

Conclusion

This study provides evidence that short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions aiming to reduce neonatal, infant, and under-five mortality in Ethiopia should target the prevention of short birth interval. These could be achieved through creating awareness on the optimum birth interval and the negative impacts of shorter birth intervals on the health of children. Further expanding the availability and accessibility of family planning services also help women achieve optimum birth interval. Birth interval counseling as per the WHO recommendation should be integrated into the maternal and child health services as part of the child survival intervention.

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Contributors

All authors (DMS, CC, EGH, and DL) contributed to the design of the study and the interpretation of data. DM performed the data analysis and drafted the manuscript. All authors (DMS, CC, EGH, and DL) read, critically revised, and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Ethics approval

The 2016 EDHS was approved by the National Research Ethics Review Committee of Ethiopia (NRERC) and ICF Macro International. Permission from The DHS Program was obtained to use the 2016 EDHS data for further analysis. This analysis was also approved by The University of Newcastle Human Research Ethics Committee (H-2018-0332).

Consent for publication

Not required

Provenance and peer review

Not commissioned; externally peer reviewed.

Data availability statement

The dataset is available from The DHS Program repository at the following link: https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0.

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590 # Figure Legend

591 **Figure 1** Direct Acyclic Graph (DAG) used to select controlling variables

592 **Figure 2** Schematic presentation of the overall steps followed in the analysis

593 **Figure 3** Balance of propensity scores before and after weighting across treatment and
594 comparison groups

595 PS= propensity score

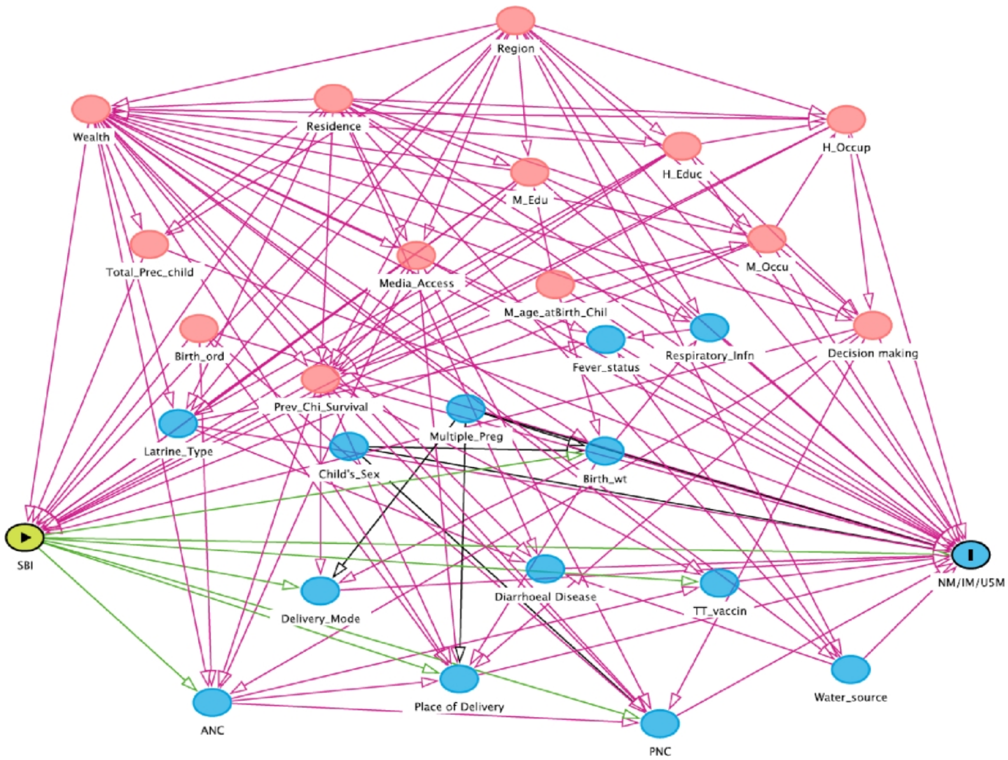

Figure 1 Direct Acyclic Graph (DAG) used to select controlling variables

157x118mm (300 x 300 DPI)

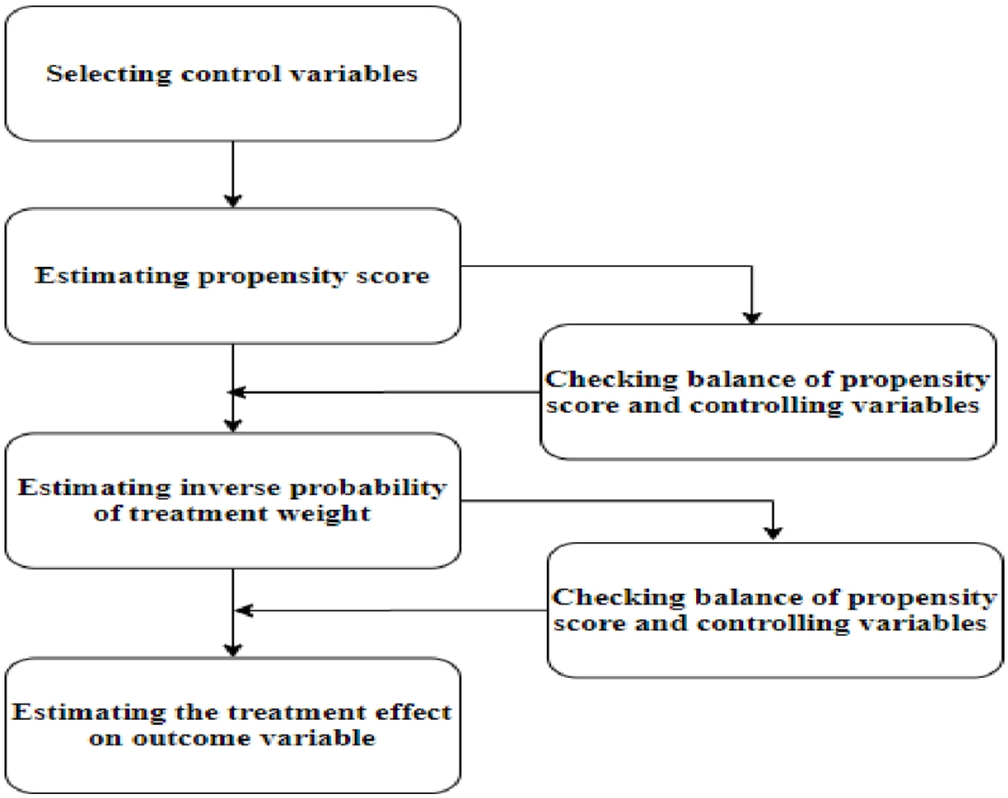

Figure 2 Schematic presentation of the overall steps followed in the analysis

115x90mm (300 x 300 DPI)

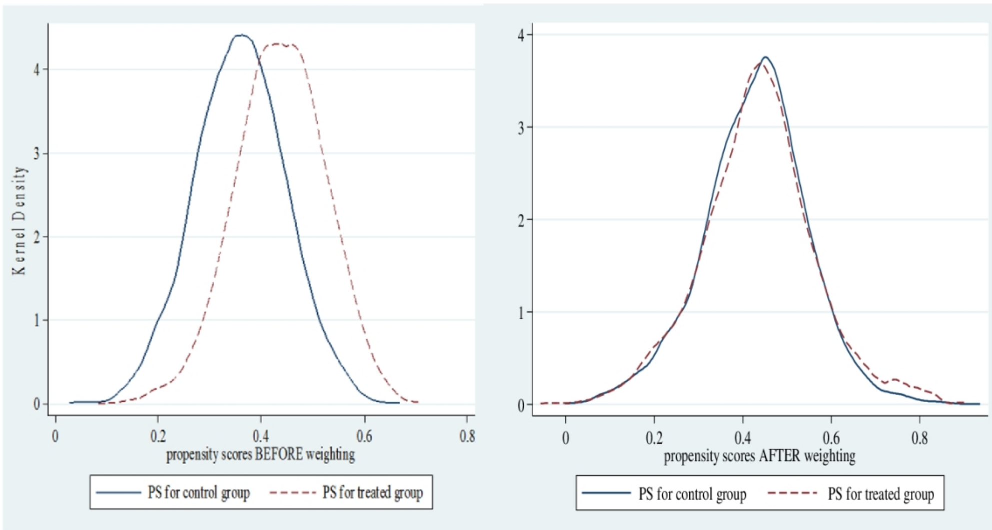

Figure 3 Balance of propensity scores before and after weighting across treatment and comparison groups; PS=propensity score

165x87mm (300 x 300 DPI)

Supplemental Material I

Table 1 Variables included in Direct Acyclic Graph

Category	Variables	Definition
Maternal background characteristics	Maternal age at birth of the index child (in years)	Maternal age at birth of the index child, which was considered as a continuous variable. It was also categorized the descriptive section of the results (1=≤19, 2= 20-24, 3=25-29, 4=30-34, and 5= ≥35).
	Educational level	Maximum educational level (1= Uneducated, 2=Primary and 3=Secondary+)
	Employment status	Maternal employment status (1=Not Employed; 2=Employed))
	Place of residence	Place of residence (1=Urban; 2=Rural)
	Region	Region of residence (1=Tigray, 2=Afar, 3=Amhara, 4=Oromia, 5=Somali, 6=Benishangul-Gumuz, 7=SNNPR*, 8=Gambella, 9=Harari, 10=Addis Ababa, 11=Dire Dawa) *SNNPR= Southern Nations, Nationalities, and Peoples' Region
	Decision making autonomy	Coded as 'yes' if the women were involved in all decisions regarding their own health care, major household purchases and visits to her family or relatives (1=Yes, 2=No).
Husband background characteristics	Husband's education	Maximum educational level of the husband (1= Uneducated, 2= Primary, 3= Secondary+)
	Husband's occupation	1= Not employed, 2=Employed
Household characteristics	Access to media	1=Access to media, 2= Have no access to media
	Wealth index	The wealth index provided with the dataset was used. DHS program provides a composite index of household amenities based on the principal component analysis (PCA) and classified the population into quintiles: (1st quintile (Poorest); 2nd quintile; 3rd quintile; 4th quintile and 5th quintile (Richest). A quintile is used as a measure of its relative socioeconomic level (i.e., 1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest)

Maternal health status and healthcare-related variables	Antenatal care	Women's antenatal care utilization categorized as 1=No visit, 2=At least one visit, 3= ≥ Four visits
	Place of delivery	1= Health facilities, 2=Home
	Postnatal care	Women received check-up at least once within 48 hours after delivery by a skilled provider; categorized as 1=Yes, 2=No
	TT vaccination	Women received at least two doses of the immunization during pregnancy (1=Yes, 2=No)
Neonatal, infant and child characteristics	Sex	Child sex (1=Male, 2=Female)
	Multiple pregnancy	1=Yes, 2=No
	Birth weight	1=Below average, 2=Average, 3=Above average
	Mode of delivery	1= Caesarean section, 2= Non caesarean section
	Survival status of the preceding child	1= Yes, 2=No
	Total number of children born before the index child	Total number of children born before the index child was considered as a continuous variable. For the descriptive statistics, this variable was categorized into 1= ≤2, 2= 3-4, and 3= ≥5. This was done after checking for the linearity assumption with the log-odds of short birth interval, which is a binary response variable. Multicollinearity was also checked among the exposure variables using the variance inflation factor (VIF). When the values of VIF were lower than 10, then the collinearity problem was considered unlikely. The VIF for birth order was 18.15 and for the total number of children born before the index child was 16.26, which indicates the presence of collinearity. Therefore, we removed the variable birth order from the model and the VIF became less than 3 for each variable included in the model.
	Birth order	Birth order is the order number of the births from first to last. Twins are given the same birth order, but the birth order of a child born after twins will be the total number of births preceding plus one.
	Diarrhoeal Disease	1= Yes, 2=No
	Fever	1=Yes, 2=No
	Respiratory infection	1=Yes, 2=No

Environmental factors	Source of water	1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well).
	Latrine facility	1 = Improved (access to flush toilet, ventilated improved pit latrine, traditional pit latrine with a slab, or composting toilet and does not share this facility with other households), 2=unimproved.

Supplemental Material II

Table 2 Standardized difference before and after weighting the propensity score

Variable	**Standardized difference**	
	Before weighting	After weighting
Maternal age at the birth of the index child (in years)*	-0.392	0.022
Maternal education		
Uneducated	0.178	0.009
Primary	-0.112	-0.017
Maternal occupation		
Not employed	0.128	0.005
Husband education		
Uneducated	0.148	0.012
Primary	-0.041	0.003
Husband occupation		
Not employed	0.159	0.006
Wealth		
Poorest	0.332	-0.004
Poorer	-0.002	0.008
Middle	-0.070	0.005
Richer	-0.061	-0.007
Total number of preceding child*	0.207	-0.006
Survival status of preceding child		
Yes	-0.029	-0.004
Residence		
Urban	-0.239	-0.006
Region		
Tigray	-0.207	0.004
Afar	0.186	0.008
Amhara	-0.282	0.014
Oromia	-0.006	0.003
Somali	0.402	-0.003
Benishangul-Gumuz	0.061	-0.006
SNNPR**	-0.069	-0.005
Gambella,	-0.087	-0.009
Harari	-0.001	-0.009
Addis Ababa	-0.180	0.014
Access to mass media		
Yes	-0.201	-0.002
Decision making autonomy		
No	0.067	-0.009

*Maternal age at the birth of the index child (in years) and total number of the preceding child were considered as continuous variables; **SNNPR= Southern Nations, Nationalities, and Peoples' Region

STROBE 2007 (v4) Statement—Checklist of items for the study

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4 , 5, & 6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7, & 8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6, 7, & 8
Bias	9	Describe any efforts to address potential sources of bias	*8, 9, & 10*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7, & 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8, 9, 10, & 11
		(*b*) Describe any methods used to examine subgroups and interactions	8, 9, 10, & 11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8, 9, 10, & 11
		(*e*) Describe any sensitivity analyses	8, 9,, 10, & 11

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11, 12, & 13
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, 12, &13
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	9 and 11, 12, & 13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15 & 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17 & 18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15, 16, 17, & 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	15, 16, 17, & 18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia: a nationally representative observational study using inverse probability of treatment weighting

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Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, Maternal medicine < OBSTETRICS, Community child health < PAEDIATRICS

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The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia: a nationally representative observational study using inverse probability of treatment weighting

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Abstract

Objective To assess the effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia.

Design A nationally representative cross-sectional survey.

Setting This study used data from the Ethiopia Demographic and Health Survey (EDHS) 2016.

Participants A total of 8,448 women who had at least two live births during the five years preceding the survey were included in the analysis.

Outcome measures Neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months) were the outcome variables.

Methods Weighted logistic regression analysis based on inverse probability of treatment weights (IPTW) was used to estimate exposure effects adjusted for potential confounders.

Results The adjusted odds of neonatal mortality were about 85% higher among women with short birth interval (AOR=1.85, 95% CI= 1.19, 2.89) than those without. The odds of infant mortality were two-fold higher (AOR=2.16, 95% CI= 1.49, 3.11) among women with short birth interval. The odds of under-five child mortality were also about two times higher (AOR=2.26, 95% CI= 1.60, 3.17) higher among women with short birth interval.

Conclusion Short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions targeting short birth interval are warranted to reduce neonatal, infant, and under-five mortality.

Strengths and limitations of this study

- The application of inverse probability of treatment weights (IPTW) mimics a randomized clinical trial by matching two comparison groups using a conditional probability of receiving exposure (short birth interval in this case) given a set of covariates.
- The study has also additional strengths, such as using data from a nationally representative survey with a large sample size.
- The application of DAGs, a graphical tool used to identify minimum adjustment sets, which defined the set of explanatory variables for the propensity scores model was another strength of this study.
- Due to the cross-sectional nature of the study, temporal associations between short birth interval and neonatal, infant, and under-five mortality may not be established.
- Another limitation of our study could be associated with the nonrandomized design of the study—propensity score-based analysis, IPTW, cannot account for unknown confounders in the same way that a randomised trial can, so the effect of residual confounders may not be avoided.

Introduction

Short birth interval, defined as a birth-to-birth interval of less than 33 months,[1] is a key public health problem with an estimated prevalence of 45.8% in Ethiopia.[2] Previous studies[2-4] have revealed the multifactorial nature of short birth interval, its spatial variation, and socioeconomic inequality in Ethiopia. Only about one-third of women in Ethiopia use modern contraceptives, which can prevent short birth interval.[5] Literature has also shown the effects of short birth interval may include, but are not limited to, preterm birth,[6 7] low birth weight,[6 7] small sizes for gestational age,[6] congenital anomalies,[8 9] autism,[10] miscarriage, preeclampsia, and premature rupture of membranes.[11 12]

Neonatal, infant, and under-five mortality are defined as the death of a child within 28 days of birth, before the age of 1 year, and before five years, respectively.[5] These mortality outcomes are regarded as a highly sensitive (proxy) measure of population health, a country's poverty and socioeconomic development status, and the availability and quality of health services and medical technology.[13 14]

The Sustainable Development Goal (SDG) 3.2 states that all countries should aim to reduce the neonatal mortality rate (NMR) to 12 deaths per 1000 live births or fewer, and reduce under-five mortality to 25 deaths per 1000 live births or fewer, by 2030.[15] The Growth and Transformation Plan of Ethiopia (GTPE) II also targets reductions in neonatal, infant, and under-five mortality rates, from 28 per 1000 live births, 44 per 1000 live births, and 64 per 1000 live births in 2014/15 to 10, 20, and 30 per 1000 live births by 2019/20, respectively.[16] However, the 2019 Ethiopia Mini Demographic and Health Survey (EMDHS) report revealed that the neonatal, infant, and under-five mortality rates in Ethiopia were 30, 43, and 55 deaths per 1,000 live births, respectively: still much higher than GTPE targets.[16 17]

Literature from Ethiopia has shown that neonatal, infant, and under-five mortality are associated with maternal education,[18 19] lack of antenatal care,[20] home delivery,[21] preterm birth,[20 22] low birth weight,[21 22] multiple births,[18 20 23 24] sex of the child,[18 20 23-26] wealth status,[27 28] place of residence,[21 24 25] sources of drinking water,[28] and lack of access to an improved toilet facility.[29]

Although previous studies[18-20 24 25 28-32] have suggested birth interval as one factor influencing neonatal, infant, under-five mortality, these studies have several limitations. Of the key limitations is that these studies[18-20 24 25 28-32] did not use the World Health Organization (WHO) recommended[1] definition of short birth interval. Understanding the impact of short birth interval on neonatal, infant, and under-five mortality, using the WHO definition,[1] is necessary for the formulation of valid, consistent policies and health planning strategies and interventions to improve child health outcomes. Second, women who were not eligible to provide birth interval information (i.e., those who had given birth only once) were included in the analysis of some studies.[20 25 29] This may result in underestimation or obscuration of the true effect of birth interval on child mortality. Third, even among studies using the same definition of short birth interval, findings have been inconsistent.[20 25] One of the studies using national data[20] did not control for a range of potential confounders including maternal education, wealth status, number of children, and region of residence, even though these data were available in the datasets used for analysis. Similarly, another previous study[30] that used national data did not condition on maternal occupation, husband education, husband occupation, the total number of preceding children, regions, access to mass media, and women's decision making autonomy. In addition, various studies did not consider short birth interval as a potential predictor of neonatal,[22 26 27 33-36] infant,[19 37 38] and under-five mortality[39-42] in their studies.

Generally, the effect of short birth interval, as per the most recent WHO recommendation,[1] on neonatal, infant, and under-five mortality has not been investigated in Ethiopia. Evidence regarding the effect of short birth interval is required for informed decision making by policy makers and health program planners. This paper aimed to assess the effect of short birth interval on neonatal, infant, and under-five mortality using the most recent WHO definition and adjusting for a comprehensive set of potential confounders.

Methods

Study design and study area

This analysis used data from the Ethiopia Demographic and Health Survey (EDHS) 2016. The EDHS is a nationally representative cross-sectional study conducted in nine geographical regions (Tigray, Afar, Amhara, Oromia, Somali, Benishangul-Gumuz, Southern Nations Nationalities and Peoples (SNNP), Gambela, and Harari) and two administrative cities (Addis Ababa and Dire Dawa). A two-stage, stratified, clustered random sampling design was employed to collect data from women who gave birth within the five years preceding the survey. Further descriptions of the sampling procedure for the EDHS are presented elsewhere.[5] A total of 8,448 women who had at least two live births during the five years preceding the 2016 survey were included in the analysis. When women had more than two births in the five years preceding the survey, the birth interval between the most recent index child and the immediately preceding child was considered for all the study participants.

Variables

Outcome variables

The outcome variables in the current study were neonatal mortality (death of the child within 28 days of birth), infant mortality (death between birth and 11 months), and under-five mortality (death between birth and 59 months).[5 43] These outcomes were coded as binary variables (1/0).

Treatment/exposure variable

Short birth interval was the treatment variable and was defined as a birth-to-birth interval of less than 33 months as per the WHO definition.[1] A preceding birth interval, the amount of time between the birth of the child under study (index child) and the immediately preceding birth, was considered in this study. Women's birth interval data were collected by extracting the date of birth of their biological children data from the children's birth /immunization certificate, and/or asking for information regarding their children's date of birth from the women. Mothers were asked to confirm the accuracy of the information before documenting children's date of birth from children's birth/immunization certificates. This crosschecking was performed to avoid errors, since in some cases the documented birth date may represent the date when the birth was recorded, rather than the actual birth date. In the absence of children's birth certificates, information regarding children's date of birth was obtained from their mothers. Further information regarding birth interval data collection is provided elsewhere.[2 3 44]

Control variables

After reviewing relevant literature,[2 18-21 23-25 28 29 39 45 46] Direct Acyclic Graphs (DAGs) were constructed using DAGitty 3.0[47] to identify confounders for the association between short birth interval and neonatal, infant, and under-five child mortality. Adjustment for such confounders is necessary to estimate the unbiased effect of SBI on neonatal, infant, and under-five mortality (figure 1). DAG is a formal system of mapping variables and the direction of causal relationships among them.[48 49] This graphical representation of causal effects among variables helps understand whether bias is potentially reduced or increased when conditioning on covariates. Moreover, it illustrates covariates that lie in the causal pathway between the treatment and outcomes, which should not be included in the analysis as a confounder. These variables are indicated by green lines in Figure 1. This is because a propensity score that includes covariates affected by the treatment (i.e., variables on the causal pathway between treatment and outcome) obscures part of the treatment effect that one is trying to estimate.[50] Identified confounders were maternal age at the birth of the index child, maternal education, maternal occupation, husband's education, husband's occupation, household wealth status, survival status of the preceding child, the total number of the preceding child, place of residence (urban/rural), regions, access to media, and decision making autonomy. A list of all variables considered in the DAG is provided in Supplementary Material I.

A yellowish-green circle with a triangle at its centre indicates the main treatment/exposure variable, a blue circle with a vertical bar at its centre indicates the outcome variable, light red circles indicate ancestors of exposure and outcome (i.e., confounders). Blue circles indicate the ancestors of the outcome variable. Green lines indicate a causal pathway. Red lines indicate open paths by which confounding may occur; this confounding can be removed by adjusting for one or several variables on the pathway.

Data analyses

Participants' characteristics were described using frequency with percent. P-values were calculated using Pearson's chi-squared test. Given that the outcomes (i.e., neonatal, infant, and under-five mortality) were relatively infrequent, the unbiased effect of short birth interval on each outcome was estimated using propensity scores (PS) with a stabilized method of inverse probability of treatment weighting (IPTW). A previous study[51] has shown that IPTW with stabilized weights preserves the sample size of the original data, provides an appropriate estimation of the variance of the main effect, and maintains an appropriate type I error rate. The other methods, such as IPTW with normalized weight and greedy algorithm with 1:1 matching methods, are discussed elsewhere.[52-54] A propensity score is defined as the probability of treatment assignment given observed baseline covariates (described in

Supplementary Material II).[54] Propensity scores are used to estimate treatment effects on outcomes using observational data when confounding bias due to non-random treatment assignment is likely.[50] Inverse probability of treatment weighting weights the entire study sample by the inverse of the propensity score;[55] a differential amount of information is used from each participant, depending on their conditional probability of receiving treatment. This means observations are less likely to be lost than when using matching for confounder adjustment.[56 57] Propensity scores are a robust alternative to covariate adjustment when the outcome variable is rare, resulting in data sparsity and estimation issues in multivariable models.[57] In this study, the weighted prevalence of the outcome variables of neonatal, infant, and under-five mortality were 2.9% (95% CI: 2.39, 3.61), 4.8% (95% CI: 4.11, 5.58), and 5.5% (95% CI: 4.73, 6.44), respectively.

The analysis procedure was as follows. First, the propensity score was estimated using a logistic regression model in which treatment assignment (short birth interval vs. non-short birth interval) was regressed on the 11 covariates identified using the DAG. The balance of measured covariates/confounders was then assessed across treatment groups (i.e., women with short birth interval) and comparison groups (i.e., women with non-short birth interval) before and after weighting, by computing standardized differences (Supplementary Material II).[57 58] For a continuous covariate, the standardized difference[58 59] is defined as:

$$d = \frac{(\bar{x}_{treatment} - \bar{x}_{control})}{\sqrt{\frac{s^2_{treatment} + s^2_{control}}{2}}}$$

where $\bar{x}_{treatment}$ and $\bar{x}_{control}$ denote the sample mean of the covariate in treated and untreated subjects, respectively and $s^2_{treatment}$ and $s^2_{control}$ denote the corresponding sample variances of the covariate. The standardized difference[58 59] for a dichotomous variable is given as:

$$d = \frac{(\hat{p}_{treatment} - \hat{p}_{control})}{\sqrt{\frac{\hat{p}_{treatment}(1-\hat{p}_{treatment}) \quad + \quad \hat{p}_{control}(1-\hat{p}_{control})}{2}}}$$

194 where $\hat{p}_{treatment}$ and $\hat{p}_{control}$ denote the prevalence of the dichotomous variable in treated
195 and untreated subjects, respectively.

196 A standard difference less than 0.1 has been suggested as indicating a negligible difference in
197 the mean or prevalence of a covariate between treatment and control groups and was used
198 here.[58] In addition, kernel densities were plotted to graphically demonstrate the propensity
199 score balance in the treatment group (i.e., women with short birth interval) and control groups
200 (women with non-short birth interval). Balance in propensity scores was considered to be
201 achieved when the kernel density line for the treatment group and control group lay closer
202 together.[60] The inverse probability of treatment weights was then calculated as 1/PS for those
203 exposed to short birth interval and $1/(1-\mathrm{PS})$ for those who were not. The sample was then
204 reweighted by the IPTW and the balance of the covariates checked in the reweighted
205 sample.[50 61] Stabilization of weights was made to preserve the sample size of the original
206 data, reduce the effect of weights of either treated subjects with low propensity scores or
207 untreated subjects with high propensity scores, and provides appropriate improve the
208 estimation of variance estimates and confidence intervals for the treatment effect.[51] Since
209 the EDHS employed a two-stage, stratified, clustered random sampling, which is a complex
210 sampling procedure, sampling weights were also used to adjust for the non-proportional
211 allocation of sample participants to different regions, including urban and rural areas, and
212 consider the possible differences in response rates.[5] Finally, a weighted logistic regression was
213 fit to estimate the effect of the treatment (short birth interval) on each outcome variable
214 (neonatal, infant, and under-five mortality). Estimation of the treatment effect on outcome
215 variables in the final model used the grand weight, which was formed as the product of the
216 survey weight and the stabilized weight. Literature has shown that combining a propensity

score method and survey weighting is necessary to estimate unbiased treatment effects which are generalizable to the original survey target population.[62] The treatment effect on the outcome variables was expressed as adjusted odds ratios (AORs) with a 95% confidence interval (CI). Statistical analysis was performed using Stata version 14 statistical software *(StataCorp. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP. 2015).* Figure 2 presents a schematic summary of the overall analysis procedure.

Patient and public involvement

Patients and/or the general public were not involved in the design, or conduct, or drafting of this secondary analysis.

Results

Respondents' characteristics

Table 1 illustrates the baseline characteristics of the study participants. The occurrence of neonatal mortality differed with maternal age at birth, with mortality rates being higher among mothers aged ≥35 (p=0.021). Neonatal mortality was also higher in rural than in urban areas (p=0.004). Similarly, infant mortality and under-five mortality were somewhat higher in rural areas (p<0.001). Under-five mortality was higher among uneducated mothers (p=0.027) and in mothers without access to mass media (p=0.043). Mortality at all ages was higher among infants with at least five siblings (p<0.0001). Both infant and under-five mortality were slightly higher among women from the richer household

Table 1 The weighted distribution of neonatal, infant, and under-five child mortality by background characteristics, EDHS 2016

Variable	Neonatal Mortality		P-value	Infant Mortality		P-value	Under-five Mortality		P-value
	No (%)	Yes (%)		No (%)	Yes (%)		No (%)	Yes (%)	
Maternal age at the birth of the index child (in years)									
≤19	291 (3.2)	17 (5.8)	0.021	283 (3.1)	25 (6.5)	0.065	280 (3.1)	28 (6.0)	0.068
20-24	1950 (23.4)	52 (18.8)		1896 (23.2)	106 (23.7)		1877 (23.3)	125 (23.0)	
25-29	2587 (30.8)	67 (26.0)		2536 (30.8)	118 (27.6)		2516 (30.8)	138 (27.4)	
30-34	1836 (22.7)	59 (22.6)		1802 (22.9)	93 (21.0)		1781 (22.7)	114 (22.9)	
≥35	1533 (19.9)	56 (26.8)		1515 (20.0)	74 (21.2)		1500 (20.1)	89 (20.7)	
Maternal education									
Uneducated	5890 (73.9)	182 (75.0)	0.859	5759 (73.8)	313 (75.9)	0.157	5694 (73.9)	378 (75.5)	0.027
Primary	1744 (22.0)	54 (19.7)		1715 (22.0)	83 (20.8)		1704 (22.0)	94 (21.1)	
Secondary+	563 (4.1)	15 (5.3)		558 (4.2)	20 (3.3)		556 (4.1)	22 (3.4)	
Maternal occupation									
Not employed	5935 (72.9)	178 (74.6)	0.604	5807 (72.9)	306 (73.2)	0.575	5747 (72.9)	366 (73.6)	0.376
Employed	2267 (27.1)	73 (25.4)		2225 (27.1)	110 (26.8)		2207 (27.1)	128 (26.4)	
Husband education									
Uneducated	4186 (49.9)	145 (53.2)	0.092	4104 (50.0)	227 (50.1)	0.346	4057 (50.0)	274 (49.0)	0.154
Primary	2482 (37.3)	69 (34.6)		2437 (37.3)	114 (36.2)		2416 (37.3)	135 (37.1)	
Secondary+	1529 (12.8)	37 (12.2)		1491 (12.7)	75 (13.7)		1481 (12.7)	85 (13.9)	
Husband occupation									
Not employed	873 (7.7)	22 (6.6)	0.339	846 (7.6)	49 (7.7)	0.421	838 (7.6)	57 (7.4)	0.482
Employed	7324 (92.3)	229 (93.4)		7186 (92.4)	367 (92.3)		7116 (92.4)	437 (92.6)	
Wealth									
Poorest	3238 (25.4)	109 (15.6)	0.248	3163 (25.3)	184 (21.5)	0.015	3118 (25.3)	229 (22.2)	<0.001
Poorer	1430 (23.4)	48 (22.5)		1400 (23.4)	78 (22.2)		1390 (23.5)	88 (21.3)	
Middle	1167 (21.1)	36 (22.8)		1147 (21.3)	56 (20.0)		1136 (21.2)	67 (20.7)	
Richer	1025 (17.8)	30 (24.8)		1000 (17.7)	55 (23.3)		993 (17.6)	62 (23.7)	
Richest	1337 (12.3)	28 (14.3)		1322 (12.3)	43 (13.0)		1317 (12.3)	48 (12.1)	

Total number of preceding child									
≤2	2627 (31.0)	57 (27.0)	<0.001	2591 (31.0)	93 (27.1)	<0.001	2575 (31.1)	109 (26.4)	<0.001
3-4	2561 (30.6)	77 (22.0)		2505 (30.7)	133 (23.6)		2482 (30.7)	156 (24.6)	
≥5	3009 (38.4)	117 (50.9)		2936 (38.2)	190 (49.3)		2897 (38.2)	229 (49.0)	
Residence									
Urban	1264 (8.8)	22 (12.0)	0.004	1251 (8.9)	35 (8.7)	<0.001	1248 (9.0)	38 (7.7)	<0.001
Rural	6933 (91.2)	229 (88.0)		6781 (91.1)	381 (91.3)		6706 (91.0)	456 (92.3)	
Region									
Tigray	765 (6.0)	23 (6.1)	0.516	762 (6.1)	26 (4.1)	0.145	752 (6.1)	36 (5.3)	0.039
Afar	808 (1.0)	20 (0.7)		779 (1.0)	49 (1.2)		762 (1.0)	66 (1.4)	
Amhara	774 (18.7)	26 (22.2)		765 (18.8)	35 (17.9)		761 (18.9)	39 (17.2)	
Oromia	1270 (44.7)	37 (45.5)		1245 (44.6)	62 (47.9)		1235 (44.6)	72 (47.1)	
Somali	1231(5.0)	52 (6.3)		1210 (4.9)	73 (5.4)		1203 (4.9)	80 (5.1)	
Benishangul-Gumuz	711 (1.1)	24 (1.0)		690 (1.1)	45 (1.3)		682 (1.1)	53 (1.4)	
SNNPR***	1021 (21.2)	23 (16.0)		995 (21.1)	49 (20.4)		987 (21.1)	57 (20.9)	
Gambella,	541 (0.2)	16 (0.2)		531 (0.2)	26 (0.2)		522 (0.2)	35 (0.2)	
Harari	443 (0.2)	13 (0.2)		429 (0.2)	27 (0.2)		427 (0.2)	29 (0.2)	
Addis Ababa	246 (1.5)	6 (1.2)		245 (1.5)	7 (1.0)		245 (1.5)	7 (0.8)	
Dire Dawa	387 (0.4)	11 (0.4)		381(0.4)	17 (0.4)		378 (0.4)	20 (0.4)	
Access to mass media									
Yes	1408 (15.8)	36 (23.2)	0.240	1383 (15.9)	61 (20.2)	0.177	1376 (15.9)	68 (19.0)	0.043
No	6789 (84.2)	215 (76.8)		6649 (84.1)	355 (79.8)		6578 (84.1)	426 (81.0)	
Decision making autonomy									
Yes	6014 (77.7)	179 (74.9)	0.469	5898 (77.8)	295 (73.8)	0.258	5848	345	0.072
No	2183 (22.3)	72 (25.1)		2134 (22.2)	121 (26.2)		2106	149	

***SNNPR= Southern Nations, Nationalities, and Peoples' Region; EDHS= Ethiopia Demographic and Health Survey

Balance diagnostics

Propensity score balance

Figure 3 presents the density plot of women in the treatment group (dashed lines) and the control group (solid lines) before and after weighting. It reveals that an adequate balance of the propensity score distribution between the treatment groups after weighting (Figure 3).

Covariate balance

After weighting adjustment, standardized differences of covariates were all less than 0.1 (10%), showing comparability between women with and without short birth interval (Supplementary Material II).

Treatment effect estimation

The prevalence of short birth interval in Ethiopia was 45.8% (95% CI: 42.91–48.62). Table 2 presents the estimated effects of short birth interval on neonatal, infant, and under-five mortality. The adjusted estimated odds of neonatal mortality were 85% higher among women who experienced short birth interval (AOR=1.85, 95% CI=1.19, 2.89) than those who did not. Similarly, the odds of infant mortality were two times higher (AOR=2.16, 95% CI=1.49, 3.11) among women who experienced short birth interval compared with women who did not. The odds of under-five child mortality were two times (AOR=2.26, 95% CI= 1.60, 3.17) higher among women who were exposed to short birth interval compared with women who were not.

Table 2 The effect of short birth interval on neonatal, infant, and under-five mortality in Ethiopia, EDHS 2016

Treatment variable	Neonatal mortality		AOR (95% CI)
	No (%)*	Yes (%)*	
Short birth interval			
No	4166 (54.5)	95 (46.1)	Ref
Yes	4031 (45.5)	156 (53.9)	1.85 (1.19, 2.89)
	Infant mortality		
Short birth interval	No (%)	Yes (%)	
No	4126 (54.9)	135 (40.5)	Ref
Yes	3906 (45.1)	281 (59.5)	2.16 (1.49, 3.11)
	Under-Five mortality		
Short Birth interval	No (%)	Yes (%)	
No	4099 (55.1)	162 (39.3)	Ref
Yes	3855 (44.9)	332 (60.7)	2.26 (1.60, 3.17)

EDHS= Ethiopia Demographic and Health Survey; AOR= Adjusted Odds Ratio; CI= Confidence Interval; Ref= reference group; (%)*=percentage are weighted

Discussion

To our knowledge, this study provides the first comprehensive assessment of the effect of short birth interval on neonatal, infant, and under-five mortality using the WHO recommendation to define short birth interval and applying rigorous analytical techniques to adjust for potential confounders. This study provides evidence that short birth interval is associated with neonatal, infant, and under-five mortality in Ethiopia. These findings will help policy makers and program planners formulate targeted interventions to increase birth intervals and contribute to achieving the GTPE and SDGs target of reducing neonatal, infant, and under-five mortality. [16 15]

In this current study, short birth interval was found to be associated with higher odds of neonatal mortality. This finding is consistent with evidence from the previous studies[23 25 63-66] which have shown a higher risk of neonatal mortality among women with a short birth interval. However, the definition of short birth interval (i.e., <33 months) used in the current study was in line with the WHO definition and longer than those used in previous studies (i.e., ranges from <18 to 24 months). Short birth interval could result in adverse neonatal child health outcomes, such as death, by causing maternal nutritional depletion, specifically folate depletion.[67 68] The maternal nutritional depletion hypothesis states that a short birth-to-pregnancy/birth interval worsens the mother's nutritional status because of inadequate time to recover from the physiological stresses of the subsequent pregnancy.[69] This may compromise maternal nutritional status and ability to support fetal growth, which could result in fetal malnutrition and increased risk of infection and death during childhood.[67] Women with short birth interval may also be less likely to attend postnatal care, which is vital for early detection and treatment of neonatal and maternal health problems. Evidence has shown that the majority of mothers and newborns in low- and middle-income countries do not receive optimal postnatal care[70], yet close to half of the newborn deaths occurred within the first 24 hours after birth, a critical time where mothers and their babies should get their first postnatal care.[71]

Our study found that infant mortality was two times higher among women who experienced short birth interval compared with women who did not. Our finding was consistent with evidence from Ethiopia,[18 32] Kenya,[72 73] Nepal,[74] and Iran[75] although the cut-off point for short birth interval in the current study was longer than the previous studies. The abovementioned previous studies also documented that the risk of infant mortality was higher among women who experienced short birth interval compared with women who did not. One of the possible reasons for the effect of short birth interval on infant mortality could be low maternal motivation to breastfeed (for example, if the pregnancy was unintended).[76] Maternal perception of being undernourished due to a short birth interval may also influence her infant feeding choices, such as the duration and intensity of breastfeeding and supplemental feeding of the infant. This could in turn affect infants' nutritional status, their resistance to infection, and may expose them to death.[76-79] The abovementioned links between short birth interval and neonatal mortality also apply to infant mortality.

Short birth interval doubled the odds of under-five mortality compared with non-short birth interval. Despite not using the WHO recommendation[1] of less than 33 months to define short birth interval, the existing literature[24 30 63 64 80] also supported our finding. The likely mechanism through which short birth interval affects under-five mortality could be competition between closely spaced siblings for limited household resources, maternal attention, and cross-infection.[76] Moreover, children born within a short birth interval may not receive their vaccination at all or complete their booster series, which is one of the risk factors that exposed children to the infectious disease and its associated death.[81-83] Women with short birth interval could be burdened with caring for highly dependent children[77] and other domestic activities. As a result, they may lack the time and motivation to take children to the health facility for vaccination and other services.

The results of this study need to be interpreted within the limitations of the observational study design. Due to the cross-sectional nature of the study, temporal associations between short birth interval and neonatal, infant, and under-five mortality may not be established. The second limitation of our study could be associated with the nonrandomized design of the study. Propensity scores based analysis, IPTW, cannot account for unknown confounders in the same way that a randomised trial can. As a result, the effect of residual confounders may not be avoided. However, the application of IPTW mimics a randomized clinical trial by matching two comparison groups using a conditional probability of receiving exposure (short birth interval in this case) given a set of covariates. The study has also additional strengths, such as using data from a nationally representative survey with large sample size. The application of DAGs,[48 49 84] a graphical tool used to identify minimum adjustment sets, which defined the set of explanatory variables for the propensity scores model was another strength of this study.

Conclusion

This study provides evidence that short birth interval has a significant effect on neonatal, infant, and under-five mortality in Ethiopia. Interventions aiming to reduce neonatal, infant, and under-five mortality in Ethiopia should target the prevention of short birth interval. These could be achieved through creating awareness of the optimum birth interval and the negative impacts of shorter birth intervals on the health of children. Further expanding the availability and accessibility of family planning services also help women achieve optimum birth interval. Birth interval counseling as per the WHO recommendation should be integrated into the maternal and child health services as part of the child survival intervention.

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Contributors

All authors (DMS, CC, EGH, and DL) contributed to the design of the study and the interpretation of data. DMS performed the data analysis and drafted the manuscript. All authors (DMS, CC, EGH, and DL) read, critically revised, and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Ethics approval

The 2016 EDHS was approved by the National Research Ethics Review Committee of Ethiopia (NRERC) and ICF Macro International. Permission from The DHS Program was obtained to use the 2016 EDHS data for further analysis. This analysis was also approved by The University of Newcastle Human Research Ethics Committee (H-2018-0332).

Consent for publication

Not required

Provenance and peer review

Not commissioned; externally peer reviewed.

Data availability statement

The dataset is available from The DHS Program repository at the following link: https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0.

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583 # Figure Legend

584 **Figure 1** Direct Acyclic Graph (DAG) used to select controlling variables

585 M_age_atBirth_chil= Maternal age at birth of the index child; M_Edu= Maternal education;
586 M_Occu= Maternal Occupation; H_Educ= Husband education; H_Occup= Husband
587 occupation; Birth_wt=Birth weight; Total_Prec_child=Total number of preceding child;
588 Respiratory_infn= respiratory infection; Prev_Chi_Survival=Previous child survival;
589 Multiple_preg= Multiple pregnancy; ANC=Antenatal care; PNC=Postnatal care;
590 TT_vaccin=Tetanus toxoid vaccination status; SBI= Short birth interval; NM=Neonatal
591 mortality; IM=Infant mortality; U5M=Under-five mortal

592 **Figure 2** Schematic presentation of the overall steps followed in the analysis

593 **Figure 3** Balance of propensity scores before and after weighting across treatment and
594 comparison groups

595 PS= propensity score

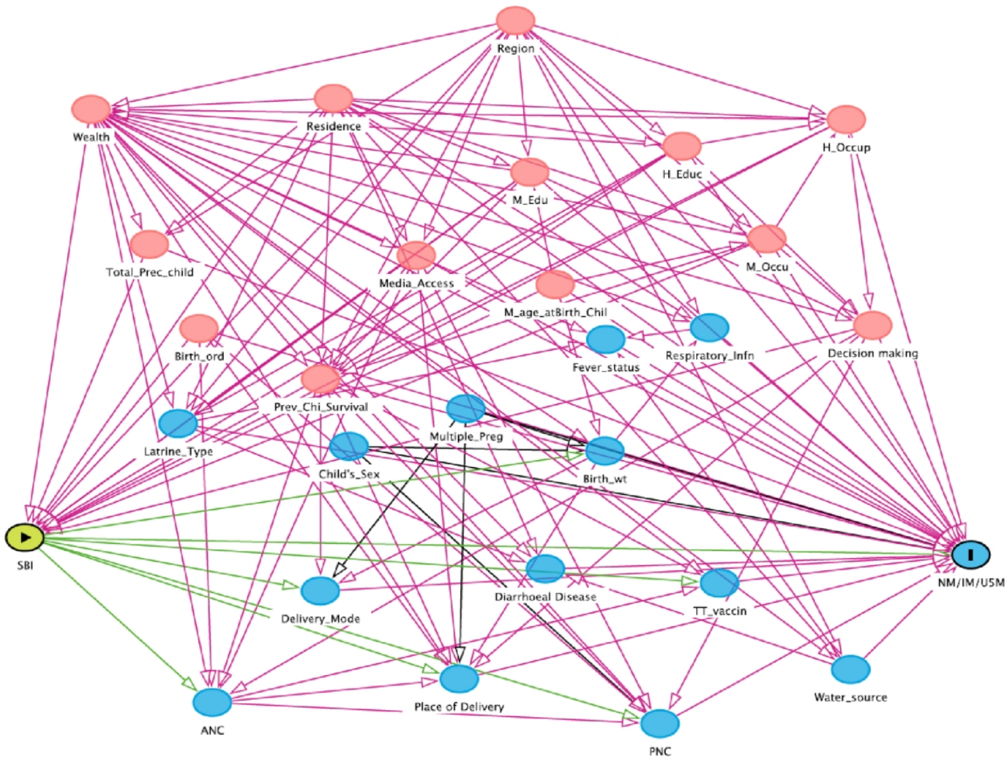

Figure 1 Direct Acyclic Graph (DAG) used to select controlling variables

157x118mm (300 x 300 DPI)

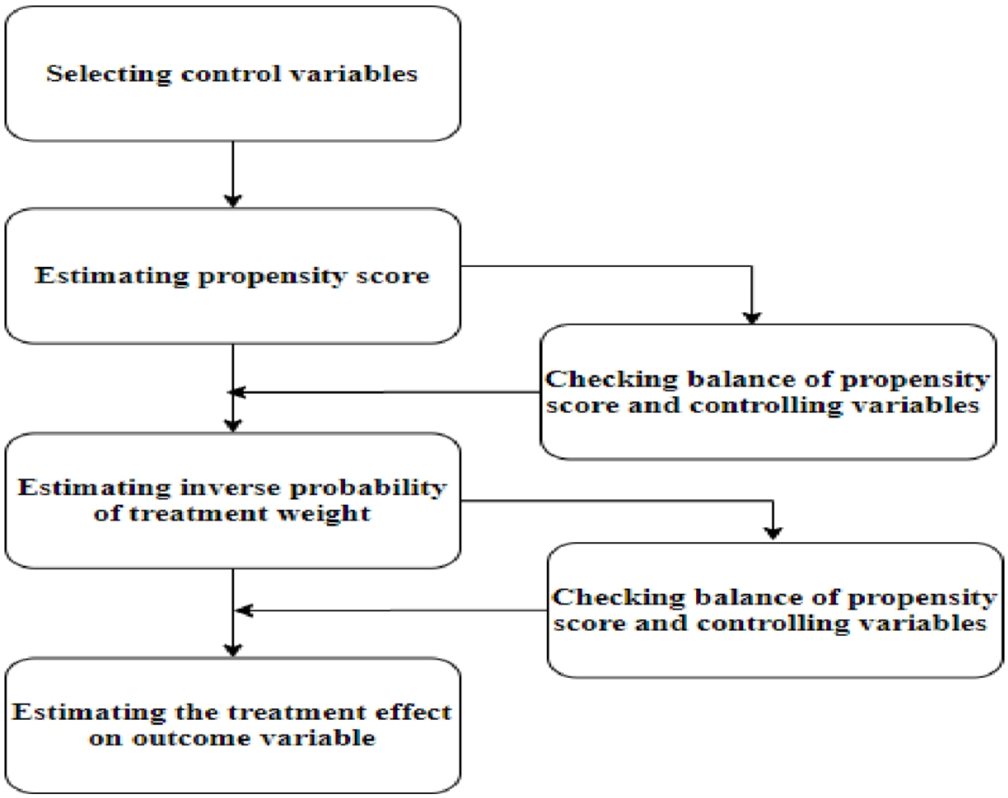

Figure 2 Schematic presentation of the overall steps followed in the analysis

115x90mm (300 x 300 DPI)

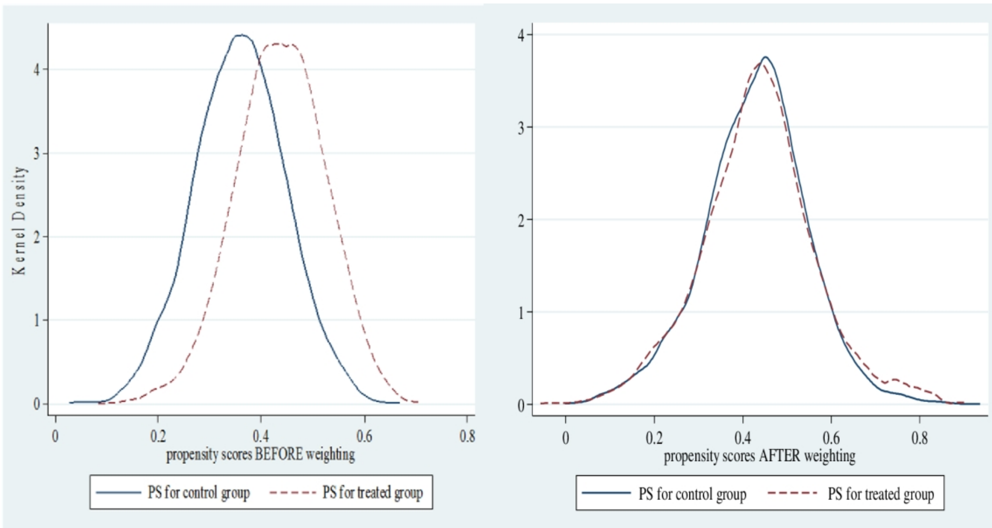

Figure 3 Balance of propensity scores before and after weighting across treatment and comparison groups; PS=propensity score

165x87mm (300 x 300 DPI)

Supplemental Material I

Table 1 Variables included in Direct Acyclic Graph

Category	Variables	Definition
Maternal background characteristics	Maternal age at birth of the index child (in years)	Maternal age at birth of the index child, which was considered as a continuous variable. It was also categorized the descriptive section of the results (1=≤19, 2= 20-24, 3=25-29, 4=30-34, and 5= ≥35).
	Educational level	Maximum educational level (1= Uneducated, 2=Primary and 3=Secondary+)
	Employment status	Maternal employment status (1=Not Employed; 2=Employed))
	Place of residence	Place of residence (1=Urban; 2=Rural)
	Region	Region of residence (1=Tigray, 2=Afar, 3=Amhara, 4=Oromia, 5=Somali, 6=Benishangul-Gumuz, 7=SNNPR*, 8=Gambella, 9=Harari, 10=Addis Ababa, 11=Dire Dawa) *SNNPR= Southern Nations, Nationalities, and Peoples' Region
	Decision making autonomy	Coded as 'yes' if the women were involved in all decisions regarding their own health care, major household purchases and visits to her family or relatives (1=Yes, 2=No).
Husband background characteristics	Husband's education	Maximum educational level of the husband (1= Uneducated, 2= Primary, 3= Secondary+)
	Husband's occupation	1= Not employed, 2=Employed
Household characteristics	Access to media	1=Access to media, 2= Have no access to media
	Wealth index	The wealth index provided with the dataset was used. DHS program provides a composite index of household amenities based on the principal component analysis (PCA) and classified the population into quintiles: (1st quintile (Poorest); 2nd quintile; 3rd quintile; 4th quintile and 5th quintile (Richest). A quintile is used as a measure of its relative socioeconomic level (i.e., 1=Poorest; 2=Poorer; 3=Middle; 4=Richer; 5=Richest)

Maternal health status and healthcare-related variables	Antenatal care	Women's antenatal care utilization categorized as 1=No visit, 2=At least one visit, 3= ≥ Four visits
	Place of delivery	1= Health facilities, 2=Home
	Postnatal care	Women received check-up at least once within 48 hours after delivery by a skilled provider; categorized as 1=Yes, 2=No
	TT vaccination	Women received at least two doses of the immunization during pregnancy (1=Yes, 2=No)
Neonatal, infant and child characteristics	Sex	Child sex (1=Male, 2=Female)
	Multiple pregnancy	1=Yes, 2=No
	Birth weight	1=Below average, 2=Average, 3=Above average
	Mode of delivery	1= Caesarean section, 2= Non caesarean section
	Survival status of the preceding child	1= Yes, 2=No
	Total number of children born before the index child	Total number of children born before the index child was considered as a continuous variable. For the descriptive statistics, this variable was categorized into 1= ≤2, 2= 3-4, and 3= ≥5. This was done after checking for the linearity assumption with the log-odds of short birth interval, which is a binary response variable. Multicollinearity was also checked among the exposure variables using the variance inflation factor (VIF). When the values of VIF were lower than 10, then the collinearity problem was considered unlikely. The VIF for birth order was 18.15 and for the total number of children born before the index child was 16.26, which indicates the presence of collinearity. Therefore, we removed the variable birth order from the model and the VIF became less than 3 for each variable included in the model.
	Birth order	Birth order is the order number of the births from first to last. Twins are given the same birth order, but the birth order of a child born after twins will be the total number of births preceding plus one.
	Diarrhoeal Disease	1= Yes, 2=No
	Fever	1=Yes, 2=No
	Respiratory infection	1=Yes, 2=No

Environmental factors	Source of water	1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well).
	Latrine facility	1 = Improved (access to flush toilet, ventilated improved pit latrine, traditional pit latrine with a slab, or composting toilet and does not share this facility with other households), 2=unimproved.

Supplemental Material II

Table 2 Standardized difference before and after weighting the propensity score

Variable	Standardized difference	
	Before weighting	After weighting
Maternal age at the birth of the index child (in years)*	-0.392	0.022
Maternal education		
Uneducated	0.178	0.009
Primary	-0.112	-0.017
Maternal occupation		
Not employed	0.128	0.005
Husband education		
Uneducated	0.148	0.012
Primary	-0.041	0.003
Husband occupation		
Not employed	0.159	0.006
Wealth		
Poorest	0.332	-0.004
Poorer	-0.002	0.008
Middle	-0.070	0.005
Richer	-0.061	-0.007
Total number of preceding child*	0.207	-0.006
Survival status of preceding child		
Yes	-0.029	-0.004
Residence		
Urban	-0.239	-0.006
Region		
Tigray	-0.207	0.004
Afar	0.186	0.008
Amhara	-0.282	0.014
Oromia	-0.006	0.003
Somali	0.402	-0.003
Benishangul-Gumuz	0.061	-0.006
SNNPR**	-0.069	-0.005
Gambella,	-0.087	-0.009
Harari	-0.001	-0.009
Addis Ababa	-0.180	0.014
Access to mass media		
Yes	-0.201	-0.002
Decision making autonomy		
No	0.067	-0.009

*Maternal age at the birth of the index child (in years) and total number of the preceding child were considered as continuous variables; **SNNPR= Southern Nations, Nationalities, and Peoples' Region

STROBE 2007 (v4) Statement—Checklist of items for the study

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4 , 5, & 6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7, & 8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6, 7, & 8
Bias	9	Describe any efforts to address potential sources of bias	*8, 9, & 10*
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6, 7, & 8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8, 9, 10, & 11
		(*b*) Describe any methods used to examine subgroups and interactions	8, 9, 10, & 11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	8, 9, 10, & 11
		(*e*) Describe any sensitivity analyses	8, 9,, 10, & 11

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	11, 12, & 13
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	11, 12, &13
		(b) Indicate number of participants with missing data for each variable of interest	N/A
Outcome data	15*	Report numbers of outcome events or summary measures	9 and 11, 12, & 13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	15 & 16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17 & 18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15, 16, 17, & 18
Generalisability	21	Discuss the generalisability (external validity) of the study results	15, 16, 17, & 18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	19

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.