

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

BMJ Open

BMJ Open

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

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-047892
Article Type:	Original research
Date Submitted by the Author:	11-Dec-2020
Complete List of Authors:	Shifti, Desalegn Markos; Saint Paul's Hospital Millennium Medical College; The University of Newcastle Faculty of Health and Medicine, School of Medicine Chojenta, Catherine; The University of Newcastle Faculty of Health and Medicine Holliday, Elizabeth; The University of Newcastle Faculty of Health and Medicine Loxton, Deborah; The University of Newcastle Faculty of Health and Medicine
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, Maternal medicine < OBSTETRICS, Community child health < PAEDIATRICS





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

3
4
5
6
7
/
8
9
10
11
12
13
14
15
16 17
18
19
20
21
22
22
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
55 54
55
56
50 57
58
59
60

The effects of short birth interval on neonatal, infant and under-five child mortality in Ethiopia Desalegn Markos Shifti^{1,2,*}, Catherine Chojenta², Elizabeth G. Holliday³, Deborah Loxton² Affiliation

⁵ ¹Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

⁶ ²Priority Research Centre for Generational Health and Ageing, School of Medicine and

- 7 Public Health, University of Newcastle, New South Wales, Australia
- 8 ³Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health,

ê jik

9 University of Newcastle, New South Wales, Australia

10

11 *Corresponding author

12 <u>desalegnmarkos@gmail.com, desalegnmarkos.shifti@uon.edu.au</u>

BMJ Open

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.

36 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 studies²⁻⁴ 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,⁶⁷ low birth weight,⁶⁷ small size for gestational age,⁶ congenital anomalies,⁸⁹ 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.⁵¹⁶

Page 5 of 36

BMJ Open

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 studies¹⁷⁻¹⁹ ²³ ²⁴ ²⁷⁻³¹ did not use the World Health Organization (WHO) recommended¹ 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.¹⁹²⁴ One of the studies using national data¹⁹ 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 mortality³⁸⁻⁴¹ 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.

86 Methods

87 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.

99 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

Page 7 of 36

BMJ Open

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 3.0⁴⁶ 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.

BMJ Open

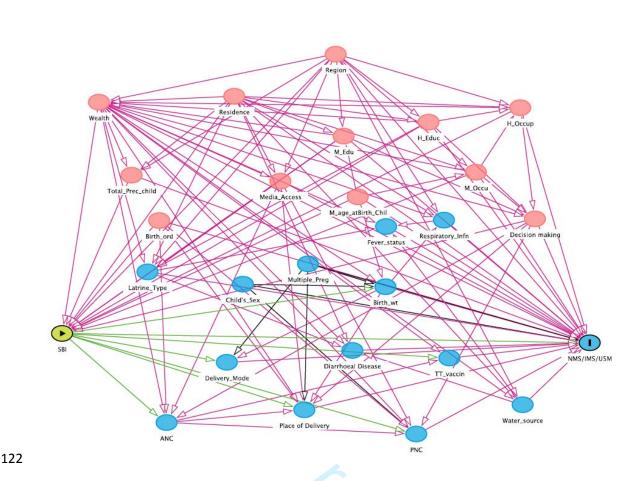


Figure 1 Direct Acyclic Graph (DAG) used to select controlling variables

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

Page 9 of 36

BMJ Open

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:

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

BMJ Open

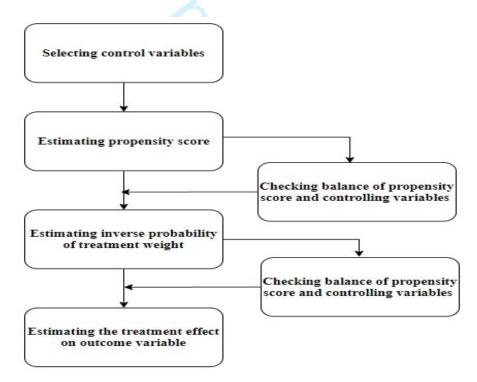
where $\overline{x}_{treatment}$ and $\overline{x}_{control}$ denote the sample mean of the covariate in treated and untreated subjects, respectively and $s_{treatment}^2$ and $s_{control}^2$ denote the corresponding sample variances of the covariate. The standardized difference^{52 53} for a dichotomous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

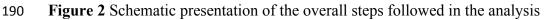
$$d = \frac{(\hat{p}_{treatment} - \hat{p}_{control})}{\sqrt{\frac{\hat{p}_{treatment}(1 - \hat{p}_{treatment}) + \hat{p}_{control}(1 - \hat{p}_{control})}{2}}$$

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.





Patient and public involvement

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

58 194

Results

Respondents' characteristics

197 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 \geq 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-ates and five mortality had slightly higher rates among wealthier families, although numbers were small.

 BMJ Open

Variable	Neonatal Mortality		P-value	Infant Mortality		P-value	Under-five	Mortality	P-value
	No (%)	Yes (%)		No (%)	Yes (%)		No (%)	Yes (%)	1
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)	1
30-34	1836 (22.7)	59 (22.6)		1802 (22.9)	93 (21.0)		1781 (22.7)	114 (22.9)	1
≥35	1533 (19.9)	56 (26.8)		1515 (20.0)	74 (21.2)		1500 (20.1)	89 (20.7)	1
Maternal education			0						
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 preseding									
Total number of preceding child									
<u>≤2</u>	2627 (31.0)	57 (27.0)	< 0.001	2591 (31.0)	93 (27.1)	< 0.001	2575 (31.1)	109 (26.4)	< 0.00
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)	< 0.00
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)	10-	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).

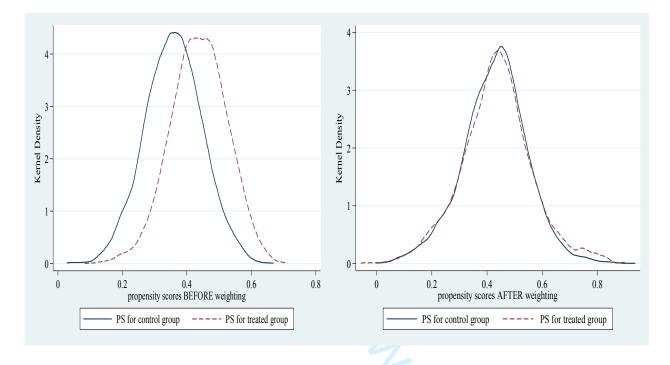


Figure 3 Balance of propensity scores before and after weighting across treatment and comparison groups

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

BMJ Open

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	Neonat	Neonatal mortality	
	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)
	Infan	t 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-H	ive 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

BMJ Open

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 underfive 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-topregnancy/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 care⁶⁵, 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 Iran⁷⁰ 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

BMJ Open

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 recommendation¹ of less than 33 months to define short birth interval, the existing literature²³ 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 children⁷² 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

Page 19 of 36

BMJ Open

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.

Author affiliations

¹ Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

²Priority Research Centre for Generational Health and Ageing, School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia

³Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health, University of Newcastle, Newcastle, New South Wales, Australia

Acknowledgment

We are grateful to The DHS Program for allowing us to use the Ethiopia Demographic and Health Survey (EDHS) data for further analysis.

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.

Funding

The authors received no specific funding for this work.

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: <u>https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0</u>.

References

- World Health Organization. Report of a WHO Technical Consultation on Birth Spacing. Geneva, Switzerland 13-15 June 2005.
- Shifti DM, Chojenta C, G. Holliday E, et al. Individual and community level determinants of short birth interval in Ethiopia: A multilevel analysis. *PloS one* 2020;15(1):e0227798.
- Shifti DM, Chojenta C, Holliday EG, et al. Application of geographically weighted regression analysis to assess predictors of short birth interval hot spots in Ethiopia. *PloS* one 2020;15(5):e0233790.
- 4. Shifti DM, Chojenta C, Holliday EG, et al. Socioeconomic inequality in short birth interval in Ethiopia: a decomposition analysis. *BMC public health* 2020;20(1):1-13.
- Central Statistical Agency (CSA) [Ethiopia] and ICF. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF 2016.
- 6. Grisaru-Granovsky S, Gordon E-S, Haklai Z, et al. Effect of interpregnancy interval on adverse perinatal outcomes—a national study. *Contraception* 2009;80(6):512-18.

- Adam I, Ismail MH, Nasr AM, et al. Low birth weight, preterm birth and short interpregnancy interval in Sudan. *The Journal of Maternal-Fetal & Neonatal Medicine* 2009;22(11):1068-71.
- 8. Chen I, Jhangri GS, Chandra S. Relationship between interpregnancy interval and congenital anomalies. *American journal of obstetrics and gynecology* 2014;210(6):564. e1-8.
- 9. Kwon S, Lazo-Escalante M, Villaran M, et al. Relationship between interpregnancy interval and birth defects in Washington State. *Journal of Perinatology* 2012;32(1):45.
- Cheslack-Postava K, Liu K, Bearman PS. Closely spaced pregnancies are associated with increased odds of autism in California sibling births. *Pediatrics* 2011;127:246-53.
- 11. DaVanzo J, Razzaque A, Rahman M, et al. The effects of birth spacing on infant and child mortality, pregnancy outcomes, and maternal morbidity and mortality in Matlab, Bangladesh. *Technical Consultation and Review of the Scientific Evidence for Birth Spacing* 2004.
- 12. DaVanzo J, Hale L, Razzaque A, et al. Effects of interpregnancy interval and outcome of the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. BJOG: An International Journal of Obstetrics & Gynaecology 2007;114(9):1079-87.
- Gonzalez RM, Gilleskie D. Infant mortality rate as a measure of a country's health: a robust method to improve reliability and comparability. *Demography* 2017;54(2):701-20.
- Reidpath DD, Allotey P. Infant mortality rate as an indicator of population health. *Journal of Epidemiology & Community Health* 2003;57(5):344-46.
- UN. Transforming our World: The 2030 Agenda For Sustainable Development Goal (A/RES/70/1). 2015.
- 16. National Planning Commission. Federal Democratic Republic of Ethiopia: Growth and Transformation Plan II (GTP II) (2015/16-2019/20). *Addis Ababa, Ethiopia* 2016.

3
4
5
6
7
/
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
33
34
35
36
36 37
38
39
40
41
42
43
44
45
46
47
48
40 49
50
51
52
53
54
55
56
57
58
59

60

17. Abate MG, Angaw DA, Shaweno T. Proximate determinants of infant mortality in Ethiopia,
2016 Ethiopian demographic and health surveys: results from a survival analysis.
Archives of Public Health 2020;78(1):1-10.

- Weldearegawi B, Melaku YA, Abera SF, et al. Infant mortality and causes of infant deaths in rural Ethiopia: a population-based cohort of 3684 births. *BMC public health* 2015;15(1):770.
- Wolde HF, Gonete KA, Akalu TY, et al. Factors affecting neonatal mortality in the general population: evidence from the 2016 Ethiopian Demographic and Health Survey (EDHS)—multilevel analysis. *BMC research notes* 2019;12(1):610.
- 20. Roro EM, Tumtu MI, Gebre DS. Predictors, causes, and trends of neonatal mortality at Nekemte Referral Hospital, east Wollega Zone, western Ethiopia (2010–2014). Retrospective cohort study. *PloS one* 2019;14(10):e0221513.
- 21. Seid SS, Ibro SA, Ahmed AA, et al. Causes and factors associated with neonatal mortality in neonatal intensive care unit (NICU) of Jimma University medical center, Jimma, south West Ethiopia. *Pediatric health, medicine and therapeutics* 2019;10:39.
- 22. Wakgari N, Wencheko E. Risk factors of neonatal mortality in Ethiopia. *Ethiopian Journal of Health Development* 2013;27(3):192-99.
- Fikru C, Getnet M, Shaweno T. Proximate Determinants of Under-Five Mortality in Ethiopia: Using 2016 Nationwide Survey Data. *Pediatric Health, Medicine and Therapeutics* 2019;10:169.
- 24. Mekonnen Y, Tensou B, Telake DS, et al. Neonatal mortality in Ethiopia: trends and determinants. *BMC public health* 2013;13(1):483.
- 25. Limaso AA, Dangisso MH, Hibstu DT. Neonatal survival and determinants of mortality in Aroresa district, Southern Ethiopia: a prospective cohort study. *BMC pediatrics* 2020;20(1):33.

- 26. Yaya Y, Eide KT, Norheim OF, et al. Maternal and neonatal mortality in south-west Ethiopia: estimates and socio-economic inequality. *PloS one* 2014;9(4):e96294.
- 27. Gebretsadik S, Gabreyohannes E. Determinants of under-five mortality in high mortality regions of Ethiopia: an analysis of the 2011 Ethiopia Demographic and Health Survey data. *International Journal of Population Research* 2016;2016.
- 28. Negera A, Abelti G, Bogale T, et al. An analysis of the trends, differentials and key proximate determinants of infant and under-five mortality in Ethiopia. Further Analysis of the 2000, 2005, and 2011 Demographic and Health Surveys. *DHS Further Analysis Reports No 79 Calverton, Maryland, USA: ICF International* 2013.
- 29. Tariku L. Effects of preceding birth intervals on child mortality in Ethiopia; Evidence from the Demographic and Health Surveys, 2016. *Epidemology International Journal* 2019;3(1).
- 30. Hailemariam A, Tesfaye M. Determinants of infant and early childhood mortality in a small urban community of Ethiopia: a hazard model analysis. *The Ethiopian Journal of Health Development (EJHD)* 1997;11(3).
- Dadi AF. A systematic review and meta-analysis of the effect of short birth interval on infant mortality in Ethiopia. *PloS one* 2015;10(5):e0126759.
- 32. Sahle-Mariam Y, Berhane Y. Neonatal mortality among hospital delivered babies in Addis Ababa, Ethiopia. *The Ethiopian Journal of Health Development (EJHD)* 1997;11(3)
- 33. Kolobo HA, Chaka TE, Kassa RT. Determinants of neonatal mortality among newborns admitted to neonatal intensive care unit Adama, Ethiopia: A case–control study. *Journal of Clinical Neonatology* 2019;8(4):232.
- 34. Bogale TN, Worku AG, Bikis GA, et al. Why gone too soon? Examining social determinants of neonatal deaths in northwest Ethiopia using the three delay model approach. *BMC pediatrics* 2017;17(1):216.

- 35. Woldeamanuel BT. Statistical analysis of neonatal mortality: a case study of Ethiopia. *Journal of Pregnancy and Child Health* 2018;5(2):1-11.
- 36. Asefa M, Drewett R, Tessema F. A birth cohort study in South-West Ethiopia to identify factors associated with infant mortality that are amenable for intervention. *Ethiopian Journal of Health Development* 2000;14(2):161-68.
- 37. Muluye S, Wencheko E. Determinants of infant mortality in Ethiopia: A study based on the 2005 EDHS data. *Ethiopian Journal of Health Development* 2012;26(2):72-77.
- 38. Deribew A, Tessema F, Girma B. Determinants of under-five mortality in Gilgel gibe field research center, Southwest Ethiopia. *Ethiopian Journal of Health Development* 2007;21(2):117-24.
- 39. Bedada D. Determinant of under-five child mortality in Ethiopia. *American Journal of Theoretical and Applied Statistics* 2017;6(4):198-204.
- 40. Ayele DG, Zewotir TT. Comparison of under-five mortality for 2000, 2005 and 2011 surveys in Ethiopia. *BMC public health* 2016;16(1):930.
- 41. Shamebo D, Sandström A, Muhe L, et al. The Butajira project in Ethiopia: a nested casereferent study of under-five mortality and its public health determinants. *Bulletin of the World Health Organization* 1993;71(3-4):389.
- 42. Croft TN, Aileen M. J. Marshall, Courtney K. Allen, et al. Guide to DHS Statistics. *Rockville, Maryland, USA: ICF* 2018.
- 43. ICF International. Demographic and Health Survey Interviewer's Manual. *MEASURE DHS Basic Documentation No 2 Calverton, Maryland, USA: ICF International* 2012
- 44. Hailu D, Gulte T. Determinants of Short Interbirth Interval among Reproductive Age Mothers in Arba Minch District, Ethiopia. *International journal of reproductive medicine* 2016;2016 doi: 10.1155/2016/6072437

- 45. Yohannes S, Wondafrash M, Abera M, et al. Duration and determinants of birth interval among women of child bearing age in Southern Ethiopia. *BMC pregnancy and childbirth* 2011;11(1):38.
- 46. Textor J, van der Zander B, Gilthorpe MS, et al. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *International journal of epidemiology* 2016;45(6):1887-94.
- 47. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika* 1983;70(1):41-55.
- 48. Garrido MM, Kelley AS, Paris J, et al. Methods for constructing and assessing propensity scores. *Health services research* 2014;49(5):1701-20.
- 49. Austin PC. A tutorial and case study in propensity score analysis: an application to estimating the effect of in-hospital smoking cessation counseling on mortality. *Multivariate behavioral research* 2011;46(1):119-51.
- 50. Guo S, Fraser MW. Propensity score analysis: Statistical methods and applications: SAGE publications 2014.
- 51. Deb S, Austin PC, Tu JV, et al. A review of propensity-score methods and their use in cardiovascular research. *Canadian Journal of Cardiology* 2016;32(2):259-65.
- Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. *Multivariate behavioral research* 2011;46(3):399-424.
- 53. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Statistics in medicine* 2015;34(28):3661-79.

- 54. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates between treatment groups in propensity-score matched samples. *Statistics in medicine* 2009;28(25):3083-107.
- 55. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched sampling methods that incorporate the propensity score. *The American Statistician* 1985;39(1):33-38.
- 56. Xu S, Ross C, Raebel MA, et al. Use of stabilized inverse propensity scores as weights to directly estimate relative risk and its confidence intervals. *Value in Health* 2010;13(2):273-77.
- 57. DuGoff EH, Schuler M, Stuart EA. Generalizing observational study results: applying propensity score methods to complex surveys. *Health services research* 2014;49(1):284-303.
- 58. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years mortality and nutritional status in developing countries: evidence from the demographic and health surveys. *International Journal of Gynecology & Obstetrics* 2005;89:S7-S24.
- 59. Kozuki N, Walker N. Exploring the association between short/long preceding birth intervals and child mortality: using reference birth interval children of the same mother as comparison. *BMC public health* 2013;13(S3):S6.
- 60. Rahman MM, Abidin S. Factors affecting neonatal mortality in Bangladesh. *Journal of Health Management* 2010;12(2):137-52.
- Ezeh OK, Agho KE, Dibley MJ, et al. Determinants of neonatal mortality in Nigeria: evidence from the 2008 demographic and health survey. *BMC Public Health* 2014;14(1):521.

- 62. Conde-Agudelo A, Rosas-Bermudez A, Castaño F, et al. Effects of birth spacing on maternal, perinatal, infant, and child health: a systematic review of causal mechanisms. *Studies in family planning* 2012;43(2):93-114.
- 63. Rousso D, Panidis D, Gkoutzioulis F, et al. Effect of the interval between pregnancies on the health of mother and child. *European Journal of Obstetrics and Gynecology and Reproductive Biology* 2002;105(1):4-6.
- 64. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or closely spaced pregnancies. *The Journal of nutrition* 2003;133(5):1732S-36S.
- 65. WHO. Maternal, newborn, child and adolescent health: Postnatal care. [cited 11 July 2020]. Available from: <u>https://www.who.int/maternal_child_adolescent/topics/newborn/postnatal_care/en/</u> accessed 2020 11 July
- 66. WHO, USAID, MCHIP, et al. Postnatal Care for Mothers and Newborns: Highlights from the World Health Organization 2013 Guidelines. 2015
- 67. Omariba DWR, Beaujot R, Rajulton F. Determinants of infant and child mortality in Kenya: an analysis controlling for frailty effects. *Population Research and Policy Review* 2007;26(3):299-321.
- 68. Fotso JC, Cleland J, Mberu B, et al. Birth spacing and child mortality: an analysis of prospective data from the Nairobi urban health and demographic surveillance system. *Journal of biosocial science* 2013;45(6):779-98.
- 69. Lamichhane R, Zhao Y, Paudel S, et al. Factors associated with infant mortality in Nepal: a comparative analysis of Nepal demographic and health surveys (NDHS) 2006 and 2011. BMC public health 2017;17(1):53.
- 70. Sharifzadeh GR, Namakin K, Mehrjoufard H. An Epidemiological study on Infant Mortality and factors affecting it in Rural Areas of Birjand, Iran. 2008.

2 3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
54
55
56
57
58
59

60

71. Boerma JT, Bicego GT. Preceding birth intervals and child survival: searching for pathways of influence. *Studies in family planning* 1992;23(4):243-56.

- 72. Dewey KG, Cohen RJ. Does birth spacing affect maternal or child nutritional status? A systematic literature review. *Maternal & child nutrition* 2007;3(3):151-73.
- 73. Stuebe A. The risks of not breastfeeding for mothers and infants. *Reviews in obstetrics and* gynecology 2009;2(4):222.
- 74. Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. *The Lancet* 2016;387(10017):475-90.
- 75. Biradar R, Patel KK, Prasad JB. Effect of birth interval and wealth on under-5 child mortality in Nigeria. *Clinical Epidemiology and Global Health* 2019;7(2):234-38.
- 76. Andre FE, Booy R, Bock HL, et al. Vaccination greatly reduces disease, disability, death and inequity worldwide. *Bulletin of the World health organization* 2008;86:140-46.
- 77. Innis BL, Snitbhan R, Kunasol P, et al. Protection against hepatitis A by an inactivated vaccine. *Jama* 1994;271(17):1328-34.
- 78. Arevshatian L, Clements C, Lwanga S, et al. An evaluation of infant immunization in Africa: is a transformation in progress? *Bulletin of the World Health Organization* 2007;85:449-57.
- 79. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC medical research methodology* 2008;8(1):70.
- 80. Attia JR, Jones MP, Hure A. Deconfounding confounding part 1: traditional explanations. *The Medical Journal of Australia* 2017;206(6):244-45.
- Attia JR, Oldmeadow C, Holliday EG, et al. Deconfounding confounding part 2: using directed acyclic graphs (DAGs). *Medical Journal of Australia* 2017;206(11):480-83.

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

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Supplemental Material II

 Table 1 Variables included in Direct Acyclic Graph

Category	Variables	Definition		
Maternal background	Age at first marriage	The age of the woman at their first marriage, which was considered		
characteristics		as a continuous variable		
	Age at birth of the index	The age of the woman during the time she gave birth to the index		
	Neonate/Infant/child	neonate, which was considered as a continuous variableMaximum educational level (1= Uneducated, 2=Primary and 3=Secondary+ (or Educated and Uneducated)		
	Educational level			
	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 visit		
		to her family or relatives (1=Yes, 2=No).		
Husband background	Husband's education	Maximum educational level of the husband (1= Uneducated, 2=		
characteristics		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 progra		
		provides a composite index of household amenities based on the		
		principal component analysis (PCA) and classified the population in		

		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	Antenatal care	Women's antenatal care utilization categorized as no visit, at least one visit, \geq four visits
variables	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	Sex	1=Male, 2=Female
characteristics	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 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 remove

BMJ Open

Diarrhoeal Disease Fever Respiratory infection Source of water Latrine facility	are given the same birth order, but the birth order of a child born afte twins will be the total number of births preceding plus one. 1=Yes, 2=No 1=Yes, 2=No 1=Yes, 2=No 1=Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well). 1 = Improved (access to flush toilet, ventilated improved pit latrine, traditional pit latrine with a slab, or composting toilet and does not
Fever Respiratory infection Source of water	1=Yes, 2=No 1=Yes, 2=No 1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well). 1 = Improved (access to flush toilet, ventilated improved pit latrine,
Respiratory infection Source of water	1=Yes, 2=No 1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well). 1 = Improved (access to flush toilet, ventilated improved pit latrine,
Source of water	 1= Piped water, 2= Other improved (protected spring and well, and rain water), 3= Unimproved (river, pond, unprotected spring and well). 1 = Improved (access to flush toilet, ventilated improved pit latrine,
Latrine facility	1 = Improved (access to flush toilet, ventilated improved pit latrine,
	share this facility with other households), 2=unimproved.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Supplemental Material III

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	0.010		
Access to mass media	0.170	0.015		
Yes	-0.194	-0.002		
Decision making autonomy	-0.174	-0.002		
No	0.069	-0.015		
*Maternal age at the birth of the index child (in				

*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.

to beet teries only

Section/Topic	ltem #	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
	ļ	(e) Describe any sensitivity analyses	8&9
Results			

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

 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

 BMJ Open

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	11, 12, & 13
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(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	15
		interval). Make clear which confounders were adjusted for and why they were included	
		(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.

BMJ Open

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

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-047892.R1
Article Type:	Original research
Date Submitted by the Author:	13-May-2021
Complete List of Authors:	Shifti, Desalegn Markos; St Paul's Hospital Millennium Medical College; The University of Newcastle Faculty of Health and Medicine, Centre for Women's Health Research Chojenta, Catherine; The University of Newcastle Faculty of Health and Medicine, Centre for Women's Health Research Holliday, Elizabeth; The University of Newcastle Faculty of Health and Medicine, Centre for Clinical Epidemiology and Biostatistics Loxton, Deborah; The University of Newcastle, Faculty of Health and Medicine, Centre for Women's Health Research
Primary Subject Heading :	Public health
Secondary Subject Heading:	Epidemiology, Obstetrics and gynaecology, Paediatrics, Reproductive medicine
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, Maternal medicine < OBSTETRICS, Community child health < PAEDIATRICS

SCHOLARONE[™] Manuscripts

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1	The effects of short birth interval on neonatal, infant and
2	under-five child mortality in Ethiopia: a nationally
3	representative observational study using inverse
4	probability of treatment weighting
5	Desalegn Markos Shifti ^{1,2,*} , Catherine Chojenta ² , Elizabeth G. Holliday ³ , Deborah Loxton ²
6	Affiliation
7	¹ Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
8	² Centre for Women's Health Research, School of Medicine and Public Health, University of
9	Newcastle, New South Wales, Australia
10	³ Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health,
11	University of Newcastle, New South Wales, Australia
12	
13	*Corresponding author
14	desalegnmarkos@gmail.com, desalegnmarkos.shifti@uon.edu.au
15	

BMJ Open

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.

1 2		
2 3 4 5	38	Strengths and limitations of this study
6 7	39	• The application of IPTW mimics a randomized clinical trial by matching two comparison
8 9	40	groups using a conditional probability of receiving exposure (short birth interval in this
10 11 12	41	case) given a set of covariates.
12 13 14	42	• The study has also additional strengths, such as using data from a nationally representative
15 16	43	survey with large sample size.
17 18 19	44	• The application of DAGs, a graphical tool used to identify minimum adjustment sets, which
20 21	45	defined the set of explanatory variables for the propensity scores model was another
22 23	46	strength of this study.
24 25 26	47	• Due to the cross-sectional nature of the study, temporal associations between short birth
20 27 28	48	interval and neonatal, infant, and under-five mortality may not be established.
29 30	49	• The second limitation of our study could be associated with the nonrandomized design of
31 32	50	the study. Propensity scores based analysis, IPTW, cannot account for unknown
33 34 35	51	confounders in the same way that a randomised trial can. As a result, the effect of residual
36 37	52	confounders may not be avoided.
37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60	52	

54 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 studies²⁻⁴ 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,⁶⁷ low birth weight,⁶⁷ small size for gestational age,⁶ congenital anomalies,⁸⁹ 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 studies¹⁸⁻²⁰ ²⁴ ²⁵ ²⁸⁻³² did not use the World Health Organization (WHO) recommended¹ 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 data²⁰ 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 study³⁰ 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 mortality³⁹⁻⁴² in their studies.

Page 7 of 39

BMJ Open

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.

106 Methods

107 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.

119 Variables

Outcome variables

121 The outcome variables in the current study were neonatal mortality (death of the child within122 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.²³⁴⁴

Control variables

After reviewing relevant literature,^{2 18-21 23-25 28 29 39 45 46} Direct Acyclic Graphs (DAGs) were constructed using DAGitty 3.0⁴⁷ 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

Page 9 of 39

BMJ Open

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 study⁵¹ 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: Page 11 of 39

BMJ Open

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

198 where $\overline{x}_{treatment}$ and $\overline{x}_{control}$ denote the sample mean of the covariate in treated and untreated 199 subjects, respectively and $s_{treatment}^2$ and $s_{control}^2$ 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.

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.⁵⁸ 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.⁶⁰ 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.^{50 61} 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.⁵¹ 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 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

Patient and public involvement

Patients and/or the general public were not involved in the design, or conduct, or drafting ofthis 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 \geq 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

$\begin{array}{c} 1 \\ 2 \\ 3 \\ 4 \\ 5 \\ 6 \\ 7 \\ 8 \\ 9 \\ 10 \\ 1 \\ 12 \\ 14 \\ 15 \\ 14 \\ 15 \\ 12 \\ 22 \\ 22 \\ 22 \\ 22 \\ 22 \\ 22$	23 15 57 3 9) 23 15 57 3 9) 23 15 57 3 9) 2 3 15 57 3 9) 2 3 15 57 3 9) 1	2
39 40) 2 	

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					i í C			~ /	
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	

244 ***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.

3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
45 46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1 2 3

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

266 Ethiopia, EDHS 2016

Treatment variable	Neonat	Neonatal mortality				
	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-F	ive 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)			

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

269 **Discussion**

To our knowledge, this study provides the first comprehensive assessment of the effect of short 270 birth interval on neonatal, infant, and under-five mortality using the WHO recommendation to 271 define short birth interval and applying rigorous analytical techniques to adjust for potential 272 confounders. This study provides evidence that short birth interval is associated with 273 neonatal, infant, and under-five mortality in Ethiopia. These findings will help policy 274 makers and program planners formulate targeted interventions to increase birth intervals and 275 contribute to achieving the GTPE and SDGs target of reducing neonatal, infant, and under-276 five mortality. ^{16 15} 277

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

Page 17 of 39

BMJ Open

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 care⁷⁰, 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 Iran⁷⁵ 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 recommendation¹ 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 children⁷⁷ 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 elle intervention.

Author affiliations

¹ Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

²Centre for Women's Health Research, School of Medicine and Public Health, University of

Newcastle, Newcastle, New South Wales, Australia

³Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health,

- University of Newcastle, Newcastle, New South Wales, Australia
 - Acknowledgment

We are grateful to The DHS Program for allowing us to use the Ethiopia Demographic and Health Survey (EDHS) data for further analysis.

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.

356 Funding

357 The authors received no specific funding for this work.

Competing interests

359 The authors declare that they have no competing interests.

360 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

366 Not required

Provenance and peer review

368 Not commissioned; externally peer reviewed.

Data availability statement

1 2		
3 4	370	The dataset is available from The DHS Program repository at the following link:
5 6 7	371	https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0.
8 9 10 11	372	References
12 13	373	1. World Health Organization. Report of a WHO Technical Consultation on Birth Spacing.
14 15 16	374	Geneva, Switzerland 13-15 June 2005.
17 18	375	2. Shifti DM, Chojenta C, G. Holliday E, et al. Individual and community level determinants
19 20	376	of short birth interval in Ethiopia: A multilevel analysis. PloS one
21 22	377	2020;15(1):e0227798.
23 24 25	378	3. Shifti DM, Chojenta C, Holliday EG, et al. Application of geographically weighted
26 27	379	regression analysis to assess predictors of short birth interval hot spots in Ethiopia. PloS
28 29	380	one 2020;15(5):e0233790.
30 31 32 33 34 35 36	381	4. Shifti DM, Chojenta C, Holliday EG, et al. Socioeconomic inequality in short birth interval
	382	in Ethiopia: a decomposition analysis. BMC public health 2020;20(1):1-13.
	383	5. Central Statistical Agency (CSA) [Ethiopia] and ICF. Ethiopia Demographic and Health
37 38	384	Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF
39 40 41	385	2016.
42 43	386	6. Grisaru-Granovsky S, Gordon E-S, Haklai Z, et al. Effect of interpregnancy interval on
44 45	387	adverse perinatal outcomes-a national study. Contraception 2009;80(6):512-18.
46 47 48	388	7. Adam I, Ismail MH, Nasr AM, et al. Low birth weight, preterm birth and short
49 50	389	interpregnancy interval in Sudan. The Journal of Maternal-Fetal & Neonatal Medicine
51 52	390	2009;22(11):1068-71.
53 54 55	391	8. Chen I, Jhangri GS, Chandra S. Relationship between interpregnancy interval and congenital
55 57 58 59 60	392	anomalies. <i>American journal of obstetrics and gynecology</i> 2014;210(6):564. e1-8.

1 2

2 3 4	393	9. Kwon S, Lazo-Escalante M, Villaran M, et al. Relationship between interpregnancy interval
5 6	394	and birth defects in Washington State. Journal of Perinatology 2012;32(1):45.
7 8	395	10. Cheslack-Postava K, Liu K, Bearman PS. Closely spaced pregnancies are associated with
9 10 11	396	increased odds of autism in California sibling births. Pediatrics 2011;127:246-53.
12 13	397	11. DaVanzo J, Razzaque A, Rahman M, et al. The effects of birth spacing on infant and child
14 15	398	mortality, pregnancy outcomes, and maternal morbidity and mortality in Matlab,
16 17 19	399	Bangladesh. Technical Consultation and Review of the Scientific Evidence for Birth
18 19 20	400	Spacing 2004.
21 22	401	12. DaVanzo J, Hale L, Razzaque A, et al. Effects of interpregnancy interval and outcome of
23 24 25	402	the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. BJOG: An
25 26 27	403	International Journal of Obstetrics & Gynaecology 2007;114(9):1079-87.
28 29	404	13. Gonzalez RM, Gilleskie D. Infant mortality rate as a measure of a country's health: a robust
30 31	405	method to improve reliability and comparability. <i>Demography</i> 2017;54(2):701-20.
32 33 34	406	14. Reidpath DD, Allotey P. Infant mortality rate as an indicator of population health. Journal
35 36	407	of Epidemiology & Community Health 2003;57(5):344-46.
37 38	408	15. UN. Transforming our World: The 2030 Agenda For Sustainable Development Goal
39 40 41	409	(A/RES/70/1). 2015.
42 43	410	16. National Planning Commission. Federal Democratic Republic of Ethiopia: Growth and
44 45	411	Transformation Plan II (GTP II) (2015/16-2019/20). Addis Ababa, Ethiopia 2016.
46 47	412	17. Ethiopian Public Health Institute (EPHI) [Ethiopia] and ICF. Ethiopia Mini Demographic
48 49 50	413	and Health Survey 2019: Key Indicators. Rockville, Maryland, USA: EPHI and ICF
51 52	414	2019.
53 54	415	18. Abate MG, Angaw DA, Shaweno T. Proximate determinants of infant mortality in Ethiopia,
55 56	416	2016 Ethiopian demographic and health surveys: results from a survival analysis.
57 58 59	417	Archives of Public Health 2020;78(1):1-10.
60		

Page 23 of 39

1 2

BMJ Open

3 4	418	1
5 6	419	
7 8 9	420	
9 10 11	421	2
12 13	422	
14 15 16	423	
10 17 18	424	2
19 20	425	
21 22 23	426	
25 24 25	427	2
26 27	428	
28 29 20	429	
30 31 32	430	2
33 34	431	
35 36	432	2
37 38 39	433	
40 41	434	
42 43	435	2
44 45 46	436	
40 47 48	437	2
49 50	438	
51 52 53	439	
55 54 55	440	2
56 57	441	
58 59 60		

418 19. Weldearegawi B, Melaku YA, Abera SF, et al. Infant mortality and causes of infant deaths
419 in rural Ethiopia: a population-based cohort of 3684 births. *BMC public health*420 2015;15(1):770.

- 421 20. Wolde HF, Gonete KA, Akalu TY, et al. Factors affecting neonatal mortality in the general
 422 population: evidence from the 2016 Ethiopian Demographic and Health Survey
 423 (EDHS)—multilevel analysis. *BMC research notes* 2019;12(1):610.
- 424 21. Roro EM, Tumtu MI, Gebre DS. Predictors, causes, and trends of neonatal mortality at
 425 Nekemte Referral Hospital, east Wollega Zone, western Ethiopia (2010–2014).
 426 Retrospective cohort study. *PloS one* 2019;14(10):e0221513.
- 4 427 22. Seid SS, Ibro SA, Ahmed AA, et al. Causes and factors associated with neonatal mortality
 428 in neonatal intensive care unit (NICU) of Jimma University medical center, Jimma,
 429 south West Ethiopia. *Pediatric health, medicine and therapeutics* 2019;10:39.
- 430 23. Wakgari N, Wencheko E. Risk factors of neonatal mortality in Ethiopia. *Ethiopian Journal* 431 of Health Development 2013;27(3):192-99.
- 432 24. Fikru C, Getnet M, Shaweno T. Proximate Determinants of Under-Five Mortality in
 433 Ethiopia: Using 2016 Nationwide Survey Data. *Pediatric Health, Medicine and* 434 *Therapeutics* 2019;10:169.
- 435 25. Mekonnen Y, Tensou B, Telake DS, et al. Neonatal mortality in Ethiopia: trends and
 436 determinants. *BMC public health* 2013;13(1):483.
 - 437 26. Limaso AA, Dangisso MH, Hibstu DT. Neonatal survival and determinants of mortality in
 438 Aroresa district, Southern Ethiopia: a prospective cohort study. *BMC pediatrics*439 2020;20(1):33.
 - 27. Yaya Y, Eide KT, Norheim OF, et al. Maternal and neonatal mortality in south-west
 Ethiopia: estimates and socio-economic inequality. *PloS one* 2014;9(4):e96294.

1

1 2		
3 4	442	28. Gebretsadik S, Gabreyohannes E. Determinants of under-five mortality in high mortality
5 6	443	regions of Ethiopia: an analysis of the 2011 Ethiopia Demographic and Health Survey
7 8 9	444	data. International Journal of Population Research 2016;2016.
10 11	445	29. Negera A, Abelti G, Bogale T, et al. An analysis of the trends, differentials and key
12 13	446	proximate determinants of infant and under-five mortality in Ethiopia. Further Analysis
14 15	447	of the 2000, 2005, and 2011 Demographic and Health Surveys DHS Further Analysis
16 17 18	448	Reports No 79 Calverton, Maryland, USA: ICF International 2013.
19 20	449	30. Laelago T. Effects of preceding birth intervals on child mortality in Ethiopia; Evidence
21 22	450	from the Demographic and Health Surveys, 2016. Epidemology International Journal
23 24 25	451	2019;3(1).
26 27	452	31. Hailemariam A, Tesfaye M. Determinants of infant and early childhood mortality in a small
28 29	453	urban community of Ethiopia: a hazard model analysis. The Ethiopian Journal of
30 31 32	454	Health Development (EJHD) 1997;11(3).
33 34	455	32. Dadi AF. A systematic review and meta-analysis of the effect of short birth interval on
35 36	456	infant mortality in Ethiopia. <i>PloS one</i> 2015;10(5):e0126759.
37 38	457	33. Sahle-Mariam Y, Berhane Y. Neonatal mortality among hospital delivered babies in Addis
39 40 41	458	Ababa, Ethiopia. The Ethiopian Journal of Health Development (EJHD) 1997;11(3).
42 43	459	34. Kolobo HA, Chaka TE, Kassa RT. Determinants of neonatal mortality among newborns
44 45	460	admitted to neonatal intensive care unit Adama, Ethiopia: A case-control study.
46 47 48	461	Journal of Clinical Neonatology 2019;8(4):232.
49 50	462	35. Bogale TN, Worku AG, Bikis GA, et al. Why gone too soon? Examining social
51 52	463	determinants of neonatal deaths in northwest Ethiopia using the three delay model
53 54 55	464	approach. BMC pediatrics 2017;17(1):216.
56 57	465	36. Woldeamanuel BT. Statistical analysis of neonatal mortality: a case study of Ethiopia.
58 59	466	Journal of Pregnancy and Child Health 2018;5(2):1-11.
60		

Page 25 of 39

1 2

BMJ Open

3 4	467	37. Asefa M, Drewett R, Tessema F. A birth cohort study in South-West Ethiopia to identify
5 6 7	468	factors associated with infant mortality that are amenable for intervention. Ethiopian
7 8 9	469	Journal of Health Development 2000;14(2):161-68.
) 10 11	470	38. Muluye S, Wencheko E. Determinants of infant mortality in Ethiopia: A study based on the
12 13	471	2005 EDHS data. Ethiopian Journal of Health Development 2012;26(2):72-77.
14 15	472	39. Deribew A, Tessema F, Girma B. Determinants of under-five mortality in Gilgel gibe field
16 17 18	473	research center, Southwest Ethiopia. Ethiopian Journal of Health Development
19 20	474	2007;21(2):117-24.
21 22	475	40. Bedada D. Determinant of under-five child mortality in Ethiopia. American Journal of
23 24 25	476	Theoretical and Applied Statistics 2017;6(4):198-204.
26 27	477	41. Ayele DG, Zewotir TT. Comparison of under-five mortality for 2000, 2005 and 2011
28 29	478	surveys in Ethiopia. BMC public health 2016;16(1):930.
30 31 32	479	42. Shamebo D, Sandström A, Muhe L, et al. The Butajira project in Ethiopia: a nested case-
32 33 34	480	referent study of under-five mortality and its public health determinants. Bulletin of the
35 36	481	World Health Organization 1993;71(3-4):389.
37 38	482	43. Croft TN, Aileen M. J. Marshall, Courtney K. Allen, et al. Guide to DHS Statistics.
39 40 41	483	Rockville, Maryland, USA: ICF 2018.
42 43	484	44. ICF International. Demographic and Health Survey Interviewer's Manual. MEASURE DHS
44 45	485	Basic Documentation No 2 Calverton, Maryland, USA: ICF International 2012.
46 47 48	486	45. Hailu D, Gulte T. Determinants of Short Interbirth Interval among Reproductive Age
49 50	487	Mothers in Arba Minch District, Ethiopia. International journal of reproductive
51 52	488	medicine 2016;2016 doi: 10.1155/2016/6072437
53 54	489	46. Yohannes S, Wondafrash M, Abera M, et al. Duration and determinants of birth interval
55 56 57	490	among women of child bearing age in Southern Ethiopia. BMC pregnancy and
58 59 60	491	<i>childbirth</i> 2011;11(1):38.

- 492 47. Textor J, van der Zander B, Gilthorpe MS, et al. Robust causal inference using directed
 493 acyclic graphs: the R package 'dagitty'. *International journal of epidemiology*494 2016;45(6):1887-94.
- 48. Attia JR, Oldmeadow C, Holliday EG, et al. Deconfounding confounding part 2: using
 directed acyclic graphs (DAGs). *Medical Journal of Australia* 2017;206(11):480-83.
- 497 49. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC medical research*498 *methodology* 2008;8(1):70.
 - 50. Garrido MM, Kelley AS, Paris J, et al. Methods for constructing and assessing propensity
 scores. *Health services research* 2014;49(5):1701-20.
- 501 51. Xu S, Ross C, Raebel MA, et al. Use of stabilized inverse propensity scores as weights to
 502 directly estimate relative risk and its confidence intervals. *Value in Health*503 2010;13(2):273-77.
- 504 52. Lee Y, Hong I, Lee MJ, et al. Identifying risk of depressive symptoms in adults with
 505 physical disabilities receiving rehabilitation services: Propensity score approaches.
 506 Annals of rehabilitation medicine 2019;43(3):250.
- 507 53. Austin PC, Mamdani MM. A comparison of propensity score methods: a case-study 508 estimating the effectiveness of post-AMI statin use. *Statistics in medicine* 509 2006;25(12):2084-106.
- 510 54. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies
 511 for causal effects. *Biometrika* 1983;70(1):41-55.
- 512 55. Austin PC. A tutorial and case study in propensity score analysis: an application to
 513 estimating the effect of in-hospital smoking cessation counseling on mortality.
 514 Multivariate behavioral research 2011;46(1):119-51.
- 56 515 56. Guo S, Fraser MW. Propensity score analysis: Statistical methods and applications: SAGE
 57 58 516 publications 2014.

Page 27 of 39

1 2 BMJ Open

517	57. Deb S, Austin PC, Tu JV, et al. A review of propensity-score methods and their use in
518	cardiovascular research. Canadian Journal of Cardiology 2016;32(2):259-65.
519	58. Austin PC. An introduction to propensity score methods for reducing the effects of
520	confounding in observational studies. Multivariate behavioral research
521	2011;46(3):399-424.
522	59. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of
523	treatment weighting (IPTW) using the propensity score to estimate causal treatment
524	effects in observational studies. Statistics in medicine 2015;34(28):3661-79.
525	60. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates
526	between treatment groups in propensity-score matched samples. Statistics in medicine
527	2009;28(25):3083-107.
528	61. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched
529	sampling methods that incorporate the propensity score. The American Statistician
530	1985;39(1):33-38.
531	62. DuGoff EH, Schuler M, Stuart EA. Generalizing observational study results: applying
532	propensity score methods to complex surveys. Health services research
533	2014;49(1):284-303.
534	63. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years
535	mortality and nutritional status in developing countries: evidence from the demographic
536	and health surveys. International Journal of Gynecology & Obstetrics 2005;89:S7-S24.
537	64. Kozuki N, Walker N. Exploring the association between short/long preceding birth
538	intervals and child mortality: using reference birth interval children of the same mother
539	as comparison. BMC public health 2013;13(S3):S6.
540	65. Rahman MM, Abidin S. Factors affecting neonatal mortality in Bangladesh. Journal of
541	Health Management 2010;12(2):137-52.
	 518 519 520 521 522 523 526 527 526 527 528 529 530 531 532 533 534 537 536 537 538 539 540

2		
2 3 4	542	66. Ezeh OK, Agho KE, Dibley MJ, et al. Determinants of neonatal mortality in Nigeria:
5 6	543	evidence from the 2008 demographic and health survey. BMC Public Health
7 8 9	544	2014;14(1):521.
10 11	545	67. Conde-Agudelo A, Rosas-Bermudez A, Castaño F, et al. Effects of birth spacing on
12 13	546	maternal, perinatal, infant, and child health: a systematic review of causal mechanisms.
14 15 16	547	Studies in family planning 2012;43(2):93-114.
17 18	548	68. Rousso D, Panidis D, Gkoutzioulis F, et al. Effect of the interval between pregnancies on
19 20	549	the health of mother and child. European Journal of Obstetrics and Gynecology and
21 22 23	550	Reproductive Biology 2002;105(1):4-6.
24 25	551	69. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or
26 27	552	closely spaced pregnancies. <i>The Journal of nutrition</i> 2003;133(5):1732S-36S.
28 29 30	553	70. WHO. Maternal, newborn, child and adolescent health: Postnatal care. [cited 11 July
31 32	554	2020]. Available from:
33 34	555	https://www.who.int/maternal_child_adolescent/topics/newborn/postnatal_care/en/
35 36 27	556	accessed 2020 11 July
37 38 39	557	71. WHO, USAID, MCHIP, et al. Postnatal Care for Mothers and Newborns: Highlights from
40 41	558	the World Health Organization 2013 Guidelines 2015
42 43	559	72. Omariba DWR, Beaujot R, Rajulton F. Determinants of infant and child mortality in Kenya:
44 45 46	560	an analysis controlling for frailty effects. Population Research and Policy Review
47 48	561	2007;26(3):299-321.
49 50	562	73. Fotso JC, Cleland J, Mberu B, et al. Birth spacing and child mortality: an analysis of
51 52 53	563	prospective data from the Nairobi urban health and demographic surveillance system.
53 54 55 56 57 58 59 60	564	Journal of biosocial science 2013;45(6):779-98.

Page 29 of 39

BMJ Open

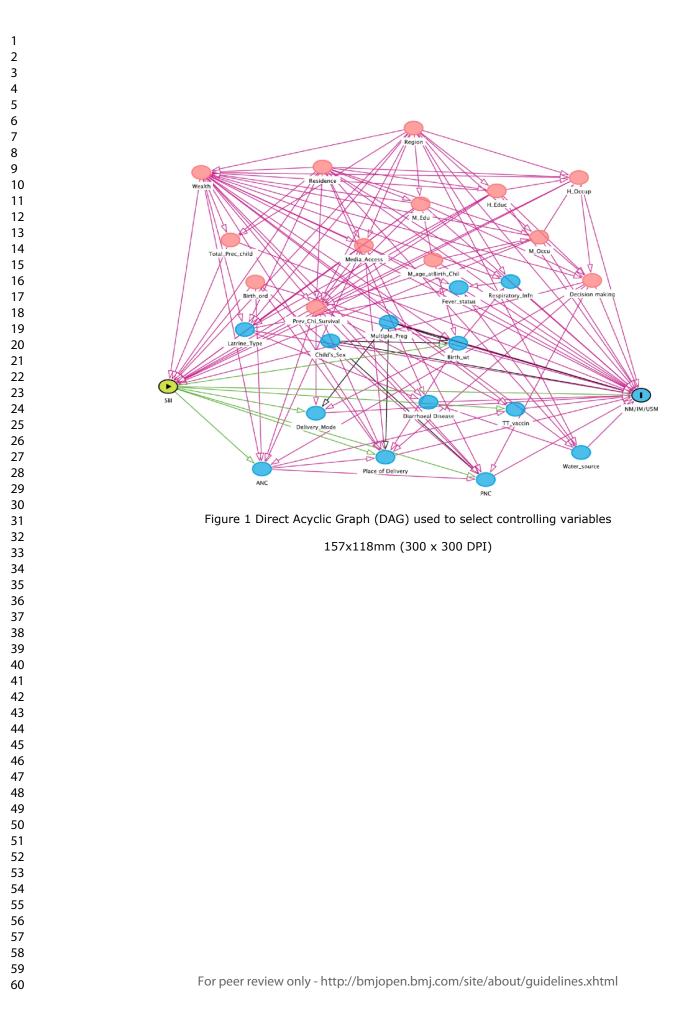
1 2		
3 4	565	74. Lamichhane R, Zhao Y, Paudel S, et al. Factors associated with infant mortality in Nepal:
5 6	566	a comparative analysis of Nepal demographic and health surveys (NDHS) 2006 and
7 8 9	567	2011. BMC public health 2017;17(1):53.
10 11	568	75. SHARIFZADEH GR, Namakin K, Mehrjoufard H. An Epidemiological study on Infant
12 13	569	Mortality and factors affecting it in Rural Areas of Birjand, Iran. 2008.
14 15 16	570	76. Boerma JT, Bicego GT. Preceding birth intervals and child survival: searching for pathways
10 17 18	571	of influence. Studies in family planning 1992;23(4):243-56.
19 20	572	77. Dewey KG, Cohen RJ. Does birth spacing affect maternal or child nutritional status? A
21 22	573	systematic literature review. Maternal & child nutrition 2007;3(3):151-73.
23 24 25	574	78. Stuebe A. The risks of not breastfeeding for mothers and infants. Reviews in obstetrics and
26 27	575	gynecology 2009;2(4):222.
28 29	576	79. Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology,
30 31 32	577	mechanisms, and lifelong effect. The Lancet 2016;387(10017):475-90.
33 34	578	80. Biradar R, Patel KK, Prasad JB. Effect of birth interval and wealth on under-5 child
35 36	579	mortality in Nigeria. Clinical Epidemiology and Global Health 2019;7(2):234-38.
37 38 30	580	81. Andre FE, Booy R, Bock HL, et al. Vaccination greatly reduces disease, disability, death
39 40 41	581	and inequity worldwide. Bulletin of the World health organization 2008;86:140-46.
42 43	582	82. Innis BL, Snitbhan R, Kunasol P, et al. Protection against hepatitis A by an inactivated
44 45	583	vaccine. Jama 1994;271(17):1328-34.
46 47 48	584	83. Arevshatian L, Clements C, Lwanga S, et al. An evaluation of infant immunization in
49 50	585	Africa: is a transformation in progress? Bulletin of the World Health Organization
51 52	586	2007;85:449-57.
53 54 55	587	84. Attia JR, Jones MP, Hure A. Deconfounding confounding part 1: traditional explanations.
56 57	588	The Medical Journal of Australia 2017;206(6):244-45.
58 59 60	589	

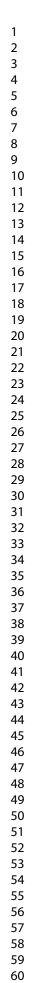
590 Figure Legend

- 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

Page 31 of 39

BMJ Open





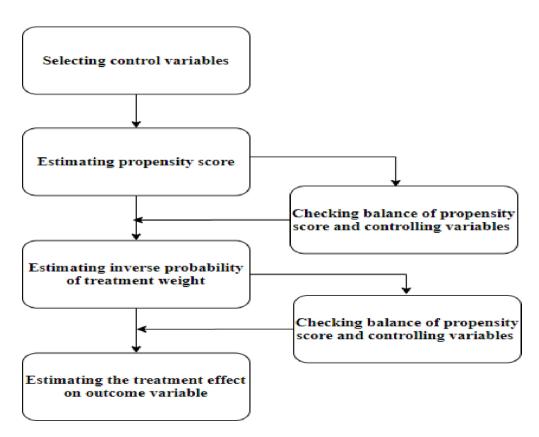
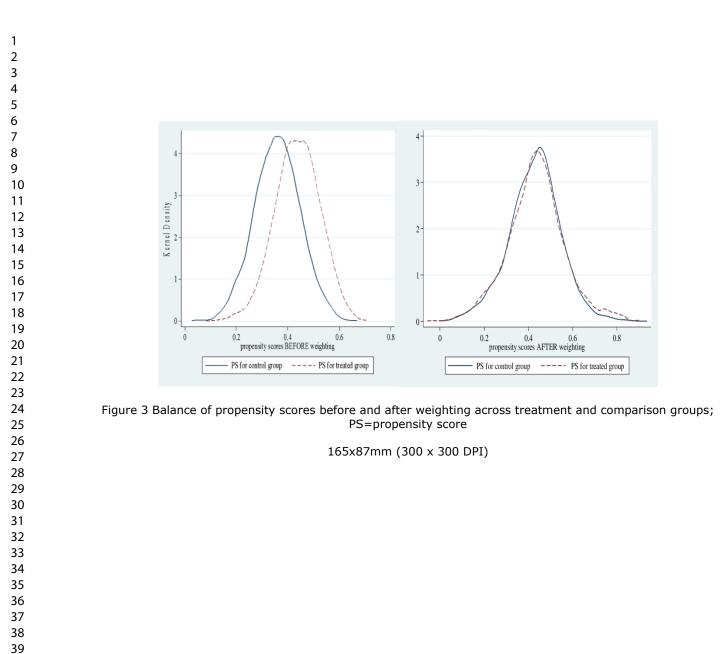


Figure 2 Schematic presentation of the overall steps followed in the analysis

115x90mm (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 continuous variable. It was also categorized the descriptive section of the results (1= \leq 19, 2= 20-24, 3=25-29, 4=30-34, and 5= \geq 35).				
	Educational level	Maximum educational level (1= Uneducated, 2=Primary and 3=Secondary+)				
	Employment status Place of residence	Maternal employment status (1=Not Employed; 2=Employed)) 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)				

Page 35 of 39

 BMJ Open

Maternal health status	Antenatal care	Women's antenatal care utilization categorized as 1=No visit, 2=At				
and healthcare-related		least one visit, $3 = \ge$ Four visits				
variables	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	Sex	Child sex (1=Male, 2=Female)				
characteristics	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	Total number of children born before the index child was considered				
	the index child	as a continuous variable. For the descriptive statistics, this variable				
		was categorized into $1 = \le 2$, $2 = 3-4$, and $3 = \ge 5$.				
		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 variable				
		using the variance inflation factor (VIF). When the values of VIF we lower than 10, then the collinearity problem was considered unlikel				
		The VIF for birth order was 18.15 and for the total number of childred				
		born before the index child was 16.26, which indicates the presence				
		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.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Supplemental Material II

Table 2 Standardized difference before and after weighting the propensity score

re weighting 92 8 12 8 8 41 9 2 02 70 61	After weighting 0.022 0.009 -0.017 0.005 0.005 0.003 0.003 0.006 -0.004 0.008 0.005 -0.007	
8 12 8 41 9 2 02 70 61	0.009 -0.017 0.005 0.012 0.003 0.006 -0.004 0.008 0.005	
12 8 8 41 9 2 02 70 61	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008 0.005	
12 8 8 41 9 2 02 70 61	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008 0.005	
12 8 8 41 9 2 02 70 61	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008 0.005	
8 8 41 9 2 02 70 61	0.005 0.012 0.003 0.006 -0.004 0.008 0.005	
8 41 9 2 02 70 61	0.012 0.003 0.006 -0.004 0.008 0.005	
8 41 9 2 02 70 61	0.012 0.003 0.006 -0.004 0.008 0.005	
41 9 2 02 70 61	0.003 0.006 -0.004 0.008 0.005	
41 9 2 02 70 61	0.003 0.006 -0.004 0.008 0.005	
9 2 02 70 61	0.006 -0.004 0.008 0.005	
2 02 70 61	-0.004 0.008 0.005	
2 02 70 61	-0.004 0.008 0.005	
02 70 61	0.008 0.005	
02 70 61	0.008 0.005	
70 61	0.005	
61		
	-0.007	
	0.007	
7	-0.006	
29	-0.004	
39	-0.006	
07	0.004	
6	0.008	
82	0.014	
06	0.003	
2	-0.003	
	-0.006	
	-0.005	
	-0.009	
	-0.009	
	0.014	
00	0.017	
01	-0.002	
01	-0.002	
7	-0.009	
	07 6 82	

*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

tor peer terier only

 BMJ Open

Section/Topic	Item #	Recommendation				
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						
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						
/ariables 7 Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable		6, 7, & 8				
Data sources/ measurement	sources/ 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe		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			

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

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	11, 12, & 13
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(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	15
		interval). Make clear which confounders were adjusted for and why they were included	
		(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	15, 16, 17, & 18
		similar studies, and other relevant evidence	
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	19
		which the present article is based	

*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.

BMJ Open

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

Journal:	BMJ Open
Manuscript ID	bmjopen-2020-047892.R2
Article Type:	Original research
Date Submitted by the Author:	05-Jul-2021
Complete List of Authors:	Shifti, Desalegn Markos; St Paul's Hospital Millennium Medical College; The University of Newcastle School of Medicine and Public Health, Centre for Women's Health Research Chojenta, Catherine; The University of Newcastle School of Medicine and Public Health, Centre for Women's Health Research Holliday, Elizabeth; The University of Newcastle School of Medicine and Public Health, Centre for Clinical Epidemiology and Biostatistics Loxton, Deborah; The University of Newcastle School of Medicine and Public Health, Centre for Women's Health Research
Primary Subject Heading :	Public health
Secondary Subject Heading:	Epidemiology, Obstetrics and gynaecology, Paediatrics, Reproductive medicine
Keywords:	PUBLIC HEALTH, EPIDEMIOLOGY, Maternal medicine < OBSTETRICS, Community child health < PAEDIATRICS

SCHOLARONE[™] Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

reliez oni

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1	The effects of short birth interval on neonatal, infant and
2	under-five child mortality in Ethiopia: a nationally
3	representative observational study using inverse
4	probability of treatment weighting
5	Desalegn Markos Shifti ^{1,2,*} , Catherine Chojenta ² , Elizabeth G. Holliday ³ , Deborah Loxton ²
6	Affiliation
7	¹ Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
8	² Centre for Women's Health Research, School of Medicine and Public Health, University of
9	Newcastle, New South Wales, Australia
10	³ Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health,
11	University of Newcastle, New South Wales, Australia
12	
13	*Corresponding author
14	desalegnmarkos@gmail.com, desalegnmarkos.shifti@uon.edu.au
15	

BMJ Open

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.

2	
3	
4	
5	
6	
/	
8	
9	
10	
11	
12 13	
14 15	
16	
17	
18	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36 37	
37 38	
30 39	
40	
40 41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57 58	
58 59	
59 60	
00	

48

1 2

38

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.

54 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 studies²⁻⁴ 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,⁶⁷ low birth weight,⁶⁷ 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) recommended¹ 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 data²⁰ 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 study³⁰ 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 mortality³⁹⁻⁴² in their studies.

Page 7 of 39

BMJ Open

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.

106 Methods

107 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.

119 Variables

Outcome variables

121 The outcome variables in the current study were neonatal mortality (death of the child within122 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.²³⁴⁴

Control variables

After reviewing relevant literature,^{2 18-21 23-25 28 29 39 45 46} Direct Acyclic Graphs (DAGs) were constructed using DAGitty 3.0⁴⁷ 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

Page 9 of 39

BMJ Open

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.

2 162 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 study⁵¹ 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

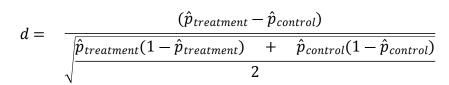
Supplementary Material II).⁵⁴ Propensity scores are used to estimate treatment effects on outcomes using observational data when confounding bias due to non-random treatment assignment is likely.⁵⁰ Inverse probability of treatment weighting weights the entire study sample by the inverse of the propensity 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:

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

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

BMJ Open



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.⁵⁸ 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.⁶⁰ 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.^{50 61} 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.⁵¹ 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 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.

223 Patient and public involvement

Patients and/or the general public were not involved in the design, or conduct, or drafting ofthis 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 \geq 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

236	Table 1 The weighted distribution of neonata	l, infant, and under-five child mortal	lity 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	· · · ·			、 <i>, , ,</i>	~ /		· · · ·		
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	

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

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

238 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.

3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14 15	
15	
16	
17	
18	
19	
20	
21	
22	
20 21 22 23 24 25 26 27 28 29 30 31	
24	
25	
26	
20	
27 20	
20	
29	
30	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
54 55	
56	
57	
58	
59	
60	

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

Ethiopia, EDHS 2016

Treatment variable	Neonat	al 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)	
	Infan	t mortality		
Short birth interval	No (%)	Yes (%)		
No	4126 (54.9)	135 (40.5)	Ref	
Yes	3906 (45.1) 281 (59.5) 2.16 (1		2.16 (1.49, 3.11)	
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

262 **Discussion**

To our knowledge, this study provides the first comprehensive assessment of the effect of short 263 birth interval on neonatal, infant, and under-five mortality using the WHO recommendation to 264 define short birth interval and applying rigorous analytical techniques to adjust for potential 265 confounders. This study provides evidence that short birth interval is associated with 266 neonatal, infant, and under-five mortality in Ethiopia. These findings will help policy 267 makers and program planners formulate targeted interventions to increase birth intervals and 268 contribute to achieving the GTPE and SDGs target of reducing neonatal, infant, and under-269 five mortality. ^{16 15} 270

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

Page 17 of 39

BMJ Open

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 care⁷⁰, 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 Iran⁷⁵ 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 recommendation¹ 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 children⁷⁷ 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 elle intervention.

Author affiliations

¹ Saint Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia

²Centre for Women's Health Research, School of Medicine and Public Health, University of

Newcastle, Newcastle, New South Wales, Australia

³Centre for Clinical Epidemiology and Biostatistics, School of Medicine and Public Health,

University of Newcastle, Newcastle, New South Wales, Australia

Acknowledgment

We are grateful to The DHS Program for allowing us to use the Ethiopia Demographic and Health Survey (EDHS) data for further analysis.

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.

349 Funding

350 The authors received no specific funding for this work.

Competing interests

352 The authors declare that they have no competing interests.

353 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

359 Not required

Provenance and peer review

361 Not commissioned; externally peer reviewed.

Data availability statement

1 2		
3 4	363	The dataset is available from The DHS Program repository at the following link:
5 6 7	364	https://www.dhsprogram.com/data/dataset/Ethiopia_Standard-DHS_2016.cfm?flag=0.
8 9 10 11	365	References
12 13	366	1. World Health Organization. Report of a WHO Technical Consultation on Birth Spacing.
14 15 16	367	Geneva, Switzerland 13-15 June 2005.
17 18 19 20	368	2. Shifti DM, Chojenta C, G. Holliday E, et al. Individual and community level determinants
	369	of short birth interval in Ethiopia: A multilevel analysis. PloS one
21 22	370	2020;15(1):e0227798.
23 24 25	371	3. Shifti DM, Chojenta C, Holliday EG, et al. Application of geographically weighted
26 27	372	regression analysis to assess predictors of short birth interval hot spots in Ethiopia. PloS
28 29	373	one 2020;15(5):e0233790.
 30 31 32 33 34 35 36 37 38 39 	374	4. Shifti DM, Chojenta C, Holliday EG, et al. Socioeconomic inequality in short birth interval
	375	in Ethiopia: a decomposition analysis. BMC public health 2020;20(1):1-13.
	376	5. Central Statistical Agency (CSA) [Ethiopia] and ICF. Ethiopia Demographic and Health
	377	Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF
39 40 41	378	2016.
42 43	379	6. Grisaru-Granovsky S, Gordon E-S, Haklai Z, et al. Effect of interpregnancy interval on
44 45	380	adverse perinatal outcomes-a national study. Contraception 2009;80(6):512-18.
46 47 48	381	7. Adam I, Ismail MH, Nasr AM, et al. Low birth weight, preterm birth and short
49 50	382	interpregnancy interval in Sudan. The Journal of Maternal-Fetal & Neonatal Medicine
51 52 53 54 55 56 57 58 59	383	2009;22(11):1068-71.
	384	8. Chen I, Jhangri GS, Chandra S. Relationship between interpregnancy interval and congenital
	385	anomalies. American journal of obstetrics and gynecology 2014;210(6):564. e1-8.
60		

1

1 2		
3 4	386	9. Kwon S, Lazo-Escalante M, Villaran M, et al. Relationship between interpregnancy interval
5 6	387	and birth defects in Washington State. Journal of Perinatology 2012;32(1):45.
7 8 9	388	10. Cheslack-Postava K, Liu K, Bearman PS. Closely spaced pregnancies are associated with
10 11	389	increased odds of autism in California sibling births. Pediatrics 2011;127:246-53.
12 13	390	11. DaVanzo J, Razzaque A, Rahman M, et al. The effects of birth spacing on infant and child
14 15	391	mortality, pregnancy outcomes, and maternal morbidity and mortality in Matlab,
16 17 18	392	Bangladesh. Technical Consultation and Review of the Scientific Evidence for Birth
19 20	393	Spacing 2004.
21 22	394	12. DaVanzo J, Hale L, Razzaque A, et al. Effects of interpregnancy interval and outcome of
23 24 25	395	the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. BJOG: An
26 27	396	International Journal of Obstetrics & Gynaecology 2007;114(9):1079-87.
28 29	397	13. Gonzalez RM, Gilleskie D. Infant mortality rate as a measure of a country's health: a robust
30 31 32 33 34	398	method to improve reliability and comparability. <i>Demography</i> 2017;54(2):701-20.
	399	14. Reidpath DD, Allotey P. Infant mortality rate as an indicator of population health. Journal
35 36	400	of Epidemiology & Community Health 2003;57(5):344-46.
37 38	401	15. UN. Transforming our World: The 2030 Agenda For Sustainable Development Goal
39 40 41	402	(A/RES/70/1). 2015.
42 43	403	16. National Planning Commission. Federal Democratic Republic of Ethiopia: Growth and
44 45	404	Transformation Plan II (GTP II) (2015/16-2019/20). Addis Ababa, Ethiopia 2016.
46 47 48 49 50 51 52 53 54	405	17. Ethiopian Public Health Institute (EPHI) [Ethiopia] and ICF. Ethiopia Mini Demographic
	406	and Health Survey 2019: Key Indicators. Rockville, Maryland, USA: EPHI and ICF
	407	2019.
	408	18. Abate MG, Angaw DA, Shaweno T. Proximate determinants of infant mortality in Ethiopia,
55 56 57	409	2016 Ethiopian demographic and health surveys: results from a survival analysis.
58 59	410	Archives of Public Health 2020;78(1):1-10.
60		

Page 23 of 39

1 2 3

BMJ Open

4	
5	
6	
7	
8	
6 7 8 9 10	
10	
11	
12	
13	
14	
15	
12 13 14 15 16 17 18 19 20	
17	
18	
19	
20	
21	
າາ	
22 23 24	
24	
25	
26	
27	
22 23 24 25 26 27 28	
29	
30	
31	
32	
33 34 35	
34	
35	
36	
37	
37 38 39	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	

60

411 19. Weldearegawi B, Melaku YA, Abera SF, et al. Infant mortality and causes of infant deaths
412 in rural Ethiopia: a population-based cohort of 3684 births. *BMC public health*413 2015;15(1):770.

- 414 20. Wolde HF, Gonete KA, Akalu TY, et al. Factors affecting neonatal mortality in the general
 415 population: evidence from the 2016 Ethiopian Demographic and Health Survey
 416 (EDHS)—multilevel analysis. *BMC research notes* 2019;12(1):610.
- 417 21. Roro EM, Tumtu MI, Gebre DS. Predictors, causes, and trends of neonatal mortality at
 418 Nekemte Referral Hospital, east Wollega Zone, western Ethiopia (2010–2014).
 419 Retrospective cohort study. *PloS one* 2019;14(10):e0221513.
- 420 22. Seid SS, Ibro SA, Ahmed AA, et al. Causes and factors associated with neonatal mortality
 421 in neonatal intensive care unit (NICU) of Jimma University medical center, Jimma,
 422 south West Ethiopia. *Pediatric health, medicine and therapeutics* 2019;10:39.
- 423 23. Wakgari N, Wencheko E. Risk factors of neonatal mortality in Ethiopia. *Ethiopian Journal* 424 of Health Development 2013;27(3):192-99.
- 425 24. Fikru C, Getnet M, Shaweno T. Proximate Determinants of Under-Five Mortality in
 426 Ethiopia: Using 2016 Nationwide Survey Data. *Pediatric Health, Medicine and* 427 *Therapeutics* 2019;10:169.
- 428 25. Mekonnen Y, Tensou B, Telake DS, et al. Neonatal mortality in Ethiopia: trends and 45 429 determinants. *BMC public health* 2013;13(1):483.
 - 430 26. Limaso AA, Dangisso MH, Hibstu DT. Neonatal survival and determinants of mortality in
 431 Aroresa district, Southern Ethiopia: a prospective cohort study. *BMC pediatrics*432 2020;20(1):33.
 - 433 27. Yaya Y, Eide KT, Norheim OF, et al. Maternal and neonatal mortality in south-west
 434 Ethiopia: estimates and socio-economic inequality. *PloS one* 2014;9(4):e96294.

1

1 2		
3 4	435	28. Gebretsadik S, Gabreyohannes E. Determinants of under-five mortality in high mortality
5 6	436	regions of Ethiopia: an analysis of the 2011 Ethiopia Demographic and Health Survey
7 8 9	437	data. International Journal of Population Research 2016;2016.
9 10 11	438	29. Negera A, Abelti G, Bogale T, et al. An analysis of the trends, differentials and key
12 13	439	proximate determinants of infant and under-five mortality in Ethiopia. Further Analysis
14 15	440	of the 2000, 2005, and 2011 Demographic and Health Surveys DHS Further Analysis
16 17 18	441	Reports No 79 Calverton, Maryland, USA: ICF International 2013.
19 20	442	30. Laelago T. Effects of preceding birth intervals on child mortality in Ethiopia; Evidence
21 22	443	from the Demographic and Health Surveys, 2016. Epidemology International Journal
23 24 25	444	2019;3(1).
26 27	445	31. Hailemariam A, Tesfaye M. Determinants of infant and early childhood mortality in a small
28 29	446	urban community of Ethiopia: a hazard model analysis. The Ethiopian Journal of
30 31 32	447	Health Development (EJHD) 1997;11(3).
32 33 34	448	32. Dadi AF. A systematic review and meta-analysis of the effect of short birth interval on
35 36	449	infant mortality in Ethiopia. <i>PloS one</i> 2015;10(5):e0126759.
37 38	450	33. Sahle-Mariam Y, Berhane Y. Neonatal mortality among hospital delivered babies in Addis
39 40 41	451	Ababa, Ethiopia. The Ethiopian Journal of Health Development (EJHD) 1997;11(3).
42 43	452	34. Kolobo HA, Chaka TE, Kassa RT. Determinants of neonatal mortality among newborns
44 45	453	admitted to neonatal intensive care unit Adama, Ethiopia: A case-control study.
46 47 48	454	Journal of Clinical Neonatology 2019;8(4):232.
49 50	455	35. Bogale TN, Worku AG, Bikis GA, et al. Why gone too soon? Examining social
51 52	456	determinants of neonatal deaths in northwest Ethiopia using the three delay model
53 54 55	457	approach. BMC pediatrics 2017;17(1):216.
56 57	458	36. Woldeamanuel BT. Statistical analysis of neonatal mortality: a case study of Ethiopia.
58 59	459	Journal of Pregnancy and Child Health 2018;5(2):1-11.
60		

Page 25 of 39

1 2

BMJ Open

3 4	460	37. Asefa M, Drewett R, Tessema F. A birth cohort study in South-West Ethiopia to identify
5 6	461	factors associated with infant mortality that are amenable for intervention. Ethiopian
7 8 9	462	Journal of Health Development 2000;14(2):161-68.
9 10 11	463	38. Muluye S, Wencheko E. Determinants of infant mortality in Ethiopia: A study based on the
12 13	464	2005 EDHS data. Ethiopian Journal of Health Development 2012;26(2):72-77.
14 15	465	39. Deribew A, Tessema F, Girma B. Determinants of under-five mortality in Gilgel gibe field
16 17 18	466	research center, Southwest Ethiopia. Ethiopian Journal of Health Development
19 20	467	2007;21(2):117-24.
21 22	468	40. Bedada D. Determinant of under-five child mortality in Ethiopia. American Journal of
23 24 25	469	Theoretical and Applied Statistics 2017;6(4):198-204.
26 27	470	41. Ayele DG, Zewotir TT. Comparison of under-five mortality for 2000, 2005 and 2011
28 29	471	surveys in Ethiopia. BMC public health 2016;16(1):930.
30 31 32	472	42. Shamebo D, Sandström A, Muhe L, et al. The Butajira project in Ethiopia: a nested case-
33 34	473	referent study of under-five mortality and its public health determinants. Bulletin of the
35 36	474	World Health Organization 1993;71(3-4):389.
37 38	475	43. Croft TN, Aileen M. J. Marshall, Courtney K. Allen, et al. Guide to DHS Statistics.
39 40 41	476	Rockville, Maryland, USA: ICF 2018.
42 43	477	44. ICF International. Demographic and Health Survey Interviewer's Manual. MEASURE DHS
44 45	478	Basic Documentation No 2 Calverton, Maryland, USA: ICF International 2012.
46 47 48	479	45. Hailu D, Gulte T. Determinants of Short Interbirth Interval among Reproductive Age
49 50	480	Mothers in Arba Minch District, Ethiopia. International journal of reproductive
51 52	481	medicine 2016;2016 doi: 10.1155/2016/6072437
53 54 55	482	46. Yohannes S, Wondafrash M, Abera M, et al. Duration and determinants of birth interval
55 56 57	483	among women of child bearing age in Southern Ethiopia. BMC pregnancy and
58 59 60	484	<i>childbirth</i> 2011;11(1):38.

- 485 47. Textor J, van der Zander B, Gilthorpe MS, et al. Robust causal inference using directed
 486 acyclic graphs: the R package 'dagitty'. *International journal of epidemiology*487 2016;45(6):1887-94.
- 488 48. Attia JR, Oldmeadow C, Holliday EG, et al. Deconfounding confounding part 2: using
 489 directed acyclic graphs (DAGs). *Medical Journal of Australia* 2017;206(11):480-83.
- 490 49. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC medical research*491 *methodology* 2008;8(1):70.
 - 492 50. Garrido MM, Kelley AS, Paris J, et al. Methods for constructing and assessing propensity
 493 scores. *Health services research* 2014;49(5):1701-20.
- 494 51. Xu S, Ross C, Raebel MA, et al. Use of stabilized inverse propensity scores as weights to
 495 directly estimate relative risk and its confidence intervals. *Value in Health*496 2010;13(2):273-77.
- 497 52. Lee Y, Hong I, Lee MJ, et al. Identifying risk of depressive symptoms in adults with
 498 physical disabilities receiving rehabilitation services: Propensity score approaches.
 499 *Annals of rehabilitation medicine* 2019;43(3):250.
- 500 53. Austin PC, Mamdani MM. A comparison of propensity score methods: a case-study 501 estimating the effectiveness of post-AMI statin use. *Statistics in medicine* 502 2006;25(12):2084-106.
- 503 54. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies
 504 for causal effects. *Biometrika* 1983;70(1):41-55.
- 505 55. Austin PC. A tutorial and case study in propensity score analysis: an application to 516 estimating the effect of in-hospital smoking cessation counseling on mortality. 527 *Multivariate behavioral research* 2011;46(1):119-51.
 - 508 56. Guo S, Fraser MW. Propensity score analysis: Statistical methods and applications: SAGE
 509 publications 2014.

Page 27 of 39

1 2 BMJ Open

3 4	510	57. Deb S, Austin PC, Tu JV, et al. A review of propensity-score methods and their use in
5 6	511	cardiovascular research. Canadian Journal of Cardiology 2016;32(2):259-65.
7 8 9 10 11 12 13	512	58. Austin PC. An introduction to propensity score methods for reducing the effects of
	513	confounding in observational studies. Multivariate behavioral research
	514	2011;46(3):399-424.
14 15 16	515	59. Austin PC, Stuart EA. Moving towards best practice when using inverse probability of
17 18	516	treatment weighting (IPTW) using the propensity score to estimate causal treatment
19 20	517	effects in observational studies. Statistics in medicine 2015;34(28):3661-79.
21 22 23	518	60. Austin PC. Balance diagnostics for comparing the distribution of baseline covariates
24 25	519	between treatment groups in propensity-score matched samples. <i>Statistics in medicine</i>
26 27	520	2009;28(25):3083-107.
28 29 30 31 32	521	61. Rosenbaum PR, Rubin DB. Constructing a control group using multivariate matched
	522	sampling methods that incorporate the propensity score. The American Statistician
33 34	523	1985;39(1):33-38.
35 36 37	524	62. DuGoff EH, Schuler M, Stuart EA. Generalizing observational study results: applying
37 38 39	525	propensity score methods to complex surveys. Health services research
40 41	526	2014;49(1):284-303.
42 43	527	63. Rutstein SO. Effects of preceding birth intervals on neonatal, infant and under-five years
44 45 46	528	mortality and nutritional status in developing countries: evidence from the demographic
47 48 49 50	529	and health surveys. International Journal of Gynecology & Obstetrics 2005;89:S7-S24.
	530	64. Kozuki N, Walker N. Exploring the association between short/long preceding birth
51 52 53	531	intervals and child mortality: using reference birth interval children of the same mother
54 55	532	as comparison. <i>BMC public health</i> 2013;13(S3):S6.
56 57	533	65. Rahman MM, Abidin S. Factors affecting neonatal mortality in Bangladesh. Journal of
58 59 60	534	Health Management 2010;12(2):137-52.

2		
2 3 4	535	66. Ezeh OK, Agho KE, Dibley MJ, et al. Determinants of neonatal mortality in Nigeria:
5 6	536	evidence from the 2008 demographic and health survey. BMC Public Health
7 8 9	537	2014;14(1):521.
) 10 11	538	67. Conde-Agudelo A, Rosas-Bermudez A, Castaño F, et al. Effects of birth spacing on
12 13	539	maternal, perinatal, infant, and child health: a systematic review of causal mechanisms.
14 15 16	540	Studies in family planning 2012;43(2):93-114.
17 18	541	68. Rousso D, Panidis D, Gkoutzioulis F, et al. Effect of the interval between pregnancies on
19 20	542	the health of mother and child. European Journal of Obstetrics and Gynecology and
21 22	543	Reproductive Biology 2002;105(1):4-6.
23 24 25	544	69. King JC. The risk of maternal nutritional depletion and poor outcomes increases in early or
26 27	545	closely spaced pregnancies. <i>The Journal of nutrition</i> 2003;133(5):1732S-36S.
28 29	546	70. WHO. Maternal, newborn, child and adolescent health: Postnatal care. [cited 11 July
30 31 32	547	2020]. Available from:
33 34	548	https://www.who.int/maternal_child_adolescent/topics/newborn/postnatal_care/en/
35 36	549	accessed 2020 11 July
37 38 20	550	71. WHO, USAID, MCHIP, et al. Postnatal Care for Mothers and Newborns: Highlights from
39 40 41	551	the World Health Organization 2013 Guidelines 2015
42 43	552	72. Omariba DWR, Beaujot R, Rajulton F. Determinants of infant and child mortality in Kenya:
44 45	553	an analysis controlling for frailty effects. Population Research and Policy Review
46 47 48	554	2007;26(3):299-321.
49 50	555	73. Fotso JC, Cleland J, Mberu B, et al. Birth spacing and child mortality: an analysis of
51 52	556	prospective data from the Nairobi urban health and demographic surveillance system.
53 54 55 56 57 58 59 60	557	Journal of biosocial science 2013;45(6):779-98.
00		

Page 29 of 39

BMJ Open

1 2		
3 4	558	74. Lamichhane R, Zhao Y, Paudel S, et al. Factors associated with infant mortality in Nepal:
5 6	559	a comparative analysis of Nepal demographic and health surveys (NDHS) 2006 and
7 8 9	560	2011. BMC public health 2017;17(1):53.
9 10 11	561	75. SHARIFZADEH GR, Namakin K, Mehrjoufard H. An Epidemiological study on Infant
12 13	562	Mortality and factors affecting it in Rural Areas of Birjand, Iran. 2008.
14 15	563	76. Boerma JT, Bicego GT. Preceding birth intervals and child survival: searching for pathways
16 17 18	564	of influence. Studies in family planning 1992;23(4):243-56.
19 20	565	77. Dewey KG, Cohen RJ. Does birth spacing affect maternal or child nutritional status? A
21 22	566	systematic literature review. Maternal & child nutrition 2007;3(3):151-73.
23 24 25	567	78. Stuebe A. The risks of not breastfeeding for mothers and infants. Reviews in obstetrics and
25 26 27	568	gynecology 2009;2(4):222.
28 29	569	79. Victora CG, Bahl R, Barros AJ, et al. Breastfeeding in the 21st century: epidemiology,
30 31	570	mechanisms, and lifelong effect. The Lancet 2016;387(10017):475-90.
32 33 34	571	80. Biradar R, Patel KK, Prasad JB. Effect of birth interval and wealth on under-5 child
35 36	572	mortality in Nigeria. Clinical Epidemiology and Global Health 2019;7(2):234-38.
37 38	573	81. Andre FE, Booy R, Bock HL, et al. Vaccination greatly reduces disease, disability, death
39 40 41	574	and inequity worldwide. Bulletin of the World health organization 2008;86:140-46.
41 42 43	575	82. Innis BL, Snitbhan R, Kunasol P, et al. Protection against hepatitis A by an inactivated
44 45	576	vaccine. Jama 1994;271(17):1328-34.
46 47	577	83. Arevshatian L, Clements C, Lwanga S, et al. An evaluation of infant immunization in
48 49 50	578	Africa: is a transformation in progress? Bulletin of the World Health Organization
51 52	579	2007;85:449-57.
53 54	580	84. Attia JR, Jones MP, Hure A. Deconfounding confounding part 1: traditional explanations.
55 56 57	581	The Medical Journal of Australia 2017;206(6):244-45.
57 58 59		
60	582	

Figure Legend

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

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

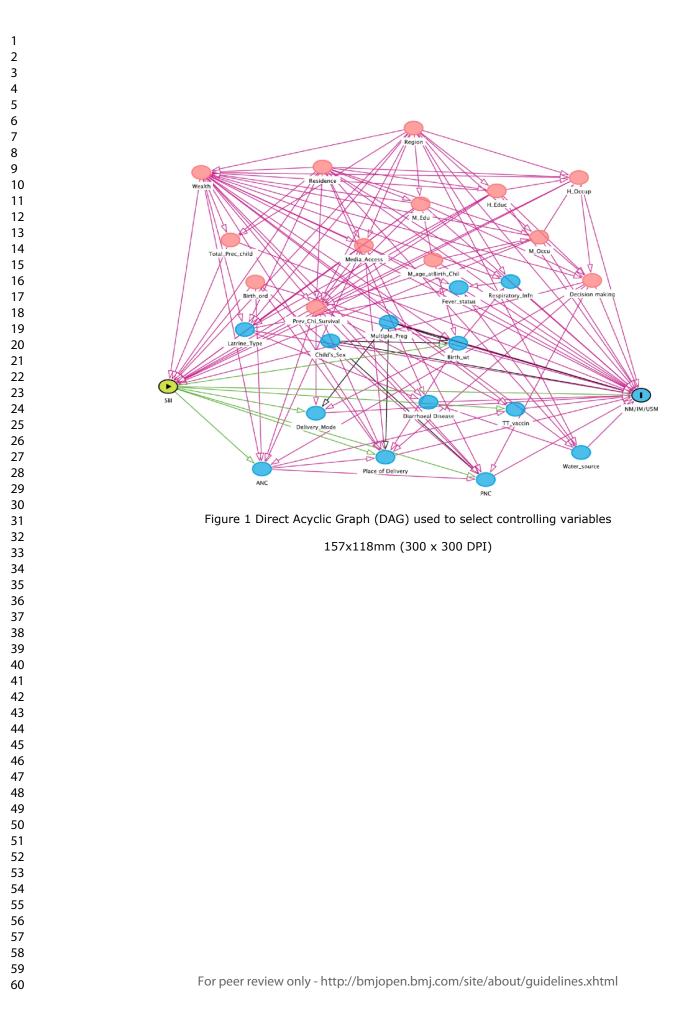
Figure 2 Schematic presentation of the overall steps followed in the analysis

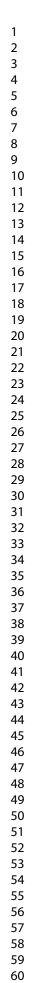
Figure 3 Balance of propensity scores before and after weighting across treatment and C.C.Z.O. comparison groups

PS= propensity score

Page 31 of 39

BMJ Open





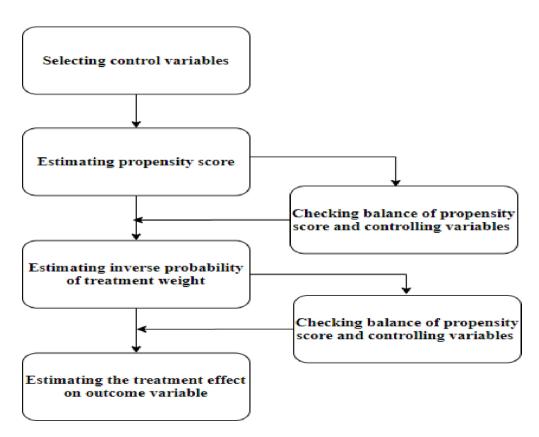
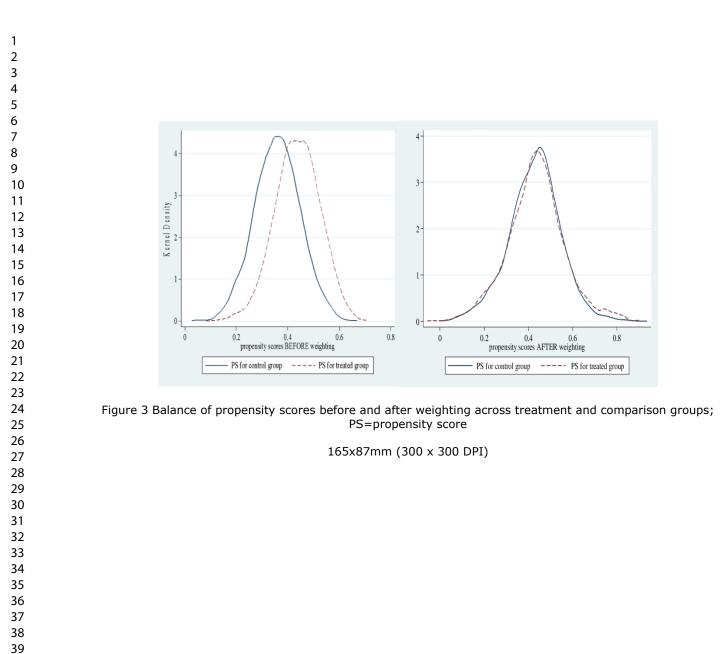


Figure 2 Schematic presentation of the overall steps followed in the analysis

115x90mm (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= \leq 19, 2= 20-24, 3=25-29, 4=30-34, and 5= \geq 35).
	Educational level	Maximum educational level (1= Uneducated, 2=Primary and 3=Secondary+)
	Employment status Place of residence	Maternal employment status (1=Not Employed; 2=Employed)) 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)

Page 35 of 39

 BMJ Open

Maternal health status	Antenatal care	Women's antenatal care utilization categorized as 1=No visit, 2=At
and healthcare-related		least one visit, $3 = \ge$ Four visits
variables	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	Sex	Child sex (1=Male, 2=Female)
characteristics	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	Total number of children born before the index child was considered
	the index child	as a continuous variable. For the descriptive statistics, this variable
		was categorized into $1 = \le 2$, $2 = 3-4$, and $3 = \ge 5$.
	ř C	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 variable
		using the variance inflation factor (VIF). When the values of VIF we lower than 10, then the collinearity problem was considered unlikel
		The VIF for birth order was 18.15 and for the total number of childred
		born before the index child was 16.26, which indicates the presence
		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.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Supplemental Material II

Table 2 Standardized difference before and after weighting the propensity score

re weighting 92 8 8 12 8 8 41 9 2 02 70	After weighting 0.022 0.009 -0.017 0.005 0.012 0.003 0.006 -0.004 0.008 0.005
8 12 8 8 41 9 2 02 70	0.009 -0.017 0.005 0.012 0.003 0.006 -0.004 0.008
12 8 8 41 9 2 02 70	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008
12 8 8 41 9 2 02 70	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008
12 8 8 41 9 2 02 70	-0.017 0.005 0.012 0.003 0.006 -0.004 0.008
8 8 41 9 2 02 70	0.005 0.012 0.003 0.006 -0.004 0.008
8 41 9 2 02 70	0.012 0.003 0.006 -0.004 0.008
8 41 9 2 02 70	0.012 0.003 0.006 -0.004 0.008
41 9 2 02 70	0.003 0.006 -0.004 0.008
41 9 2 02 70	0.003 0.006 -0.004 0.008
9 2 02 70	0.006 -0.004 0.008
2 02 70	-0.004 0.008
2 02 70	-0.004 0.008
02 70	0.008
02 70	0.008
70	
	0.005
51	-0.007
7	-0.006
29	-0.004
39	-0.006
7	
07	0.004
6	0.008
82	0.014
06	0.003
2	-0.003
	-0.006
	-0.005
	-0.009
	-0.009
	0.014
30	0.017
71	-0.002
	-0.002
51	1
	39 07 6 82 06 2 1 59 87 01 80

*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

tor peer terier only

 BMJ Open

Section/Topic	ltem #	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

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

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility,	11, 12, & 13
		confirmed eligible, included in the study, completing follow-up, and analysed	
		(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	15
		interval). Make clear which confounders were adjusted for and why they were included	
		(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	15, 16, 17, & 18
		similar studies, and other relevant evidence	
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	19
		which the present article is based	

*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.