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Exploring spatial distribution and associated factors of stillbirth among births from reproductive-age women in Ethiopia based on the Ethiopian demographic health survey 2016: Spatial and Multilevel Analysis

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thiopia, Multilevel analysis, Spatial analysis





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1	Exploring spatial distribution and associated factors of stillbirth among births
2	from reproductive-age women in Ethiopia based on the Ethiopian
3	demographic health survey 2016: Spatial and Multilevel Analysis
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17 Abstract

Objective: Although the stillbirth rate has been reduced globally, the rate is still very high in developing countries. So far, only ten countries carry the burden of over 65% of stillbirth in the world including Ethiopia in the seventh position. Exploring the spatial variation is important to monitor and design effective intervention programs but there is no available study on spatial distribution and factors associated with a stillbirth at the national level. Therefore, this study aimed to explore the spatial distribution and associated factors of stillbirth.

Methods: secondary data analysis was conducted using the 2016 Ethiopian Demographic and Health Survey data. Weighted samples of 11,375 women were included for analysis. The Bernoulli model was fitted using spatial scan statistics version 9.6 to identify hotspot areas and ArcGIS version 10.6 to explore the spatial distribution of stillbirth. For associated factors, a multilevel logistic regression model that accounts for the hierarchical structure of the data was fitted using STATA 14.

Result: the study showed geographic variability of stillbirth across the country (Global Moran's I = 0.017, p< 0.05). The SaTScan spatial analysis identified primary cluster in Northeast Somali region (LLR=13.4, p<0.001) while the secondary cluster was detected in the border area between Oromia and Amhara region (LLR=8.8, p<0.05). Rural residence (AOR=4.83, 95%CI:1.44-16.19), primary education (AOR=0.39, 95%CI:0.20-0.74), not having ANC visit(AOR=2.77, 95%CI:1.70-4.51), caesarean delivery (AOR=5.07, 95%CI: 1.65-15.58), birth interval <24 month (AOR=1.95, 95%CI: 1.20,3.10), and height<150 cm(AOR=2.73, 95%CI:1.45-4.97) were significant predictors of stillbirth.

Conclusion and recommendation: In Ethiopia, stillbirth had spatial variation across the 39 country. Residence, maternal stature, preceding birth interval, cesarean delivery, education, and

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ANC visit were significant predictors of stillbirth. This has public health implications to target
interventions to identified hotspot areas of stillbirth and the government should scale up maternal
health programs in rural areas
Keywords: stillbirth, Ethiopia, multilevel logistic regression, spatial analysis
Strength and limitation of the study
The study used national survey by weighted the data since some regions were oversampled

and some under sampled to make it nationally representative, the study has the potential to
 inform policy-makers, planners and programmers to design appropriate intervention at
 national and regional levels

As a study was a cross—sectional study, the study are unable to show temporal relationship.
 However, our method used multilevel modeling which took into account the effect of
 clustering to get reliable estimate and standard error.

The EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or caregivers report

The study was based on self-reports of respondents. There may have the possibility of social desirability and recall bias since stillbirth is not culturally acceptable though CSA claim that strong effort was made to minimize it mainly through extensive training of data collectors,

- recruiting experienced data collectors and supervisors this might underestimate our finding
- The SaTScan detect only circular clusters, irregular shaped clusters were not detected

60 BACKGROUND

For international comparison, the World Health Organization (WHO) defines stillbirth as fetal death (death before the complete expulsion or extraction of a product of conception from its mother) in the third trimester (>28 completed weeks of gestation) or birth weight >1000 gram or length \geq 35 centimeter(1, 2). Globally, stillbirth is a huge public health concern, especially in Sub-Saharan Africa (SSA) and South Asia (SA) including Ethiopia (3). Around 2.6 million stillbirths occur annually, 98% of which occur in developing countries (4). An overwhelming majority (67%) of the world's stillbirth occurred in Sub-Saharan Africa and South Asia, and most of the stillbirth occurs during the intrapartum period which is preventable by improving obstetrics services (5).

More than half of the 2.6 million stillbirths occur during labor and delivery, indicating poor quality of healthcare services in many of the developing countries with a high burden of stillbirth (6). It is considered to be an important indicator of access to and quality of obstetric care, including the utilization of services in a geographic location (7). According to the most recent global estimate of the World Health Organization (WHO), the average global stillbirth rates was 18.4 per 1000 births (8), while developing countries have the stillbirth rates ten-fold higher than developed countries (9). Sub-Saharan Africa is particularly affected by the highest stillbirth rate globally 28.3 per 1000 births (10).

The rate of stillbirth varies across countries and remains a huge challenge to achieve Every Newborn Action Plan (ENAP) of the target of 12 or fewer stillbirths per 1000 births in every country by 2030 (1). Even though many high-income countries and upper-middle-income countries have already met this target, developing countries particularly Africa will have to more than double present progress to reach this target (1).

Despite the various international and national commitments and interventions on improving newborn and maternal health (11), stillbirth has been grossly under-reported and invisible in policies and programs worldwide, with little recognition of potential strategies for intervention (12). Like many countries in SSA, stillbirth is not routinely recorded and monitored in Ethiopia. Stillbirth has been reduced more slowly than maternal mortality or under 5 mortality, which remains invisible in global policies with an Annual Average Rate of Reduction (ARR) of 2.0% in comparison to ARR of 3.0% for maternal death or 3.1% for neonatal death (13). The death of a fetus in utero or at birth is a devastating experience for the affected mothers and families (14). It has been associated with extensive psychosocial consequences for parents and family and has been linked to a post-traumatic stress disorder, anxiety, depression, suicide, fear of the next pregnancy and reduced relation with their partner (15, 16).

In Ethiopia, a study conducted based on Ethiopian Demographic and Health Survey (EDHS) 2011 revealed a stillbirth rate of 25.5 per 1000 births with significant variability across regions and they recommend researchers to conduct spatial analysis to investigate the spatial variability of experiencing stillbirth (17). A study done at the Amhara region based on Ethiopian Mini Demographic and Health Survey 2014 reported that a stillbirth rate of 85 per 1000 births(18). Different studies done on experiencing stillbirth showed that rural residence, parity, educational status, mode of delivery, ANC utilization, and place of delivery, maternal nutritional status, and maternal obstetric factors were the significant predictors of experiencing stillbirth (14, 19-21).

There is a wide gap in the stillbirth rate not only among different countries but also within the
country (17, 22). A high rate of stillbirth has been reported among rural, poor and marginalized
societies that are the least beneficial of maternal health promotion activities and services (12).
Thus, the identification of geographic areas with a high rate of stillbirth using Geographic

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Information System (GIS) and Spatial Scan statistical analysis (SaTScan) has become fundamental to guide targeted public health interventions. However, previous studies in Ethiopia have focused on the prevalence and associated factors of stillbirth (18, 23, 24), by using standard logistic regression models despite the hierarchical structure of DHS data this could result in biased estimate since the data is nested within-cluster and violates the independent assumption unless we take into account by using multilevel models (17). The findings of these studies are insufficient and limited to capture the spatial distribution of stillbirth and community-level factors contributing to stillbirth. Therefore, the current study was done to explore the spatial distribution and associated factors of stillbirth among births from reproductive-age women in Ethiopia using Spatial and multilevel Analysis. Thus, understanding the spatial epidemiology of stillbirth is crucial for evidence-based decision making to improve pregnancy outcomes by designing effective maternal health programs.

118 Method and materials

119 Study design, setting and period

A community-based cross-sectional study was conducted from January 18 to June 27, 2016. The
study was conducted in Ethiopia, which is situated in the Horn of Africa. It has 9 Regional states
(Afar, Amhara, Benishangul-Gumuz, Gambela, Harari, Oromia, Somali, Southern Nations,
Nationalities, and People's Region (SNNP) and Tigray) and two Administrative Cities (Addis
Ababa and Dire-Dawa) (Figure 1).

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Ethiopia is an agrarian country and agriculture accounts for 43 percent of the gross domestic product (GDP) and 84% of the population lives in rural areas. More than 80 percent of the country's total population lives in the regional states of Amhara, Oromia, and SNNP(25).

In 2016, the population was 102 million of which 43.47% the population ages less than 14 years with birth rate of 36.5 births per 1000 population and fertility rate of 4.46, Ethiopia is the13th in the world and 2nd in Africa most populous country Ethiopia has 3 tiers health systems, Primary health care unit (Primary hospital, health center, health post, primary clinic, and medium clinic); Secondary health care (General hospital, specialty clinics and specialty centers); and Tertiary health care (Specialized hospital). The number of hospitals varies from region to region in response to differences in population size. The most populous region, Oromia has 30 hospitals. The other two predominant regions Amhara and SNNPR have 19 and 20 respectively with Tigray in fourth place with 16 hospitals, Gambela has only one hospital and Benishangul-Gumuz two had two hospitals (26).

138 Sample and population

The source population was all births from reproductive age women within five years before the survey in Ethiopia and all births from reproductive-age women in the selected enumeration areas within five years before the survey were the study population. The EDHS used a stratified two-stage cluster sampling technique selected in two stages using 2007 the Population and Housing Census as a sampling frame. Stratification was achieved by separating each region into urban and rural areas. In total, 21 sampling strata have been created because the Addis Ababa region is entirely urban. In the first stage, 645 EAs (202 in the urban area) were selected with probability proportional to the EA size and with independent selection in each sampling stratum. In the second stage, because the time has passed since the PHC, a complete household listing operation was carried out in all selected EAs before the start of fieldwork and on average 28 households were systematically selected. Of these, 18,008 households and 16,583 eligible women included. The detailed sampling procedure was presented in the full EDHS 2016 report (27).

151 Study variables

Outcome variables

The 2016 EDHS asked women to report any pregnancy loss that occurred in the five years preceding the survey. For each pregnancy that did not end in a live birth, the duration of the pregnancy was recorded. Pregnancy losses occurring after seven completed months of gestation are defined as stillbirths. The response variable of this study is the occurrence of stillbirth among mothers of childbearing age.

The response variable for the ith mother is represented by a random variable Y_i with two possible values coded as 1 and 0. So, the response variable of the ith mother Y_i was measured as a dichotomous variable with possible values $Y_i = 1$, if _{ith} mother had experienced stillbirth and $Y_i =$ 0 if mother had a live birth.

Independent variables

Consistent with the objective of the study and given the hierarchical structure of EDHS data where women were nested within the cluster/community, two levels of independent variables were considered. Level 1 contained individual socio-demographic and economic factors (Age, marital status, religion, maternal education, paternal education, wealth index, maternal occupation, maternal working Status), pregnancy and pregnancy-related factors (Mother's height, BMI, ANC visit, Parity, Preceding birth interval, contraceptive use, Place of delivery, Birth order, Mode of delivery, wanted pregnancy, Maternal anemia), and behavioral factors (Smoking, media exposure) and that of community-level factors (region, residence, community women education, community poverty, community media exposure, and community ANC utilization) at level 2, which included the characteristics of the community in which each woman resided. In EDHS data no variable describes the cluster except region and place of residence.

Therefore, Individual-level variables were aggregated at the cluster level to generate communitylevel variables to see whether cluster-level variables had an effect on stillbirth and which were categorized by their proportion as higher or lower based on national median value since it was not normally distributed. Community-level variables used in the analysis were from two sources; direct community-level variables that were used without any manipulation and aggregated community-level variables that were generated by aggregating individual-level variables at the cluster level.

181 Data collection procedure

The study was conducted based on EDHS data by accessing from the DHS program official database<u>www.measuredhs.com</u> after permission was granted through an online request by explaining the objective of our study. The raw data was collected from all parts of the country on childbearing aged women using a structured and pre-tested questionnaire. We used the EDHS 2016 birth data set and extracted the outcome and independent variables. Geographic coordinate data (longitude and latitude coordinates) was taken at the cluster level/ enumeration area level.

188 Data management and analysis

Before the actual data collection, the Pre-test was conducted which consisted of in-class training, biomarker training, and field practice days. The questionnaires were pretested in all three local languages (Amharic, Oromia, and Tigrigna) to make sure that the questions were clear and could be understood by the respondents. The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey and to tell the STATA to take into account the sampling design when calculating standard errors to get reliable statistical estimates. Cross tabulations and summary statistics were

conducted to describe the study population. Descriptive and summary statistics were conducted using STATA version 14 software.

In EDHS data, women are nested within a cluster and we expect that women within the same cluster may be more similar to each other than women in the rest of the country. This violates the assumption of the traditional regression model which is the independence of observations and equal variance across clusters. This implies that the need to take into account the between cluster variability by using an advanced model. Therefore, a multilevel logistic regression model (both fixed and random effect) was fitted, since the outcome variable was binary. Model comparison was done based on Deviance since the models were nested. Likelihood ratio test, ICC (Intra-class correlation), MOR (median odds ratio) and PCV (proportional change in variance) were computed to measure the variation between clusters. The intra-class correlation coefficient (ICC) quantifies the degree of heterogeneity of stillbirth between clusters (the proportion of the total observed individual variation in stillbirth that is attributable to between cluster variations).

ICC= $\sigma^2/(\sigma^2 + \pi^2/3)(28)$, but MOR is quantifying the variation or heterogeneity in outcomes between clusters and is defined as the median value of the odds ratio between the cluster at high risk of stillbirth and cluster at lower risk when randomly picking out two clusters (EAs).

¹ 212 MOR= exp (
$$\sqrt{2*\partial 2*0.6745}$$
) ~MOR=exp (0.95* ∂)(29)

 ∂^2 indicates that cluster variance

PCV measures the total variation attributed to individual-level factors and community-level factors in the multilevel model as compared to the null model.

- PCV= var (null model) var full model))

Var (null model)

Two-level multilevel multivariable logistic regression was used to analyze factors associated with a stillbirth at two levels, at individual and community (cluster) levels. Four models were constructed for the multilevel logistic regression analysis. The first model was an empty model without any explanatory variables, to determine the extent of cluster variation on stillbirth. The second model was adjusted with individual-level variables; the third model was adjusted for community-level variables while the fourth was fitted with both individual and community level variables simultaneously. A model with the lowest deviance was chosen.

Variables with p-value ≤ 0.2 in the bi-variable analysis for both individual and community-level factors were fitted in the multivariable model. Adjusted Odds Ratio (AOR) with a 95% Confidence Interval (CI) and p-value < 0.05 in the multivariable model were used to declare significant association with experiencing stillbirth. Multi-collinearity was also checked using the variance inflation factor (VIF) which indicates that there is no multi-collinearity since all variables have VIF<5 and tolerance greater than 0.1.

231 Spatial analysis

For the spatial analysis ArcGIS version 10.6 software and SaTScan version 9.6 software.

233 Incremental spatial autocorrelation

It measures spatial autocorrelation for a series of distances and creates a line graph of those distances and their corresponding Z-score. Z-scores reflect the intensity of spatial clustering and statistically significant peak Z-scores. Z-scores indicate where the spatial clustering of stillbirth is more pronounced. The maximum peak distance was used as a distance band for hotspot analysis.

239 Spatial autocorrelation analysis

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The spatial autocorrelation (Global Moran's I) statistic measures whether stillbirth patterns were dispersed, clustered or randomly distributed in the study area(30). Moran's I is a spatial statistics used to measure spatial autocorrelation by taking the entire data set and produce a single output value which ranges from -1 to +1. Moran's I Values close to -1 indicate disease dispersed, whereas Moran's I close to +1 indicate disease clustered and disease distributed randomly if I value is zero. A statistically significant Moran's I (p < 0.05) leads to rejection of the null hypothesis (stillbirth is randomly distributed) and indicates the presence of spatial autocorrelation.

Anselin Local Moran's I used to investigate the local level cluster locations of stillbirth in terms of positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high). A positive value for 'I' indicated that a case had neighboring cases with similar values, part of a cluster. A negative value for 'I' indicated that a case was surrounded by cases with dissimilar values an outlier.

253 Hot spot analysis (Getis-OrdGi* statistic)

Getis-OrdGi* statistics were computed to measure how spatial autocorrelation varies over the study location by calculating GI* statistic for each area. Z-score is computed to determine the statistical significance of clustering, and the p-value computed for the significance. Statistical output with high GI* indicates "hotspot" whereas low GI* means a "cold spot"(31).

258 Spatial interpolation

It is very expensive and laborious to collect reliable data in all areas of the country to know the burden of a certain event. Therefore, part of a certain area can be predicted by using observed data using a method called interpolation. Spatial interpolation technique is used to predict

stillbirth on the un-sampled areas in the country based on sampled EAs. There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best method since it incorporates the spatial autocorrelation and it statistically optimizes the weight(32). Ordinary Kriging spatial interpolation method was used for this study for predictions of stillbirth in unobserved areas of Ethiopia.

268 Spatial scan statistical analysis

Spatial scan statistical analysis Bernoulli based model was employed to test for the presence of statistically significant spatial clusters of stillbirth using Kuldorff's SaTScan version 9.6software. The spatial scan statistic uses a circular scanning window that moves across the study area. Women with stillbirth were taken as cases and those who have live birth as controls to fit the Bernoulli model. The numbers of cases in each location had Bernoulli distribution and the model required data for cases, controls, and geographic coordinate. The default maximum spatial cluster size of <50% of the population was used, as an upper limit, which allowed both small and large clusters to be detected and ignored clusters that contained more than the maximum limit.

For each potential cluster, a likelihood ratio test statistic and the p-value was used to determine if the number of observed stillbirth within the potential cluster was significantly higher than expected or not. The scanning window with maximum likelihood was the most likely performing cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis testing by comparing the rank of the maximum likelihood from the real data with the maximum likelihood from the random datasets. The primary and secondary clusters were identified and assigned pvalues and ranked based on their likelihood ratio test, based on 999 Monte Carlo replications(33)

285 Patient and public involvement statement

Patients and public involvement were not involved in this study since we have conducted a secondary data analysis based on already available DHS data which was collected to provide estimates of common health and health related indicators. For the original project from which data were obtained, patient and public involvement statement was essential since biomarker data's such as anemia, HIV testing and anthropometric measurements were collected (34).

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of Institute of Public Health, CMHS, and the University of Gondar. Permission for data access was obtained from major demographic and health survey through an online request from <u>http://www.dhsprogram.com</u>. The data used for this study were publicly available with no personal identifier.

Result

299 Socio-demographic and economic characteristics of respondents

A total of 11,375 women who gave birth within five years preceding the survey were included for the analysis. Of 11,375 of women, 10,149 (89.2%) were rural residents and half of the respondent were in the age group 20-29 years. Regarding maternal education status, 7,606 (66.9%) had no formal education (Table 1).

304 Pregnancy and maternal health service-related characteristics of respondents

Among 11375 respondents who gave birth within five years, two-third 7,468 (65.7%) of the respondents delivered at home and 194 (1.7%) gave birth through cesarean section. With regard to ANC utilization, 2,602 (22.9 %) had no ANC visit during pregnancy (Table 2).

The overall rate of stillbirth among births from childbearing age women within five years preceding the survey in Ethiopia was 9.2 [95% CI; 7.9, 11.1] per 1000 birth. Stillbirth rate was highest in the Amhara region (19.7) and lowest in Diredawa (3.0) (Figure 2).

311 Spatial distribution of stillbirth

A total of 622 clusters were considered for the spatial analysis of stillbirth. Each point on the map represents one enumeration area with the proportion of stillbirth cases in each cluster. The red color indicates areas with a high proportion of stillbirth whereas blue color indicates EAs with a lower proportion of stillbirth. A higher proportion of stillbirth has occurred in the south and east Amhara, east Benishangul-Gumuz, East Gambella, central Oromia, north Tigray, southwest and northeast Somali, and northeast SNNPR whereas, a low proportion of stillbirth were aggregated in Afar, southwest Benishangul, west Gambella and SNNPR (Figure 3).

319 Incremental spatial autocorrelation

Totally 10 distance bands were detected by a beginning distance of 121,803 meters, the first peak of 136,586.06 meters and the maximum peak (clustering) was observed at 166152.17 meters. The maximum peak was used as the distance band for hotspot analysis (Figure 4).

323 Spatial autocorrelation

This study revealed that the spatial distribution of stillbirth was found to be non-random in Ethiopia with Global Moran's I 0.017 (p< 0.05) (Figure 5). The clustered patterns (on the right sides) show high rates of stillbirth occurred over the study area. The outputs have automatically generated keys on the right and left sides of each panel. Given the z-score of 2.4 indicated that there is less than 1.5% likelihood that this clustered pattern could be the result of chance. The bright red and blue colors to the end tails indicate an increased significance level (Figure 5).

330 Cluster and outlier analysis of stillbirth

The significant cluster was detected in Tigray, Amhara, Oromia, Addis Ababa, SNNPR, Benishangul-Gumuz, Somali and Gambella regions. Hot spot areas for stillbirth were found in southwest Somali, southern Amhara, and west SNNPR, While the cold spot regions were found in south and west Benishangul-Gumuz, Addis Ababa, southwest of Oromia region, west Gambella and Northeast SNNPR. Outliers were found in the central and southern parts of Amhara, north Tigray, southeast Gambella and Somali regions (Figure 6).

337 Hot spot analysis of stillbirth

The red color indicates that significant hotspot areas (high rate of stillbirth). Which was found in the central and southern part of Amhara, west SNNPRs, south and north Tigray, and south West Somali region (p-value< 0.05), whereas, the blue and yellow color indicates significant more non-risky areas (cold spot areas). This was found in Addis Ababa, central Oromia, and east
SNNPRs when the level of confidence increases in both directions its significant level also
increases (Figure 7).

Interpolation of stillbirth

North West Tigray, northern and North West Oromia, east and south Amhara, east Benishangul,
East Gambella, Harari, and Northwest SNNPR were detected as predicted more risky areas of
stillbirth compared to other regions. Predicted low-risk areas were found in Oromia, Afar, and
Gambella regions. Continuous images produced by interpolating (Kriging interpolation method)
stillbirth among birth from reproductive-age women (Figure 8).

350 Spatial scan statistical analysis

A total of 56 significant clusters were identified of which 22 clusters were primary (most likely clusters) and 34 secondary clusters of stillbirth were identified. The primary cluster spatial window was located in the northeast Somali region, which was centered 7.829198 N, 43.706264 E of geographic location with 166.48 km radius, a relative risk of 22.5 and Log-Likelihood ratio (LLR) of 13.4, at p < 0.001. It showed that women within the spatial window had 22.5 times higher risk for stillbirth than women outside the window. The secondary clusters scanning window was located between the border area of the south Amhara region and the north Oromia region, and the southern Afar region (Table 3). The red circular ring indicates that the most statistically significant spatial window contains the primary cluster of stillbirth. There was a higher risk of stillbirth within the circular window than outside the spatial window (Figure 9).

- **Factors associated with stillbirth**
- 362 Model comparison

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363 ICC and LR test were checked, and multilevel model was chosen because the likelihood ratio test 364 was significant and the ICC was 47%. Therefore, the two-level multilevel logistic regression 365 model was used to get an unbiased standard error and to make a valid inference. Deviance was 366 used for model comparison; the final model was the best-fitted model with the lowest deviance 367 (Table 4).

368 Random effect model

ICC in the empty model indicated that 47% of the total variability for stillbirth was due to differences between clusters/EA, with the remaining unexplained 53% attributable to individual differences. Moreover, the median odds ratio for stillbirth was 5.03 in the null model which indicates that there was variation between clusters. If we randomly select women from two different clusters of women at the cluster with a higher risk of stillbirth had 5.03 times higher odds of experiencing stillbirth as compared with women at cluster with a lower risk of stillbirth. About 15.3 percent of the variability in stillbirth was explained by the full model (Table 4).

The

The fixed effect analysis result

In the multilevel logistic regression model, residence, region, religion, wealth status, maternal education, birth order, parity, ANC visit, media exposure, maternal height, contraceptive use, birth interval, mode of delivery, community media exposure, and community women education were significant in the bi-variable analysis at p-value<0.05. However, in the multivariable multilevel logistic regression residence, region, religion, preceding birth interval, cesarean delivery, maternal height, ANC visit, and maternal education were significant predictors of stillbirth.

The odds of experiencing stillbirth for those women residing in a rural area were 4 .83 times higher than that of those women residing in urban areas (AOR= 4.83, 95% CI 1.44-16.19). protestant and catholic religious followers had 89% decreased odds of experiencing stillbirth as compared to orthodox religious followers (AOR= 0.11, 95% CI 0.03- 0.37). Educational level of women was significantly associated with experiencing stillbirth, Though women having secondary and higher education have no significant difference in experiencing stillbirth with those having no educational attainment, women having primary education decreases the odds of experiencing stillbirth by 61% as compared to those with no educational attainment (AOR= 0.39, 95% CI 0.20 - 0.74). The odds of experiencing stillbirth in Tigray, Afar, Somali, SNNPR, Benishangul, Gambella and Harari were not significantly different from that of experiencing stillbirth in Amhara. Women's in the Oromia region had 75% decreased odds of experiencing stillbirth as compared to women in the Amhara region (AOR= 0.25, 95% 0.07- 0.83). besides, Women who had no antenatal care visit during pregnancy were 2.77 times higher odds of experiencing stillbirth than those who have 4 and above ANC visits (AOR= 2.77, 95% CI 1.70 - 4.51). Women who gave birth through cesarean delivery were 5.07times higher odds of experiencing stillbirth than those women who gave birth through vaginal delivery (AOR= 5.07, 95% CI 1.65– 15.58).

The preceding birth interval was a significant predictor of experiencing stillbirth outcomes. Women having preceding birth interval less than 24 months had 1.93 times higher odds of experiencing stillbirth compared to women having preceding birth interval 24 months and above (AOR= 1.93, 95% CI 1.20 - 3.10). also, maternal height less than 150 cm were 2.73 times higher odds of experiencing stillbirth as compared to those mother's greater than or equal to 150 cm (AOR= 2.73, 95% CI 1.50-4.97) (Table 4).

Discussion

In Ethiopia, the stillbirth rate was found to be 9.2 per 1000 birth with marked spatial heterogeneity. The spatial scan statistics detected a total of three statistically significant SaTScan clusters areas with a high rate of stillbirth. This could be attributed to the disparity in the distribution of maternal health service, and the inaccessibility of infrastructure in the border areas of regions (35). In the multivariable multilevel analysis, the odds of stillbirth were lower among women who lived in the Oromia region as compared to those in the Amhara region. This might be due to availability and accessibility of maternal health facility since Oromia regions are relatively around Addis Ababa and Dire-Dawa in which health facilities are accessible as compared to other regions and high turnover rate of health professionals in Amhara region and Addis Ababa is the place of destination for them (36). Catholic or protestant religion followers were significantly associated with lower odds of stillbirth as compared with orthodox religious followers. This could be due to miss-perception of religious followers may shape their reproductive health decision making and practices, thereby govern the women's desire for using maternal health services (37) like some religious followers consider as giving birth at home as blessed, using contraceptive as committing sin and not expose their body to health professionals during delivery this might be the possible reason which needs further qualitative study to explore the detailed reasons.

The study has shown that the odds of stillbirth were higher among women who lived in rural areas. This was consistent with previous study findings in South Africa(38), African Great lake Regions(12), Nigeria(19), Northern Ghana(14) and Ethiopia(17). This could be attributed to the

disparity in mothers health care access, availability and accessibility of health facilities and
women in urban areas are relatively had improved health-seeking behavior (35) and more aware
of maternal health service but in rural area health facilities may not be easily reachable and may
end up with poor pregnancy outcome during emergency cases (39).

This study noted lower odds of stillbirth among women who had primary education as compared to women with no education. This finding was in line with previous studies done in Kenya(40) and Nigeria(19). This could be attributed to having maternal education could lead to the corresponding improvement in health-seeking behavior such as the timely decision to seek care appropriate care during pregnancy, give better care for their health and their fetus, awareness to the danger sign of pregnancy and maternal health service utilization(41).

The odds of stillbirth were higher among short stature women. A similar finding was reported in Pakistan(21). this might be for the reason that short stature women are associated with adverse pregnancy outcomes like Cephalo pelvic disproportion, contracted pelvis, intra-uterine growth restriction(IUGR), intra-uterine Fetal death(IUFD) and birth injury hence short stature reflects longstanding malnutrition or childhood infection that start in uretro or during early childhood this kind of women may end up with poor pregnancy outcome unless we screen them as at-risk during ANC follow up(42).

In addition, having no ANC visit had a significant association with increased stillbirth. This study could support previous studies done in low-middle countries (43), Ghana(44) and Kenya(40). ANC follow up could help a pregnant woman to seek early treatment for her potential pregnancy-associated complications, early screening of underlying medical conditions and may improve birth outcomes by promoting deliveries in health facilities where complications can be better managed and have access to information related to nutrition, and danger signs of

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pregnancy (44, 45). On the other hand, women who did not have longer ANC follow up may notbe benefited from basic ANC packages.

454 Consistent with studies done in Nigeria based on the 2013 DHS(19) and cross-sectional study in 455 Gambia(46), cesarean deliveries in this study showed higher odds of stillbirth when compared 456 with normal vaginal delivery. This may be due to the reason that cesarean sections are probably 457 applied too late in hospital since most of women's are referred from the distant health facility and 458 there may be delay in referral or transportation problem resulting to not to save the baby's life 459 because the cesarean section is not done with the right time (47, 48).

In this study, having a short inter-pregnancy interval was associated with higher odds of stillbirth. This was consistent with studies done sub-Saharan Africa (49), Bangladesh (50) and Amhara Region(18). This could be explained by short preceding birth interval are less able to provide nourishment for the fetus because her body has had less time to recuperate from the previous pregnancy, the uterus had less time to recover and also lactation will deplete maternal nutrition and may end up with poor pregnancy outcomes (50).

466 The strength of this study was using weighted data to make it representativeness at national and regional levels: therefore, it can be generalized to all women who gave birth during the study 467 period in Ethiopia. Moreover, the use of GIS and SaTScan statistical tests helped to detect 468 469 similar and statistically significant hotspot areas of stillbirth and to design effective public health programs. However, the SaTScan detect only circular clusters, irregular shaped clusters were not 470 detected. Furthermore, the EDHS survey did not incorporate clinically confirmed data rather it 471 relied on mothers or caregivers report and might have the possibility of social desirability and 472 recall bias since stillbirth is not culturally acceptable though CSA claim that strong effort was 473

474 made to minimize it mainly through extensive training of data collectors, recruiting experienced475 data collectors and supervisors this might underestimate our finding.

The findings of this study have valuable policy implications for health program design and interventions. Stillbirth high-risk areas can be easily identified to make effective local interventions. In general, these findings are of supreme importance for the minister of health, regional health bureaus, and NGO's to design intervention programs to reduce stillbirth in identified hotspot areas.

Conclusions

In Ethiopia, stillbirth had spatial variations across the country. Statistically, significant-high hotspots of stillbirth were found in the central and southern parts of Amhara, west SNNPRs, south and north Tigray, and south West Somali region. Whereas, cold spot areas were found in Addis Ababa, central Oromia, and east SNNPRs. Short preceding birth interval, short maternal stature, ANC visit, rural residence, region, religion, maternal education, and cesarean delivery were significant predictors of stillbirth.

488 Abbreviations

ANC; Antenatal Care, AOR; Adjusted Odds Ratio, ARR; Annual Rate of Reduction, BMI; Body
Mass Index, CI; Confidence Interval, COR; Crude Odds Ratio, CSA; Central Statistical Agency,
DHS; Demographic Health Survey, EA; Enumeration Area, EDHS; Ethiopian Demographic
Health Survey, GIS; Geographic Information System, ICC; Intra-cluster Correlation
Coefficient, IUFD; Intra Uterine Fetal Death, IUGR; Intra Uterine Growth Restriction,
LLR; log-likelihood Ratio, LR; Likelihood Ratio, MOR; Median Odds Ratio, PCV; Proportional

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3 4	495	Change in Variance, PHC; Population and Housing census, SBR; Stillbirth Rate, SNN	PRs;
5 6 7 8	496	Southern Nations and Nationality People Regional state, WHO; World Health Organization.	
9 10 11	497	Declarations	
12 13 14 15	498	Availability of data and materials	
16 17	499	Data is available online and you can access it from <u>www.measuredhs.com</u> .	
18 19 20	500	Competing Interests	
21 22 23	501	Authors declare that they have no conflict of interest	
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32 33 34	505	Conceptualization: Getayeneh Antehunegn Tesema	
35 36 37	506	Data curation: Getayeneh Antehunegn Tesema	
38 39	507	Funding acquisition: Getayeneh Antehunegn Tesema	
40 41 42	508	Investigation: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu	
43 44	509	Methodology: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu	
45 46 47	510 511	Project administration: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh Resources: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh	
48 49	512	Software: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh	
50 51 52	513	Supervision: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh	
53 54 55	514	Validation: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh	
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- 515 Visualization: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh
- 516 Writing: Getayeneh Antehunegn Tesema
 - 517 Writing review and editing: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Derseh

Consent for publication

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² 522 **References**

523 1. Organization WH. Every newborn: an action plan to end preventable deaths. 2014.

524 2. Smith GC, Fretts RC. Stillbirth. The Lancet. 2007;370(9600):1715-25.

525 3. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and 526 stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC 527 pregnancy and childbirth. 2010;10(1):S1.

528 4. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. The Lancet. 2016;387(10018):587-603.

5 530 5. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? 6 531 When? Why? How to make the data count? The Lancet. 2011;377(9775):1448-63.

532 6. Temmerman M, Lawn JE. Stillbirths count, but it is now time to count them all. The Lancet.
 533 2018;392(10158):1602-4.

534
 7. Admasu K, Haile-Mariam A, Bailey P. Indicators for availability, utilization, and quality of
 535 emergency obstetric care in Ethiopia, 2008. International Journal of Gynecology & Obstetrics.
 536 2011;115(1):101-5.

537 8. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and
46 538 worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet
47 539 Global Health. 2016;4(2):e98-e108.

540 9. Saleem S, Tikmani SS, McClure EM, Moore JL, Azam SI, Dhaded SM, et al. Trends and
541 determinants of stillbirth in developing countries: results from the Global Network's Population-Based
542 Birth Registry. Reproductive health. 2018;15(1):100.

543 10. McClure EM, Pasha O, Goudar SS, Chomba E, Garces A, Tshefu A, et al. Epidemiology of stillbirth
54 in low-middle income countries: a Global Network Study. Acta obstetricia et gynecologica Scandinavica.
55 545 2011;90(12):1379-85.

- 546 11. Bamford L. Maternal, newborn and child health: service delivery. South African health review.
 547 2012;2012(2012/2013):49-66.
- 548 12. Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: A
 549 pooled analysis of Demographic and Health Surveys. PloS one. 2018;13(8):e0202603.
- Solution
 Sol
- 1455414.Badimsuguru AB, Nyarko KM, Afari EA, Sackey SO, Kubio C. Determinants of stillbirths in15555Northern Ghana: a case control study. The Pan African medical journal. 2016;25(Suppl 1).
- 16
 17
 18
 15. Ogwulu CB, Jackson LJ, Heazell AE, Roberts TE. Exploring the intangible economic costs of stillbirth. BMC pregnancy and childbirth. 2015;15(1):188.
- 19 558 16. Meaney S, Everard CM, Gallagher S, O'donoghue K. Parents' concerns about future pregnancy
 20 559 after stillbirth: a qualitative study. Health Expectations. 2017;20(4):555-62.
- 2256017.Berhie KA, Gebresilassie HG. Logistic regression analysis on the determinants of stillbirth in23561Ethiopia. Maternal health, neonatology and perinatology. 2016;2(1):10.
- 24
 25 562 18. Lakew D, Tesfaye D, Mekonnen H. Determinants of stillbirth among women deliveries at Amhara
 26 563 region, Ethiopia. BMC pregnancy and childbirth. 2017;17(1):375.
- 27
 28
 29
 564
 19. Dahiru T, Aliyu AA. Stillbirth in Nigeria: rates and risk factors based on 2013 Nigeria DHS. Open
 29
 565
 Access Library Journal. 2016;3(08):1.
- 566 20. Ali AAA, Adam I. Anaemia and stillbirth in Kassala hospital, eastern Sudan. Journal of tropical
 567 pediatrics. 2010;57(1):62-4.
- 3356821.Badshah S, Mason L, Lisboa PJ. Risk Factors Associated with Stillbirths in Public-Hospitals in34569Peshawar, Pakistan. The Journal of Humanities and Social Sciences. 2011;19(2):15.
- 35
 36 570 22. Berhan Y, Berhan A. Perinatal mortality trends in Ethiopia. Ethiopian journal of health sciences.
 37 571 2014;24:29-40.
- Welegebriel TK, Dadi TL, Mihrete KM. Determinants of stillbirth in Bonga General and Mizan
 Tepi University Teaching Hospitals southwestern Ethiopia, 2016: a case–control study. BMC research
 notes. 2017;10(1):713.
- 42 575 24. Tilahun D, Assefa T. Incidence and determinants of stillbirth among women who gave birth in
 43 576 Jimma University specialized hospital, Ethiopia. Pan African Medical Journal. 2017;28(1).
- 4557725.Central statistical agency(CSA) I. Ethiopian Demographic and Health survey. Addis Abeba: Addis46578Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF, 2016.
- 47 48 579 26. Adugna A. Health Institutions and Services. Addis Abeba: July 2014.
- 49 580 27. ICF CSACEa. Ethiopia Demographic and Health Survey 2016 Addis Ababa, Ethiopia, and Rockville
 50 581 , maryland, USA: CSA and ICF. 2016.
- 52 582 28. Rodriguez G, Elo I. Intra-class correlation in random-effects models for binary data. The Stata
 53 583 Journal. 2003;3(1):32-46.
 54
- 57 58

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60

55 56

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584 29. Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial of
 585 multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to
 586 investigate contextual phenomena. Journal of Epidemiology & Community Health. 2006;60(4):290-7.

⁷ 587 30. Waldhör T. The spatial autocorrelation coefficient Moran's I under heteroscedasticity. Statistics
 ⁸ 588 in Medicine. 1996;15(7-9):887-92.
 9

1058931.Tsai P-J, Lin M-L, Chu C-M, Perng C-H. Spatial autocorrelation analysis of health care hotspots in11590Taiwan in 2006. BMC Public Health. 2009;9(1):464.

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16 594 33. Kulldorff M. SaTScanTM user guide. Boston; 2006.

18 595 34. 2016. CSACEal. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and
 19 596 Rockville, Maryland, USA: CSA and ICF. 2016.
 20

21 597 35. Adugna A. Health instituition and Services in Ethiopia. 2014.

598 36. Assefa T, Mariam DH, Mekonnen W, Derbew M, Enbiale W. Physician distribution and attrition
 599 in the public health sector of Ethiopia. Risk management and healthcare policy. 2016;9:285.

- 600 37. Tarekegn SM, Lieberman LS, Giedraitis V. Determinants of maternal health service utilization in
 601 Ethiopia: analysis of the 2011 Ethiopian Demographic and Health Survey. BMC pregnancy and childbirth.
 602 2014;14(1):161.
- 603 38. Nfii FN. Levels, trends and household determinants of stillbirths and miscarriages in South Africa
 604 (2010-2014) 2017.
 31

605 39. Babalola S, Fatusi A. Determinants of use of maternal health services in Nigeria-looking beyond
 606 individual and household factors. BMC pregnancy and childbirth. 2009;9(1):43.

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- Ahmed S, Creanga AA, Gillespie DG, Tsui AO. Economic status, education and empowerment:
 implications for maternal health service utilization in developing countries. PloS one. 2010;5(6):e11190.
- 40 611 42. Liselele HB, Boulvain M, Tshibangu KC, Meuris S. Maternal height and external pelvimetry to
 41 612 predict cephalopelvic disproportion in nulliparous African women: a cohort study. BJOG: An
 42 613 International Journal of Obstetrics & Gynaecology. 2000;107(8):947-52.
- 44 614 43. McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in low45 615 middle income countries 2010-2013: a population-based, multi-country study from the Global Network.
 46 616 Reproductive health. 2015;12(2):S7.
- 47
 48 617 44. Afulani PA. Determinants of stillbirths in Ghana: does quality of antenatal care matter? BMC
 49 618 pregnancy and childbirth. 2016;16(1):132.
- 619
 619
 45. Bhutta ZA, Darmstadt GL, Haws RA, Yakoob MY, Lawn JE. Delivering interventions to reduce the
 620
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 62
- 622 46. Jammeh A, Vangen S, Sundby J. Stillbirths in rural hospitals in the gambia: a cross-sectional
 623 retrospective study. Obstetrics and gynecology international. 2010;2010.
- 57

1 2

2 3 4 5 6	624 625 626			, Leveno KJ, Varner MW, et al. mes. New England Journal of M	-				
7 8 9	627 628		C, Pell JP, Bobbie R. Caesarea .ancet. 2003;362(9398):1779-	n section and risk of unexplaine 84.	d stillbirth in subsequent				
10 11	629 630	tertiary hospital in sub-Sahara Africa: a case control study. BMC research notes. 2017;10(1):44							
12 13 14 15 16 17	631 632 633 634	the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. BJOG: An International Jourr of Obstetrics & Gynaecology. 2007;114(9):1079-87.							
18 19 20 21	635								
22 23 24	636								
25 26	637	Table 1: Sociodemographic characteristics of women who gave birth within 5 years before the							
27 28 29	638	survey in Ethio	pia, 2016.						
30 31 32		Variables	Category	Unweighted frequency (%)	Weighted frequency (%)				
33 34		Residence	Urban	1,994 (18.0)	1,226 (10.8)				
35 36 37			Rural	9,091 (82.0)	10,149 (89.2)				
37 38 39		Region	Tigray	1,021 (9.2)	709 (6.2)				
40 41			Afar	1,102 (9.9)	119 (1.0)				
42 43			Amhara	1,004 (9.1)	2,122 (18.7)				
44 45 46			Oromia	2,617 (23.6)	5,280 (46.4)				
47 48			Somali	1,623 (14.6)	554 (4.9)				
49 50			Benishangul Gumuz	962 (8.7)	133 (1.2)				
51 52 53			SNNPR	1,334 (12.0)	2,402 (21.1)				
54 55			Gambella	789 (7.1)	29 (0.3)				
56 57 58 50		L	1	1	28				

	Harari	633 (5.7)	27 (0.2)
Religion	Orthodox	3,127 (28.2)	3,844 (33.8)
	Muslim	5,710 (51.5)	4,696 (41.3)
	Catholic and	2,248 (20.3)	2,835 (24.9)
	protestant		
Maternal	No education	7,241 (65.3)	7,606 (66.9)
education	Primary education	2,708 (24.4)	2,961 (26.0)
	Secondary and	1,136 (10.3)	808 (7.1)
	higher education		
Maternal age	<20 year	395 (3.6)	374 (3.3)
	20-29 year	5,556 (50.1)	5,599 (49.2)
	30-39 year	4,234 (38.2)	4,381 (38.5)
	≥40 year	900 (8.1)	1,021 (9.0)
Husband	No education	5,331 (51.2)	5,339 (49.6)
education	Primary education	3,260 (31.3)	4,139 (38.5)
	Secondary and higher	1,817 (17.5)	1,284 (11.9)
	education		
Maternal	Had occupation	6,584 (59.4)	6,352 (55.8)
occupation status	No occupation	4,501 (40.6)	5,023 (44.2)
Wealth status	Poor	6,081 (54.9)	5,360 (47.1)
	Middle	1,512 (13.6)	2,318 (20.4)
	Rich	3,492 (31.5)	3,697 (32.5)

Table 2: pregnancy and health service-related characteristics of women who gave birth within 5

640 years preceding the survey in Ethiopia, 2016.

Variable	Category	Unweighted frequency (%)	Weighted frequency (%		
Pregnancy and materna	l service-related facto	prs	I		
Place of delivery	Home	6,737 (60.8)	7,468 (65.7)		
	Health facility	4,348 (39.2)	3,907 (34.3)		
Parity	Only one birth	1,435 (13.0)	1,419 (12.5)		
	2-4 birth	5,042 (45.5)	5,022 (44.1)		
	\geq 5 birth	4,608 (41.5)	4,934 (43.4)		
Birth order	1-3	5,806 (52.4)	5,703 (50.1)		
	4-5	2,584 (23.3)	2,655 (23.4)		
	≥6	2,695 (24.3)	3,017 (26.5)		
BMI	Thin	2,981 (26.9)	2,483 (21.8)		
	Normal	7,106 (64.1)	8,164 (71.8)		
	Overweight	998 (9.0)	728 (6.4)		
Maternal height	< 150 cm	1,018 (9.2)	1,228 (10.8)		
	≥150 cm	10,067 (90.8)	10,147 (89.2)		
ANC visit	No ANC visit	2,321 (20.9)	2,602 (22.9)		
	1-3 ANC visit	1,917 (17.3)	2,145 (18.9)		
	\geq 4 ANC visit	6,847 (61.8)	6,628 (58.2)		
Preceding birth	< 24 month	2,347 (21.2)	2,145 (18.9)		
interval	≥24 month	8,738 (78.8)	9,230 (81.1)		

Maternal anemia	Not anemic	6,696 (60.4)	7,590 (66.7)
	Anemic	4,389 (39.6)	3,785 (33.3)
Ever use of	Yes	4,101 (37.0)	5,238 (46.0)
contraceptive	No	6,984 (63.0)	6,137 (54.0)
Mode of delivery	Vaginal delivery	10,813 (97.5)	11, 181 (98.3)
	Cesarean delivery	272 (2.5)	194 (1.7)
Number of gestation	Single	10,798 (97.4)	11,072 (97.3)
	Twin	287 (2.6)	303 (2.7)
Behavioral and commun	nity-level factors		I
Smoking cigarettes	Yes	10,976 (99.0)	11,286 (99.2)
	No	109 (1.0)	89 (0.8)
Media exposure	Yes	9,747 (87.9)	10,020 (88.1)
	No	1,338 (12.1)	1,355 (11.9)
Community media	Lower	5,503 (49.6)	4,640 (40.8)
exposure	Higher	5,582 (50.4)	6,735 (59.2)
Community poverty	Lower	6,909 (62.3)	7,617 (67.0)
	Higher	4,176 (37.7)	3,758 (33.0)
Community ANC	Lower	5,387 (48.6)	6,665 (58.6)
utilization	Higher	5,698 (51.4)	4,710 (41.4)
Community women	Lower	6,909 (62.3)	7,617 (67.0)
education	Higher	4,176 (37.7)	3,758 (33.0)

Table 3: SaTScan analysis results of stillbirth in Ethiopia, 2016.

2								
3 4	Cluster	Enumeration area(cluster)identified	Coordinate/radius	Population	Case	RR	LLR	p-value
5 6 7	1	497, 95, 198, 521, 588, 553, 458,	(7.829198 N,	532	17	22.5	13.4	0.00069
7 8 9		171, 214, 251, 573, 239, 116, 22,	43.706264 E) /	'				
9 10 11		543, 490, 492, 92, 568, 33, 277, 527	166.48 km	'				
12 13				'				
14 15	2	350, 229, 482, 531, 218, 510, 206,	(10.195460 N,	384	14	3.6	8.84	0.04
16 17		10, 474, 267, 375, 423, 120, 176,		'				
18 19		572, 517, 460, 24, 403, 429, 38, 3,		'				
20 21 22			172.00 Km	'				
22 23 24		485, 456, 274, 167, 463, 112, 399,		'				
24 25 26		532		'				
20 27 28		1		'				
29 30				!				
31 32	3	564, 39, 230, 51	(9.555410 N,	50	4	8.83	8.55	0.05
33 34			40.326165 E) /	۱ ۱				
35 36 37			34.04 km					
37 [38 39	642]	Table 4: Multivariable multilevel logis	stic regression analy	ysis result of	f both	individ	ual and	1 1
40 41	643 c	community-level factors associated with s	stillbirth in Ethiopia,	, EDHS 2016	J			
	idividual a	and community- Null model	Model II	Model III		M	Iodel IV	7
44 4 3 e 46	evel charac	teristics	AOR (95% CI)	AOR (95%	όCI)	A	OR (95	% CI)
	esidence							
49 50	rban			1		1		
	ural			3.75[1.33, 1	10.56]	4.	.83[1.44	4, 16.19]*
53 5 A	egion							
55 56 57								
57 58 59							32	2
60		For peer review only - http://b	omjopen.bmj.com/site/a	about/guideline	es.xhtml			

2				
³ Amhara 4			1	1
⁵ ₆ Tigray			0.54[0.18, 1.63]	0.63[0.19, 2.17]
7 8 Afar 9			0.28[0.08, 0.94]	0.24[0.05, 1.06]
⁹ 10romia 11			0.20[0.07, 0.55]	0.25[0.07, 0.83]*
12 13 Somali			0.84[0.32, 2.21]	0.98[0.27, 3.56]
14 1 B enishangul Gumuz			0.25[0.07, 0.92]	0.37[0.09, 1.53]
16 13SNNPR 18			0.21[0.06, 0.69]	0.56[0.14, 2.18]
19 20Gambella			0.26[0.06, 1.07]	1.02[0.20, 5.22]
21 2Harari			0.71[0.19, 2.63]	0.77[0.16, 3.72]
23 2 Religion				
25 ²⁶ Orthodox 27		1		1
28 29Muslim		0.59[0.31, 1.12]		0.75[0.32, 1.77]
30 3Protestant/catholic		0.12[0.04, 0.35]		0.11[0.03, 0.37]**
32 ³ Wealth status 34				
35 36 36		1.12[0.60, 2.11]		0.87[0.45, 1.69]
37 3ðMiddle		1.58[0.78, 3.19]		1.21[0.60, 2.47]
39 4Rich		1		1
41 ⁴² Women's education				
44 4No education		1		1
46 4 P rimary education		0.39[0.21, 0.75]		0.39[0.20, 0.74]**
48 ⁴⁹ Secondary and 50	higher	0.49[0.18, 1.33]		0.63[0.23, 1.71]
51 5° ducation				
53 5 Birth order				
55 56				
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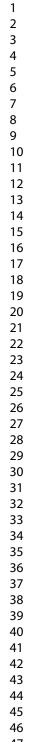
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³ / ₄ 1-3	1	1
5 6 4-5	0.49[0.24, 1.03]	0.50[0.24, 1.03]
7 86 and above 9	0.66[0.25, 1.75]	0.66[0.25, 1.73]
¹ Parity 11		
$^{12}_{13}$ Only one birth	1	1
14 1 2 -4 birth	0.68[0.37, 1.28]	0.65[0.35, 1.22]
16 1 <u>≯</u> 5 birth 18	0.45[0.16, 1.28]	0.42[0.15, 1.20]
¹⁹ ANC visit		
21 22No ANC visit 23	2.85[1.76, 4.62]	2.77[1.70, 4.51]**
25 24-3 visit 25	1.22[0.68, 2.19]	1.11[0.62, 2.00]
²⁶ 4 and above visit 27	1	1
28 29 Media exposure		
30 3¶Yes 32	1	1
33 _{No} 34	2.11[0.85, 5.24]	1.63[0.66, 4.04]
³⁵ Maternal height		
37 3≰ 150 cm 39	2.66[1.47, 4.79]	2.73[1.50, 4.97]**
4⊵150 cm	1	1
⁴² Contraceptive use		
44 45 ^y es	0.74[0.43, 1.26]	0.72[0.41, 1.24]
46 4No 48	1	1
⁴⁹ Preceding birth interval		
51 52⁄24 month	1.92[1.19, 3.07]	1.93[1.20, 3.10]**
53 5≹24 month 55	1	1
56 57 58		34
59 60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xht	

2				
³ ₄ Mode of delivery				
⁵ ₆ Vaginal delivery		1		1
9 8Cesarean delivery		4.00[1.35, 11.85]		5.07[1.65, 15.58]**
¹ Community media				
12 1 3exposure				
14 1 £ ower community exposure 16			1	1
¹ Higher community exposure			0.96[0.51, 1.80]	1.02[0.51, 2.04]
¹⁹ ₂₀ Community women's				
21 2 £ducation				
 23 24 ower community education 25 			1	1
²⁶ Higher community education			1.28[0.61,2.71]	1.88[0.80, 4.42]
28 29 Constant	0.003[0.002, 0.005]	0.003[0.001,	0.002[0.0005,0.0096]	0.001[0.0002, 0.01]
30 31		0.01]		
32 ³³ Model comparison and 34				
³⁴ ³⁵ ₃ Random effects				
37 3 § CC	0.47(0.35, 0.59)			
39 4 0 Log-likelihood 41	-599.02	-551.2	-584.36	-540.50
⁴¹ ⁴² ⁴³ Deviance	1198.04	1102.2	1168.72	1081
44 49CV	Ref	21.5	9.3	15.3
46 4MOR 48	5.03[3.19, 7.13]	5.91[3.44, 8.90]	4.66[2.84, 6.69]	5.69[3.31, 8.56]
10	Odds Ratio, CI; Con	fidence Interval, IC	CC; Intra-class Correlat	ion, MOR;
51 52 645 Median Odds Rati	on, PCV; Proportional	Change in Variance.		
53 54				
55 646 56				
57 58				35
59 60 Fo	r peer review only - http://b	mjopen.bmj.com/site/a	bout/guidelines.xhtml	

1 2		
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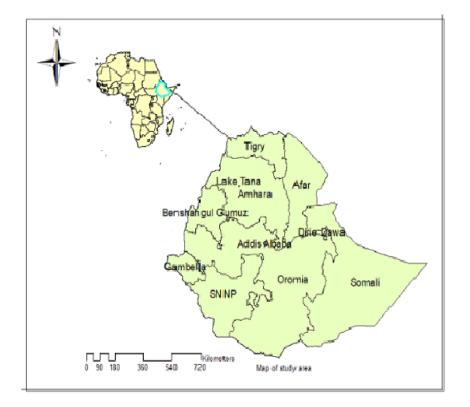


Figure 1: Map of the study area 215x279mm (300 x 300 DPI)



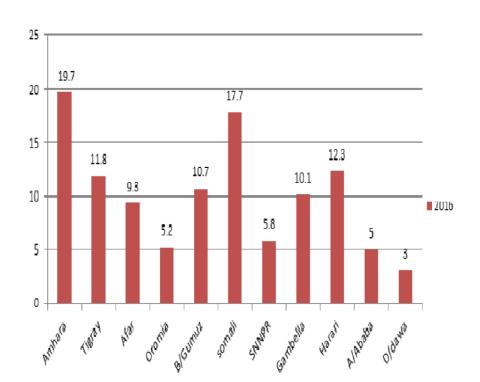
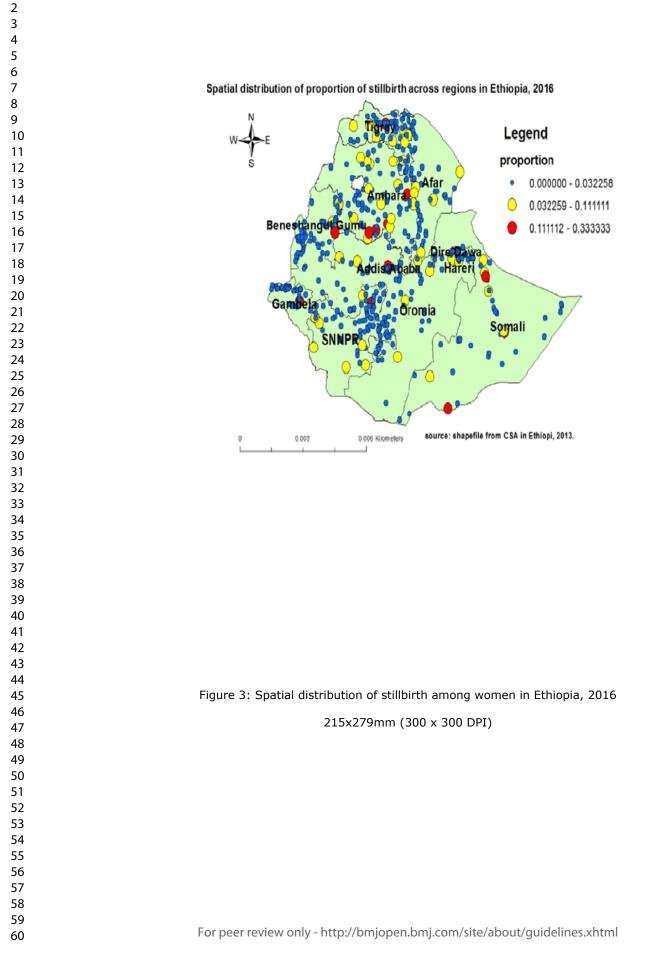
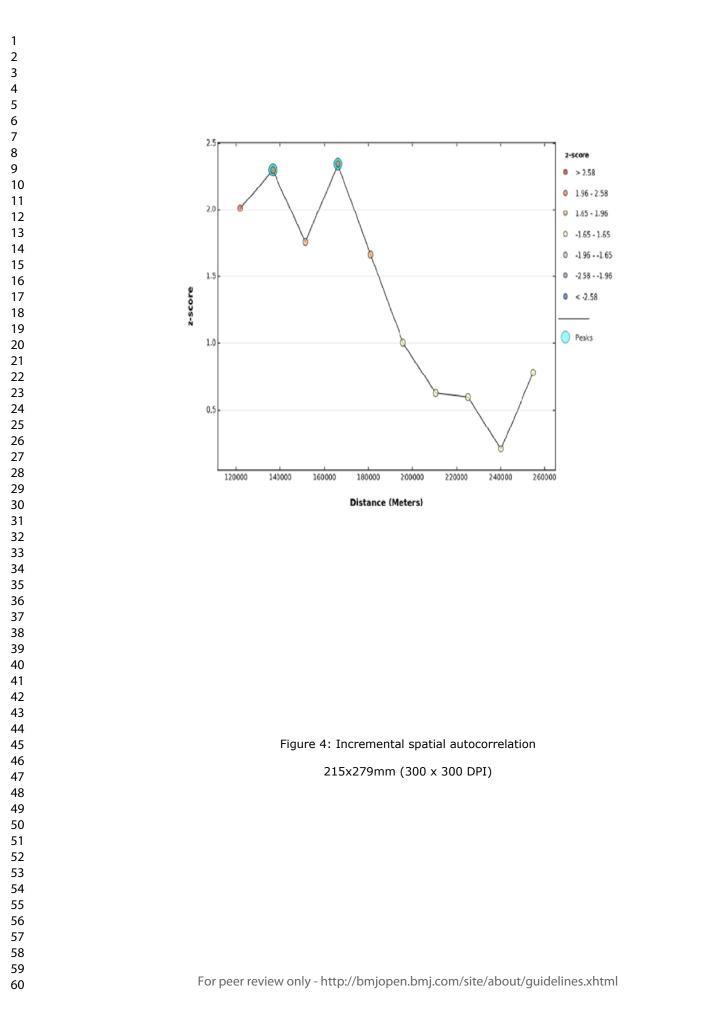
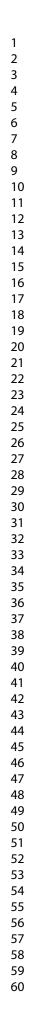


Figure 2:The rate of stillbirth among reproductive-age women across regions in Ethiopia, 2016 215x279mm (300 x 300 DPI)







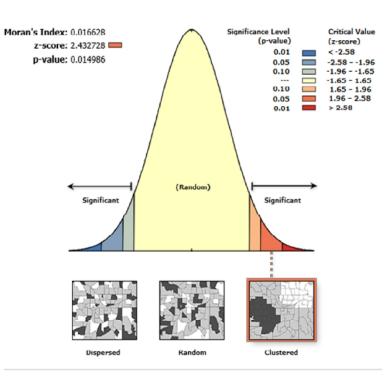
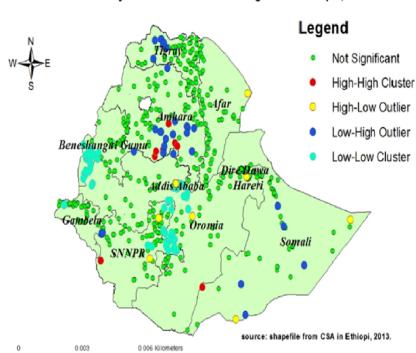


Figure 5: Global spatial autocorrelation of stillbirth among women in Ethiopia, 2016

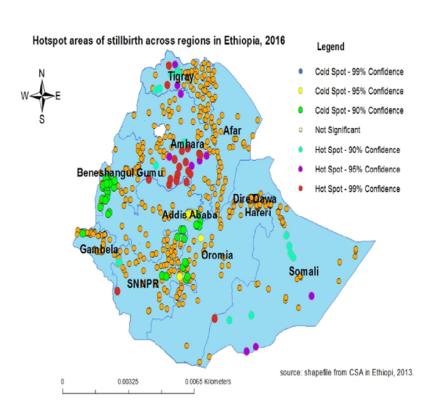
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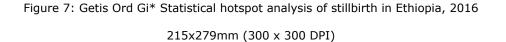


Cluster and Outlier analysis of stillbirth accross regions in Ethiopia, 2016

Figure 6: Cluster and outlier analysis of stillbirth among women in Ethiopia, 2016

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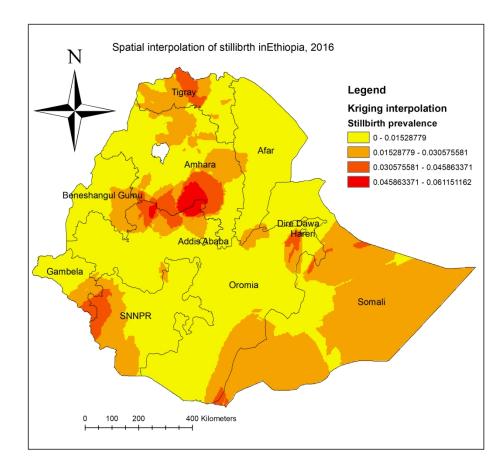
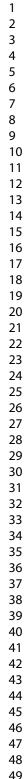


Figure 8: Kriging interpolation of stillbirth among women in Ethiopia, 2016

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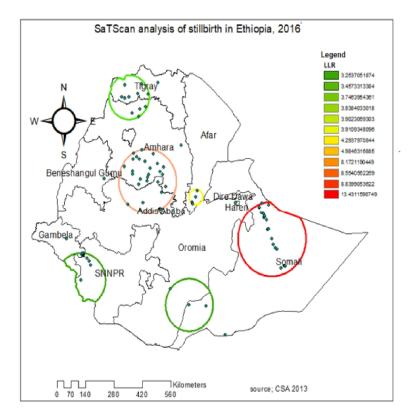


figure 9: SaTScan analysis of hotspot areas of stillbirth in Ethiopia, 2016

215x279mm (300 x 300 DPI)

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Spatial distribution of stillbirth and associated factors in Ethiopia: Spatial and Multilevel Analysis

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Keywords:	Stillbirth, Ethiopia, Multilevel analysis, Spatial analysis





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Spatial distribution of stillbirth and associated factors in Ethiopia: Spatial

and Multilevel Analysis Getayeneh Antehunegn Tesema^{1*}, Lemma Derseh Gezie¹, Solomon Gedlu Nigatu¹ ¹ Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia E-mail: (getayenehanten... lemmagezie@gmail.com) (sol.gondar@gmail.com) Corresponding author Getayeneh Antehunegn Tesema E-mail: getayenehantehunegn@gmail.com For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

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16 Abstract

Objective: Although stillbirth rates have been reduced globally, it is still very high in developing countries. So far, only ten countries carry the burden of over 65% of stillbirths in the world including Ethiopia in the seventh position. Exploring the spatial distribution is important to monitor and design effective intervention programs but there is no available study on spatial distribution and factors associated with a stillbirth at the national level. Therefore, this study aimed to explore the spatial distribution, and associated factors of stillbirths.

Methods: Secondary data analysis was conducted based on the 2016 Ethiopian Demographic and Health Survey data. Weighted samples of 11,375 women were included for analysis. The Bernoulli model was fitted using spatial scan statistics version 9.6 to identify hotspot areas and ArcGIS version 10.6 to explore the spatial distribution of stillbirths. For associated factors, a multilevel logistic regression model that accounts for the hierarchical structure of the data was fitted using STATA 14.

Result: There were significant variations of stillbirth across regions of Ethiopia. The SaTScan spatial analysis identified primary clusters in the Northeast Somali region (LLR=13.4, p<0.001) while the secondary cluster was detected in the border area between Oromia and Amhara regions (LLR=8.8, p<0.05). Rural residence (AOR=4.83, 95%CI:1.44-16.19), primary education (AOR=0.39, 95%CI:0.20-0.74), not having ANC visit(AOR=2.77, 95%CI:1.70-4.51), caesarean delivery (AOR=5.07, 95%CI: 1.65-15.58), birth interval <24 month (AOR=1.95, 95%CI: 1.20,3.10), and height<150 cm(AOR=2.73, 95%CI:1.45-4.97) were significant predictors of stillbirths.

37 Conclusion and recommendation: In Ethiopia, stillbirths had significant spatial variations
38 across the country. Residence, maternal stature, preceding birth interval, cesarean delivery,

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education, and ANC visit were significant predictors of stillbirth. This could have public health

40 implications to target interventions to identified hotspot areas of stillbirth and the government

41 should scale up maternal health programs in rural areas

42 Keywords: stillbirth, Ethiopia, multilevel logistic regression, spatial analysis

44 Strength and limitation of the study

The study used national survey by weighted the data since some regions were oversampled
 and some under-sampled to make it nationally representative, the study has the potential to
 inform policy-makers, planners and programmers, to design appropriate intervention at
 national and regional levels

As a study was a cross-sectional study, the study is unable to show a temporal relationship.
However, our method used multilevel modeling which took into account the effect of
clustering to get reliable estimates and standard error.

The EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or caregivers report

- The study was based on self-reports of respondents. Therefore, it may have the possibility of
 social desirability and recall bias
- The SaTScan detect only circular clusters, irregularly shaped clusters were not detected

57 BACKGROUND

The World Health Organization (WHO) defines stillbirth as fetal death (death before the complete expulsion or extraction of a product of conception from its mother) in the third trimester (≥ 28 completed weeks of gestation) or birth weight ≥ 1000 grams or length ≥ 35 centimeters (1, 2). Globally, stillbirth is a huge public health concern, especially in Sub-Saharan Africa (SSA) and South Asia (SA) including Ethiopia(3). Around 2.6 million stillbirths occur annually, 98% of which occur in developing countries(4). An overwhelming majority (67%) of the world's stillbirth occurred in SSA and SA, and most of the stillbirths occur during the intrapartum period which is preventable by improving obstetrics services(5).

More than half of the 2.6 million stillbirths occur during labor and delivery (6) and is considered as an indicator of access to and quality of obstetric care(7). According to the most recent global estimate of WHO, the average global stillbirth rates were 18.4 per 1000 births(8), while developing countries have the stillbirth rates ten-fold higher than developed countries(9).Sub-Saharan Africa has the highest stillbirth rate of 28.3 per 1000 births(10). Stillbirth rates have been varied across countries and remain a huge challenge to achieve Every Newborn Action Plan (ENAP) of the target of 12 or fewer stillbirths per 1000 births in every country by 2030(1). Even though many high-income countries and upper-middle-income countries have already met this target, developing countries particularly Africa will have to more than double present progress to reach this target(1).

Despite the various international and national commitments on improving newborn and maternal health (11), stillbirth has been grossly under-reported and invisible in policies and programs worldwide(12). Like many countries in SSA, stillbirth is not routinely recorded and monitored in Ethiopia. Stillbirth has been reduced more slowly than maternal mortality or under 5 mortality,

80 which remains invisible in global policies with an Annual Average Rate of Reduction (ARR) of 81 2.0% in comparison to ARR of 3.0% for maternal death or 3.1% for neonatal death(13). The 82 death of a fetus in uterus or at birth is a devastating experience for the affected mothers and 83 families(14). It has been associated with extensive psychosocial consequences for parents and 84 family and has been linked to post-traumatic stress disorder, anxiety, depression, suicide, fear of 85 the next pregnancy and reduced relation with their partner(15, 16).

In Ethiopia, a study conducted based on Ethiopian Demographic and Health Survey (EDHS) 2011 revealed that a stillbirth rate of 25.5 per 1000 births with significant variability across regions and the researchers recommended conducting spatial analysis to investigate the spatial variability of experiencing stillbirth in Ethiopia(17). A study done at the Amhara region based on Ethiopian Mini Demographic and Health Survey 2014 reported that stillbirth rates of 85 per 1000 births(18).Different studies done on experiencing stillbirth showed that rural residence, parity, educational status, mode of delivery, ANC utilization, and place of delivery, maternal nutritional status, and maternal obstetric factors were the significant predictors of experiencing stillbirth (14, 19-21).

There is a wide gap of stillbirth rates not only among different countries but also within the country(17, 22). A high rate of stillbirths has been reported among rural, poor and marginalized societies that are the least beneficial of maternal health promotion activities and services(12). Thus, the identification of geographic areas with a high rate of stillbirth using Geographic Information System (GIS) and Spatial Scan statistical analysis (SaTScan) has become fundamental to guide targeted public health interventions. However, previous studies in Ethiopia have been focused on the prevalence and associated factors of stillbirth (18, 23, 24), by using standard logistic regression models despite the hierarchical structure of EDHS data. These

could result in a biased estimate since the data is nested within-cluster and violates the
 independent assumption (17). The findings of these studies are insufficient and limited to capture
 the spatial distribution of stillbirth and community-level factors contributing to stillbirth.
 Therefore, the current study attempts to explore the spatial distribution and associated factors of
 stillbirth in Ethiopia using Spatial and multilevel Analysis.

- Method and materials
- 109 Study design, setting and period

A community-based cross-sectional study was conducted from January 18 to June 27, 2016. The study was conducted in Ethiopia, which is situated in the Horn of Africa. It has 9 Regional states (Afar, Amhara, Benishangul-Gumuz, Gambela, Harari, Oromia, Somali, Southern Nations, Nationalities, and People's Region (SNNP) and Tigray) and two Administrative Cities (Addis Ababa and Dire-Dawa). In Ethiopia, 84% of the population lives in rural areas and more than 80 percent of the country's total population lives in the regional states of Amhara, Oromia, and SNNP(25). Ethiopia is the13th in the world and 2nd in Africa's most populous country. The number of hospitals varies from region to region in response to differences in population size (26).

43 119 Sample and population

The source population was all births from reproductive age women within five years before the survey in Ethiopia, whereas all births from reproductive-age women in the selected enumeration areas within five years before the survey were the study population. The EDHS used a stratified two-stage cluster sampling technique selected in two stages using 2007 the Population and Housing Census as a sampling frame. Stratification was achieved by separating each region into

urban and rural areas. In total, 21 sampling strata have been created. In the first stage, 645 EAs
(202 in the urban area) were selected with probability proportional to the EA size and with
independent selection in each sampling stratum. In the second stage, on average 28 households
were systematically selected. The detailed sampling procedure was presented in the full EDHS
2016 report (27).

130 Study variables

Outcome variables

2016 Ethiopian Demographic and Health Survey (EDHS) asked women to report any pregnancy loss that occurred in the five years preceding the survey. For each pregnancy that did not end in a live birth, the duration of the pregnancy was recorded. Pregnancy losses occurring after seven completed months of gestation were considered as stillbirth (28). The response variable of this study was the occurrence of stillbirth among mothers of childbearing age. The response variable for the ith mother is represented by a random variable Y_i with two possible values coded as 1 and 0. So, the response variable of the ith mother Y_i was measured as a dichotomous variable with possible values $Y_i = 1$, if ith mother had experienced stillbirth and $Y_i = 0$ if mother had a live birth.

141 Independent variables

142 Consistent with the objective of the study and given the hierarchical structure of EDHS data 143 where women were nested within the cluster/community, two levels of independent variables 144 were considered. Level 1 contained individual socio-demographic and economic factors (Age, 145 marital status, religion, maternal education, paternal education, wealth index, maternal 146 occupation, maternal working Status), pregnancy and pregnancy-related factors (Mother's 147 height, BMI, ANC visit, Parity, Preceding birth interval, contraceptive use, Place of delivery, Page 9 of 42

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Birth order, Mode of delivery, wanted pregnancy, Maternal anemia), and behavioral factors (Smoking, media exposure). The community-level factors(region, residence, community women education, community poverty, community media exposure, and community ANC utilization) at level 2, which included the characteristics of the community in which each woman resided. In EDHS data no variable describes the cluster except region and place of residence. Therefore, Individual-level variables were aggregated at the cluster level to generate community-level variables to see whether cluster-level variables had an effect on stillbirth and which were categorized by their proportion as higher or lower based on national median value since it was not normally distributed. Community-level variables used in the analysis were from two sources; direct community-level variables that were used without any manipulation and aggregated community-level variables that were generated by aggregating individual-level variables at the elie cluster level.

Data collection procedure

The study was conducted based on EDHS data and geographic coordinate data by accessing the data from the DHS program official database www.measuredhs.com after permission was granted through an online request by explaining the objective of our study. We used the EDHS 2016 birth data (BR) set for the study. Geographic coordinate data (longitude and latitude coordinates) were taken at the cluster level/ enumeration area level.

Data management and analysis

The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey and to take into account the

sampling design to get reliable statistical estimates. Descriptive and summary statistics wereconducted using STATA version 14 software.

In EDHS data, women are nested within a cluster and we expect that women within the same cluster may be more similar to each other than women in the rest of the country. This violates the assumption of the traditional regression model which is the independence of observations and equal variance across clusters. This implies that the need to take into account the between cluster variability by using an advanced model. Therefore, a multilevel random intercept logistic regression model was fitted to estimate the association between the individual and community level variables and the likelihood of experiencing stillbirth. Model comparison was done based on Deviance(The negative 2 log-likelihood (-2LL)) since the models were nested. Likelihood ratio test, ICC (Intra-class correlation), MOR (median odds ratio) and PCV (proportional change in variance) were computed to measure the variation between clusters. The intra-class correlation coefficient (ICC) quantifies the degree of heterogeneity of stillbirth between clusters (the proportion of the total observed individual variation in stillbirth that is attributable to between cluster variations).

184 ICC= $\sigma^2/(\sigma^2 + \pi^2/3)(29)$, but MOR is quantifying the variation or heterogeneity in outcomes 185 between clusters and is defined as the median value of the odds ratio between the cluster at high 186 risk of stillbirth and cluster at lower risk when randomly picking out two clusters (EAs).

187 MOR= exp (
$$\sqrt{2 * \partial 2 * 0.6745}$$
) ~MOR=exp (0.95* ∂)(30)

 ∂^2 indicates that cluster variance

PCV measures the total variation attributed to individual-level factors and community-levelfactors in the multilevel model as compared to the null model.

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191 PCV= <u>var (null model) - var full model</u>))

Var (null model)

Multilevel random intercept logistic regression was used to analyze factors associated with a stillbirth at two levels to take into account the hierarchical structure of the data, at individual and community (cluster) levels. Four models were constructed for the multilevel logistic regression analysis. The first model (a multilevel random intercept logistic regression model without covariates) was an empty model without any explanatory variables, to determine the extent of cluster variation on stillbirth. The second model (determined the association between the individual level predictors and stillbirth) was adjusted with individual-level variables; the third model (determined the association between community-level predictors and stillbirth) was adjusted for community-level variables while the fourth (individual and community level model) was fitted with both individual and community level variables simultaneously. The final model(a model with individual and community level factors) was chosen since it had the lowest deviance. Variables with p-value ≤ 0.2 in the bi-variable analysis for both individual and community-level factors were fitted in the multivariable model. Adjusted Odds Ratio (AOR) with a 95% Confidence Interval (CI) and p-value <0.05 in the multivariable model were used to declare significant predictors of stillbirth. Multi-collinearity was also checked using the variance inflation factor (VIF) which indicates that there is no multi-collinearity since all variables have VIF<5and tolerance greater than 0.1.

210 Spatial analysis

For the spatial analysis ArcGIS version 10.6 software and SaTScan version 9.6 software.
Incremental spatial autocorrelation was done to get the maximum peak distance where stillbirth

clustering is pronounced. It measures spatial autocorrelation for a series of distances and creates a line graph of those distances and their corresponding Z-score. Z-scores reflect the intensity of spatial clustering and statistically significant peak Z-scores. Z-scores indicate where the spatial clustering of stillbirth is more pronounced. The maximum peak distance is the distance where maximum spatial autocorrelation occurs and this was used as a distance band for hotspot analysis. Totally 10 distance bands were detected by a beginning distance of 121,803 meters, the first peak of 136,586.06 meters and the maximum peak (clustering) was observed at 166152.17 meters. The maximum peak was used as the distance band for the hotspot analysis.

221 Spatial autocorrelation analysis

The spatial autocorrelation (Global Moran's I) was done to test whether there is spatial clustering of stillbirth or not. It is a statistic that measures whether stillbirth patterns were dispersed, clustered or randomly distributed in the study area(31). Moran's I is a spatial statistics used to measure spatial autocorrelation by taking the entire data set and produce a single output value which ranges from -1 to +1. Moran's I Values close to -1 indicate dispersed, whereas Moran's I close to +1 indicate disease clustered and disease distributed randomly if I value is zero. A statistically significant Moran's I (p < 0.05) leads to rejection of the null hypothesis (stillbirth is randomly distributed) and indicates the presence of spatial autocorrelation.

230 Hot spot analysis of stillbirth

Anselin Local Moran's I used to investigate the local level cluster locations of stillbirth in terms of positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high). A positive value for 'I' indicated that a case had neighboring cases with similar values, part of a cluster. A negative value for 'I' indicated that a case was surrounded by cases with dissimilar values an outlier(32).Spatial scan statistical analysis Bernoulli based model was

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employed to test for the presence of statistically significant spatial clusters of stillbirth using Kuldorff's SaTScan version 9.6software. The spatial scan statistic uses a circular scanning window that moves across the study area. Women with stillbirth were taken as cases and those who have live birth as controls to fit the Bernoulli model. The numbers of cases in each location had Bernoulli distribution and the model required data for cases, controls, and geographic coordinates. The default maximum spatial cluster size of <50% of the population was used, as an upper limit, which allowed both small and large clusters to be detected and ignored clusters that contained more than the maximum limit.

For each potential cluster, a likelihood ratio test statistic and the p-value was used to determine if the number of observed stillbirth within the potential cluster was significantly higher than expected or not. The scanning window with maximum likelihood was the most likely performing cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis testing by comparing the rank of the maximum likelihood from the real data with the maximum likelihood from the random datasets. The primary and secondary clusters were identified and assigned p-values and ranked based on their likelihood ratio test, based on 999 Monte Carlo replications(33).

252 Spatial interpolation

It is very expensive and laborious to collect reliable data in all areas of the country to know the burden of a certain event. Therefore, part of a certain area can be predicted by using observed data using a method called interpolation. The spatial interpolation technique is used to predict stillbirth on the un-sampled areas in the country based on sampled EAs. There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best method since it incorporates the

spatial autocorrelation and it statistically optimizes the weight(34). Ordinary Kriging spatial
interpolation method was used for this study for predictions of stillbirth in unobserved areas of
Ethiopia.

2 Patient and public involvement statement

Patients and public involvement were not involved in this study since we have conducted a secondary data analysis based on already available DHS data which was collected to provide estimates of common health and health-related indicators. For the original project from which data were obtained, patient and public involvement statements were essential since biomarker data such as anemia, HIV testing, and anthropometric measurements were collected(35).

268 Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of Institute of Public Health,
CMHS, and the University of Gondar. Permission for data access was obtained from major
demographic and health survey through an online request from http://www.dhsprogram.com.
The data used for this study were publicly available with no personal identifier.

Result

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75 Socio-demographic and economic characteristics of respondents

A total of 11,375 women who gave birth within five years preceding the survey were included for the analysis. Of 11,375 of women, 10,149 (89.2%) were rural residents and half of the respondent were in the age group 20-29 years. Regarding maternal education status, 7,606 (66.9%) had no formal education (Table1).

280 Pregnancy and maternal health service-related characteristics of respondents

Among 11375 respondents who gave birth within five years, two-third 7,468 (65.7%) of the respondents delivered at home and 194 (1.7%) gave birth through cesarean section. Concerning ANC utilization, 2,602 (22.9 %) had no ANC visit during pregnancy (Table 2).

The overall rate of stillbirth among births from childbearing age women within five years preceding the survey in Ethiopia was 9.2 [95% CI; 7.9, 11.1] per 1000 birth. Stillbirth rate was highest in the Amhara region (19.7) and lowest in Diredawa (3.0) (Figure 1).

287 Spatial analysis

288 Spatial Global autocorrelation

This study revealed that the spatial distribution of stillbirth was found to be non-random in Ethiopia with Global Moran's I 0.017 (p< 0.05). The clustered patterns (on the right sides) show high rates of stillbirth occurred over the study area. The outputs have automatically generated keys on the right and left sides of each panel. Given the z-score of 2.4 indicated that there is less than 1.5% likelihood that this clustered pattern could be the result of chance. The bright red and blue colors to the end tails indicate an increased significance level (Figure 2).

Hotspot analysis of stillbirth

In the cluster and outlier analysis, the significant cluster was detected in Tigray, Amhara, Oromia, Addis Ababa, SNNPR, Benishangul-Gumuz, Somali and Gambella regions. Hot spot areas for stillbirth were found in southwest Somali, southern Amhara, and west SNNPR, While the cold spot regions were found in south and west Benishangul-Gumuz, Addis Ababa, southwest of Oromia region, west Gambella and Northeast SNNPR. Outliers were found in the central and southern parts of Amhara, north Tigray, southeast Gambella and Somali regions (Figure 3).

In the Spatial scan statistical analysis, a total of 56 significant clusters were identified of which 22 clusters were primary (most likely clusters) and 34 secondary clusters of stillbirth were identified. The primary cluster spatial window was located in the northeast Somali region, which was centered 7.829198 N, 43.706264 E of geographic location with a 166.48 km radius, a relative risk of 22.5 and Log-Likelihood ratio (LLR) of 13.4, at p < 0.001. It showed that women within the spatial window had 22.5 times higher risk for stillbirth than women outside the window. The secondary clusters scanning window was located between the border area of the south Amhara region and the north Oromia region, and the southern Afar region (Table 3). The red circular ring indicates that the most statistically significant spatial window contains the primary cluster of stillbirth. There was a higher risk of stillbirth within the circular window than outside the spatial window (Figure 4).

314 Interpolation of stillbirth

North West Tigray, northern and North West Oromia, east and south Amhara, east Benishangul,
East Gambella, Harari, and Northwest SNNPR were detected as predicted most risky areas of
stillbirth compared to other regions. Predicted low-risk areas were found in Oromia, Afar, and

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Gambella regions. Continuous images produced by interpolating (Kriging interpolation method)stillbirth among birth from reproductive-age women (Figure 5).

320 Factors associated with stillbirth

321 ICC and LR tests were checked, and the multilevel model was. Therefore, the two-level 322 multilevel logistic regression model was used to get an unbiased standard error and to make a 323 valid inference. Deviance was used for model comparison; the final model was the best-fitted 324 model with the lowest deviance (Table 4).

The intra-class correlation coefficient (ICC) was 47% in the empty model indicated that 47% of 325 the total variability for stillbirth was due to differences between clusters/EA, with the remaining 326 unexplained 53% attributable to individual differences. Moreover, the median odds ratio for 327 stillbirth was 5.03 in the null model which indicates that there was variation between clusters. If 328 we randomly select women from two different clusters of women at the cluster with a higher risk 329 of stillbirth had 5.03 times higher odds of experiencing stillbirth as compared with women at 330 cluster with a lower risk of stillbirth. About 15.3 percent of the variability in stillbirth was 331 explained by the full model (Table 4). 332

The final multilevel logistic regression model found residence, region, religion, preceding birth 333 interval, cesarean delivery, maternal height, ANC visit, and maternal education were 334 significantly associated with stillbirth. At the community level (level 2), two variables were 335 significantly associated with stillbirth. The odds of experiencing among women residing in rural 336 337 areas were 4.83 times more likely to that of women residing in the urban area (AOR= 4.83, 95%) CI 1.44-16.19). The odds of experiencing stillbirth in Tigray, Afar, Somali, SNNPR, 338 Benishangul, Gambella and Harari were not significantly different from that of experiencing 339 stillbirth in Amhara. A woman who lives in the Oromia region was 75% decreased odds of 340

experiencing stillbirth as compared to a woman in the Amhara region (AOR= 0.25, 95% 0.07-0.83).

At the individual level (level 1), Six variables were significantly associated with stillbirth. Women who were protestant and catholic religious followers had 89% decreased odds of experiencing stillbirth as compared to orthodox religious followers (AOR= 0.11, 95% CI 0.03-0.37). The educational level of women was significantly associated with experiencing stillbirth. Though women having secondary and higher education have no significant difference in experiencing stillbirth with those having no educational attainment, women having primary education decreases the odds of experiencing stillbirth by 61% as compared to those with no educational attainment (AOR= 0.39, 95% CI 0.20 - 0.74).besides, Women who had no antenatal care visit during pregnancy were 2.77 times higher odds of experiencing stillbirth than those who have 4 and above ANC visits (AOR= 2.77, 95% CI 1.70 - 4.51). Women who gave birth through cesarean delivery were 5.07times higher odds of experiencing stillbirth than those women who gave birth through vaginal delivery (AOR= 5.07, 95% CI 1.65– 15.58).

The preceding birth interval was a significant predictor of experiencing stillbirth outcomes. Women having preceding birth interval less than 24 months had 1.93 times higher odds of experiencing stillbirth compared to women having preceding birth interval 24 months and above (AOR= 1.93, 95% CI 1.20 - 3.10). also, maternal height less than 150 cm were 2.73 times higher odds of experiencing stillbirth as compared to those mother's greater than or equal to 150 cm (AOR= 2.73, 95% CI 1.50-4.97) (Table 4).

Discussion

In Ethiopia, the stillbirth rate was found to be 9.2 per 1000 birth with marked spatial heterogeneity. The spatial distribution of stillbirth was non-random in Ethiopia. The spatial scan statistics detected a total of three statistically significant SaTScan clusters areas with a high rate of stillbirth. The SaTScan analysis identified significant hotspot areas of stillbirth in northeast Somali, south Afar, south Amhara, and north Oromia region. These areas are more of pastoralist areas where people did not have permanent resident and due to this relatively health facilities are not accessible and available as compared to agrarian people and cities. Besides, these areas are more rural, which had a poor network of health facilities. Also, this could be attributed to the disparity in the distribution of maternal health service, and the inaccessibility of infrastructure in the border areas of regions(36). Whereas, the cold spot areas of stillbirth were found in south and west Benishangul-Gumuz, Addis Ababa, southwest of Oromia region, west Gambella and Northeast SNNPR. This could be these areas were relatively had better availability and accessibility of health services (Addis Ababa, Dire-Dawa)(37). Therefore, women are more likely to have antenatal care visits, and institutional delivery, this could contribute to the decrement of antepartum and intrapartum stillbirth. This result provides public health planners and programmers for designing effective public health intervention to identified hotspot areas of stillbirth that need special attention.

In the multilevel analysis, different individual and community factors were significantly associated with stillbirth. Among the community level variables, it was found that the odds of stillbirth were lower among women who lived in the Oromia region as compared to those in the Amhara region. This might be due to the availability and accessibility of maternal health facilities since Oromia regions are relatively around Addis Ababa and Dire-Dawa in which

health facilities are accessible as compared to other regions. Also, the high turnover rate of health professionals in the Amhara region especially physicians didn't stay in the districts and they prefer to work in the capital city of Ethiopia (Addis Ababa) this could be contributed to the high rate of intrapartum stillbirth in districts because of lack of skilled health professionals (38). The study has shown that the odds of stillbirth were higher among women who lived in rural areas. This was consistent with previous study findings in South Africa(39), African Great lake Regions(12), Nigeria(19), Northern Ghana(14) and Ethiopia(17). This could be attributed to the disparity in mother's health care access, availability and accessibility of health facilities and women in urban areas are relatively had improved health-seeking behavior (36). Moreover, urban residents have better aware of maternal health service but in rural areas, health facilities may not be easily reachable and may end up with poor pregnancy outcomes during emergency cases (40).

Amongst the individual-level factors, catholic or protestant religion followers were significantly associated with lower odds of stillbirth as compared with orthodox religious followers. This might be related to the miss-perception of religious followers and this could shape their reproductive health decision making and practices, thereby govern the women's desire for using maternal health services(41). It could also be related to the feeding practice of women. Commonly orthodox religious followers may not eat animal products during pregnancy especially in the fasting period this might be related to poor fetal outcomes (42). Animal products are the main source of micro and macronutrients like folate and iron. Orthodox religious followers considered giving birth at home are blessed, using contraceptive as sinning and not expose their body to health professionals during delivery this might be the possible reason which needs further qualitative study to explore the detailed reasons.

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This study noted lower odds of stillbirth among women who had primary education as compared to women with no education. This finding was in line with previous studies done in Kenya(43) and Nigeria(19). This could be attributed to having maternal education that could lead to the corresponding improvement in health-seeking behavior. Like the timely decision to seek care appropriate care during pregnancy, give better care for their health and their fetus, awareness of the danger sign of pregnancy and maternal health service utilization(44).

The odds of stillbirth were higher among short stature women. A similar finding was reported in Pakistan(21). This might be for the reason that short stature women are associated with adverse pregnancy outcomes like Cephalo pelvic disproportion, contracted pelvis, intra-uterine growth restriction(IUGR), intra-uterine Fetal death(IUFD) and birth injury. Short stature reflects longstanding malnutrition or childhood infection that start in uretro or during early childhood, this kind of women may end up with poor pregnancy outcome unless we screen them as at-risk during ANC follow up(45).

Besides, having no ANC visit had a significant association with increased stillbirth. This study
could support previous studies done in low-middle countries (46), Ghana(47) and Kenya(43).
ANC follow up could help a pregnant woman to seek early treatment for her potential
pregnancy-associated complications, early screening of underlying medical conditions and may
improve birth outcomes (47, 48). On the other hand, women who did not have longer ANC
follow up may not be benefited from basic ANC packages.

426 Consistent with studies done in Nigeria based on the 2013 DHS(19) and cross-sectional study in
427 Gambia(49), cesarean deliveries in this study showed higher odds of stillbirth when compared
428 with normal vaginal delivery. This may be due to the reason that cesarean sections are probably
429 applied too late in hospital since most women are referred to from distant health facilities. there

may be a delay in referral or transportation problems resulting in not to save the baby's lifebecause the cesarean section is not done at the right time (50, 51).

In this study, having a short inter-pregnancy interval was associated with higher odds of stillbirth. This was consistent with studies done sub-Saharan Africa (52), Bangladesh (53) and Amhara Region(18). This could be explained by short preceding birth interval are less able to provide nourishment for the fetus because her body has had less time to recuperate from the previous pregnancy, the uterus had less time to recover. Furthermore, lactation will deplete maternal nutrition and may end up with poor pregnancy outcomes(53).

The strength of this study was using weighted data to make it representativeness at national and regional levels: therefore, it can be generalized to all women who gave birth during the study period in Ethiopia. Moreover, the use of GIS and SaTScan statistical tests helped to detect similar and statistically significant hotspot areas of stillbirth and to design effective public health programs. However, the SaTScan detect only circular clusters, irregularly shaped clusters were not detected. Furthermore, the EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or caregivers report and might have the possibility of social desirability and recall bias since stillbirth(27).

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The findings of this study have valuable policy implications for health program design and interventions. Stillbirth high-risk areas can be easily identified to make effective local interventions. In general, these findings are of supreme importance for the minister of health, regional health bureaus, and NGO's to design intervention programs to reduce stillbirth in identified hotspot areas. To reduce the overall stillbirth rate in Ethiopia, Somali, Afar, Amhara and Oromia regions should emphasize the identified SaTScan clusters through developing local interventional strategies like improving accessibility and availability of maternal health facility.

Conclusions

In Ethiopia, stillbirth had spatial variations across the country. Statistically, significant-high hotspots of stillbirth were found in the central and southern parts of Amhara, west SNNPRs, south and north Tigray, and south West Somali region. Whereas, cold spot areas were found in Addis Ababa, central Oromia, and east SNNPRs. Short preceding birth interval, short maternal stature, ANC visit, rural residence, region, religion, maternal education, and cesarean delivery were significant predictors of stillbirth.

Abbreviations

ANC; Antenatal Care, AOR; Adjusted Odds Ratio, ARR; Annual Rate of Reduction, BMI; Body Mass Index, CI; Confidence Interval, COR; Crude Odds Ratio, CSA; Central Statistical Agency, DHS; Demographic Health Survey, EA; Enumeration Area, EDHS; Ethiopian Demographic Health Survey, GIS; Geographic Information System, ICC; Intra-cluster Correlation Coefficient, IUFD; Intra Uterine Fetal Death, IUGR; Intra Uterine Growth Restriction, LLR; log-likelihood Ratio, LR; Likelihood Ratio, MOR; Median Odds Ratio, PCV; Proportional

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2 3 4	467	Change in Variance, PHC; Population and Housing census, SBR; Stillbirth Rate, SNNPRs;
5 6 7 8	468	Southern Nations and Nationality People Regional state, WHO; World Health Organization.
9 10 11	469	Declarations
12 13 14 15	470	Availability of data and materials
15 16 17	471	Data is available online and you can access it from <u>www.measuredhs.com</u> .
18 19 20	472	Competing Interests
21 22 23	473	Authors declare that they have no conflict of interest
24 25 26	474	Funding
27 28 29	475	No funding was obtained for this study.
30 31 32	476	Authors' contribution
33 34	477	Conceptualization: Getayeneh Antehunegn Tesema
35 36 37	478	Data curation: Getayeneh Antehunegn Tesema
38 39	479	Funding acquisition: Getayeneh Antehunegn Tesema
40 41 42	480	Investigation: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
43 44	481	Methodology: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
45 46	482	Project administration: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu
47 48	483	Nigatu
49 50 51	484	Resources: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
52 53	485	Software: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
54 55 56 57 58 59	486	Supervision: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu 23

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- 3 4	487	Validation: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
5 6	488	Visualization: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon Gedlu Nigatu
7 8 9	489	Writing: Getayeneh Antehunegn Tesema
10 11	490	Writing - review and editing: Getayeneh Antehunegn Tesema, Lemma Derseh Gezie, Solomon
12 13	491	Gedlu Nigatu
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26 27 28	496	References
29 30	497	1. Organization WH. Every newborn: an action plan to end preventable deaths. 2014.
31 32	498	2. Smith GC, Fretts RC. Stillbirth. The Lancet. 2007;370(9600):1715-25.
33 34 35 36	499 500 501	3. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC pregnancy and childbirth. 2010;10(1):S1.
37 38 39	502 503	4. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. The Lancet. 2016;387(10018):587-603.
40 41	504 505	5. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? The Lancet. 2011;377(9775):1448-63.
42 43 44	506 507	6. Temmerman M, Lawn JE. Stillbirths count, but it is now time to count them all. The Lancet. 2018;392(10158):1602-4.
45 46 47 48	508 509 510	7. Admasu K, Haile-Mariam A, Bailey P. Indicators for availability, utilization, and quality of emergency obstetric care in Ethiopia, 2008. International Journal of Gynecology & Obstetrics. 2011;115(1):101-5.
49 50 51 52	511 512 513	8. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet Global Health. 2016;4(2):e98-e108.
53 54 55 56	514 515 516	9. Saleem S, Tikmani SS, McClure EM, Moore JL, Azam SI, Dhaded SM, et al. Trends and determinants of stillbirth in developing countries: results from the Global Network's Population-Based Birth Registry. Reproductive health. 2018;15(1):100.
57 58		24
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

McClure EM, Pasha O, Goudar SS, Chomba E, Garces A, Tshefu A, et al. Epidemiology of stillbirth

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in low-middle income countries: a Global Network Study. Acta obstetricia et gynecologica Scandinavica. 2011;90(12):1379-85. 11. Bamford L. Maternal, newborn and child health: service delivery. South African health review. 2012;2012(2012/2013):49-66. 12. Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: A pooled analysis of Demographic and Health Surveys. PloS one. 2018;13(8):e0202603. 13. You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. The Lancet. 2015;386(10010):2275-86. 14. Badimsuguru AB, Nyarko KM, Afari EA, Sackey SO, Kubio C. Determinants of stillbirths in Northern Ghana: a case control study. The Pan African medical journal. 2016;25(Suppl 1). 15. Ogwulu CB, Jackson LJ, Heazell AE, Roberts TE. Exploring the intangible economic costs of stillbirth. BMC pregnancy and childbirth. 2015;15(1):188. Meaney S, Everard CM, Gallagher S, O'donoghue K. Parents' concerns about future pregnancy 16. after stillbirth: a qualitative study. Health Expectations. 2017;20(4):555-62. Berhie KA, Gebresilassie HG. Logistic regression analysis on the determinants of stillbirth in 17. Ethiopia. Maternal health, neonatology and perinatology. 2016;2(1):10. 18. Lakew D, Tesfaye D, Mekonnen H. Determinants of stillbirth among women deliveries at Amhara region, Ethiopia. BMC pregnancy and childbirth. 2017;17(1):375. Dahiru T, Aliyu AA. Stillbirth in Nigeria: rates and risk factors based on 2013 Nigeria DHS. Open 19. Access Library Journal. 2016;3(08):1. 20. Ali AAA, Adam I. Anaemia and stillbirth in Kassala hospital, eastern Sudan. Journal of tropical pediatrics. 2010;57(1):62-4. Badshah S, Mason L, Lisboa PJ. Risk Factors Associated with Stillbirths in Public-Hospitals in 21. Peshawar, Pakistan. The Journal of Humanities and Social Sciences. 2011;19(2):15. 22. Berhan Y, Berhan A. Perinatal mortality trends in Ethiopia. Ethiopian journal of health sciences. 2014;24:29-40. Welegebriel TK, Dadi TL, Mihrete KM. Determinants of stillbirth in Bonga General and Mizan 23. Tepi University Teaching Hospitals southwestern Ethiopia, 2016: a case-control study. BMC research notes. 2017;10(1):713. 24. Tilahun D, Assefa T. Incidence and determinants of stillbirth among women who gave birth in Jimma University specialized hospital, Ethiopia. Pan African Medical Journal. 2017;28(1). 25. Central statistical agency(CSA) I. Ethiopian Demographic and Health survey. Addis Abeba: Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF, 2016. 26. Adugna A. Health Institutions and Services. Addis Abeba: July 2014. 27. ICF CSACEa. Ethiopia Demographic and Health Survey 2016 Addis Ababa, Ethiopia, and Rockville , maryland, USA: CSA and ICF. 2016.

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556 28. Goldenberg RL, McClure EM, Bhutta ZA, Belizán JM, Reddy UM, Rubens CE, et al. Stillbirths: the 557 vision for 2020. The lancet. 2011;377(9779):1798-805.

558 29. Rodriguez G, Elo I. Intra-class correlation in random-effects models for binary data. The Stata 559 Journal. 2003;3(1):32-46.

560 30. Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial of 561 multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to 562 investigate contextual phenomena. Journal of Epidemiology & Community Health. 2006;60(4):290-7.

563 31. Waldhör T. The spatial autocorrelation coefficient Moran's I under heteroscedasticity. Statistics 564 in Medicine. 1996;15(7-9):887-92.

565 32. Tsai P-J, Lin M-L, Chu C-M, Perng C-H. Spatial autocorrelation analysis of health care hotspots in
 566 Taiwan in 2006. BMC Public Health. 2009;9(1):464.

18 567 33. Kulldorff M. SaTScanTM user guide. Boston; 2006.

568 34. Bhunia GS, Shit PK, Maiti R. Comparison of GIS-based interpolation methods for spatial distribution of soil organic carbon (SOC). Journal of the Saudi Society of Agricultural Sciences. 22 570 2018;17(2):114-26.

571 35. 2016. CSACEal. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF. 2016.

573 36. Adugna A. Health instituition and Services in Ethiopia. 2014.

2857437.Asefa A, Bekele D. Status of respectful and non-abusive care during facility-based childbirth in a29575hospital and health centers in Addis Ababa, Ethiopia. Reproductive health. 2015;12(1):33.

576 38. Assefa T, Mariam DH, Mekonnen W, Derbew M, Enbiale W. Physician distribution and attrition 577 in the public health sector of Ethiopia. Risk management and healthcare policy. 2016;9:285.

55 578 39. Nfii FN. Levels, trends and household determinants of stillbirths and miscarriages in South Africa 579 (2010-2014) 2017.

- 580 40. Babalola S, Fatusi A. Determinants of use of maternal health services in Nigeria-looking beyond
 581 individual and household factors. BMC pregnancy and childbirth. 2009;9(1):43.
- 3958241.Tarekegn SM, Lieberman LS, Giedraitis V. Determinants of maternal health service utilization in40583Ethiopia: analysis of the 2011 Ethiopian Demographic and Health Survey. BMC pregnancy and childbirth.415842014;14(1):161.
- 4358542.Dugan B. Religion and food service. Cornell Hotel and Restaurant Administration Quarterly.445861994;35(6):80-5.
- 587 43. Cheptum JJ, Oyore JP, Okello Agina BM. Poor pregnancy outcomes in public health facilities in Kenya. African Journal of Midwifery and Women's Health. 2012;6(4):183-8.
- 48 589 44. Ahmed S, Creanga AA, Gillespie DG, Tsui AO. Economic status, education and empowerment:
 49 590 implications for maternal health service utilization in developing countries. PloS one. 2010;5(6):e11190.

51 591 45. Liselele HB, Boulvain M, Tshibangu KC, Meuris S. Maternal height and external pelvimetry to 52 592 predict cephalopelvic disproportion in nulliparous African women: a cohort study. BJOG: An 53 593 International Journal of Obstetrics & Gynaecology. 2000;107(8):947-52.

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 46. McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in low-middle income countries 2010-2013: a population-based, multi-country study from the Global Network. Reproductive health. 2015;12(2):S7.

7 597 47. Afulani PA. Determinants of stillbirths in Ghana: does quality of antenatal care matter? BMC
 8 598 pregnancy and childbirth. 2016;16(1):132.
 9

599 48. Bhutta ZA, Darmstadt GL, Haws RA, Yakoob MY, Lawn JE. Delivering interventions to reduce the
 600 global burden of stillbirths: improving service supply and community demand. BMC pregnancy and
 601 childbirth. 2009;9(1):S7.

602 49. Jammeh A, Vangen S, Sundby J. Stillbirths in rural hospitals in the gambia: a cross-sectional
 15 603 retrospective study. Obstetrics and gynecology international. 2010;2010.

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60851. Smith GC, Pell JP, Bobbie R. Caesarean section and risk of unexplained stillbirth in subsequent
pregnancy. The Lancet. 2003;362(9398):1779-84.

609 52. Tolefac PN, Tamambang RF, Yeika E, Mbwagbaw LT, Egbe TO. Ten years analysis of stillbirth in a
 610 tertiary hospital in sub-Sahara Africa: a case control study. BMC research notes. 2017;10(1):447.

611 53. DaVanzo J, Hale L, Razzaque A, Rahman M. Effects of interpregnancy interval and outcome of
612 the preceding pregnancy on pregnancy outcomes in Matlab, Bangladesh. BJOG: An International Journal
613 of Obstetrics & Gynaecology. 2007;114(9):1079-87.

	616	Table 1: Socio-demographic characteristics o	of women who gave birth within 5	years before the
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617 survey in Ethiopia, 2016.

Variables	Category	Unweighted frequency (%)	Weighted frequency (%)
Residence	Urban	1,994 (18.0)	1,226 (10.8)
	Rural	9,091 (82.0)	10,149 (89.2)
Region	Tigray	1,021 (9.2)	709 (6.2)
	Afar	1,102 (9.9)	119 (1.0)
	Amhara	1,004 (9.1)	2,122 (18.7)
	Oromia	2,617 (23.6)	5,280 (46.4)
	Somali	1,623 (14.6)	554 (4.9)
	Benishangul Gumuz	962 (8.7)	133 (1.2)
	SNNPR	1,334 (12.0)	2,402 (21.1)
	Gambella	789 (7.1)	29 (0.3)
	Harari	633 (5.7)	27 (0.2)
Religion	Orthodox	3,127 (28.2)	3,844 (33.8)
	Muslim	5,710 (51.5)	4,696 (41.3)
	Catholic and	2,248 (20.3)	2,835 (24.9)
	protestant	2	
Maternal	No education	7,241 (65.3)	7,606 (66.9)
education	Primary education	2,708 (24.4)	2,961 (26.0)
	Secondary and	1,136 (10.3)	808 (7.1)
	higher education		
Maternal age	<20 year	395 (3.6)	374 (3.3)
	20-29 year	5,556 (50.1)	5,599 (49.2)
	30-39 year	4,234 (38.2)	4,381 (38.5)
	≥40 year	900 (8.1)	1,021 (9.0)
Husband	No education	5,331 (51.2)	5,339 (49.6)
education	Primary education	3,260 (31.3)	4,139 (38.5)

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	Secondary and higher	1,817 (17.5)	1,284 (11.9)
	education		
Maternal	Had occupation	6,584 (59.4)	6,352 (55.8)
occupation status	No occupation	4,501 (40.6)	5,023 (44.2)
Wealth status	Poor	6,081 (54.9)	5,360 (47.1)
	Middle	1,512 (13.6)	2,318 (20.4)
	Rich	3,492 (31.5)	3,697 (32.5)

Table 2: pregnancy and health service-related characteristics of women who gave birth within 5

620 years preceding the survey in Ethiopia, 2016.

Variable	Category	Unweighted frequency (%)	Weighted frequency (%)
Pregnancy and mater	mal service-related factor	ors	
Place of delivery	Home	6,737 (60.8)	7,468 (65.7)
	Health facility	4,348 (39.2)	3,907 (34.3)
Parity	Only one birth	1,435 (13.0)	1,419 (12.5)
	2-4 birth	5,042 (45.5)	5,022 (44.1)
	\geq 5 birth	4,608 (41.5)	4,934 (43.4)
Birth order	1-3	5,806 (52.4)	5,703 (50.1)
	4-5	2,584 (23.3)	2,655 (23.4)
	≥6	2,695 (24.3)	3,017 (26.5)
BMI	Thin	2,981 (26.9)	2,483 (21.8)
	Normal	7,106 (64.1)	8,164 (71.8)
	Overweight	998 (9.0)	728 (6.4)
Maternal height	< 150 cm	1,018 (9.2)	1,228 (10.8)
	≥150 cm	10,067 (90.8)	10,147 (89.2)
ANC visit	No ANC visit	2,321 (20.9)	2,602 (22.9)
	1-3 ANC visit	1,917 (17.3)	2,145 (18.9)
	\geq 4 ANC visit	6,847 (61.8)	6,628 (58.2)

Preceding birth	< 24 month	2,347 (21.2)	2,145 (18.9)
interval	\geq 24 month	8,738 (78.8)	9,230 (81.1)
Maternal anemia	Not anemic	6,696 (60.4)	7,590 (66.7)
	Anemic	4,389 (39.6)	3,785 (33.3)
Ever use of	Yes	4,101 (37.0)	5,238 (46.0)
contraceptive	No	6,984 (63.0)	6,137 (54.0)
Mode of delivery	Vaginal delivery	10,813 (97.5)	11, 181 (98.3)
	Cesarean delivery	272 (2.5)	194 (1.7)
Number of gestation	Single	10,798 (97.4)	11,072 (97.3)
	Twin	287 (2.6)	303 (2.7)
Behavioral and commu	nity-level factors		1
Smoking cigarettes	Yes	10,976 (99.0)	11,286 (99.2)
	No	109 (1.0)	89 (0.8)
Media exposure	Yes	9,747 (87.9)	10,020 (88.1)
	No	1,338 (12.1)	1,355 (11.9)
Community media	Lower	5,503 (49.6)	4,640 (40.8)
exposure	Higher	5,582 (50.4)	6,735 (59.2)
Community poverty	Lower	6,909 (62.3)	7,617 (67.0)
	Higher	4,176 (37.7)	3,758 (33.0)
Community ANC	Lower	5,387 (48.6)	6,665 (58.6)
		5,698 (51.4)	4,710 (41.4)
2	Higher		
utilization Community women	Higher Lower	6,909 (62.3)	7,617 (67.0)

Table 3: SaTScan analysis results of stillbirth in Ethiopia, 2016.

50 51	Cluster	Enumeration area(cluster)identified	Coordinate/radius	Population	Case	RR	LLR	p-value
52	1	497, 95, 198, 521, 588, 553, 458,	(7.829198 N,	532	17	22.5	13.4	0.00069
53		171, 214, 251, 573, 239, 116, 22,	43.706264 E) /					
54		543, 490, 492, 92, 568, 33, 277, 527	166.48 km					
55 56								
50 [57								<u> </u>]

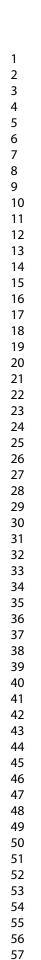
2	350, 229, 482,	531, 218, 510, 206,	(10.195460 N,	384 14	3.6	8.84	0.04
	10, 474, 267, 3	375, 423, 120, 176,	38.150574 E) /				
	572, 517, 460,	24, 403, 429, 38, 3,	142.05 km				
	485, 456, 274,	167, 463, 112, 399,					
	532						
3	564, 39, 230, 51		(9.555410 N,	50 4	8.83	8.55	0.05
5	504, 59, 250, 51		40.326165 E) /	50 4	0.05	0.55	0.05
			34.04 km				
623							
624 Ta	ble 1: Multivari	able multilevel logistic	regression analysis	esult of both indivi	dual and	1	
		actors associated with	• •		dual and	1	
025 00	initiality-level is	actors associated with	sunonui in Eunopia,	2010			
ndividual ar	nd community-	Null model	Model II	Model III	N	Iodel IV	7
vel characte	eristics		AOR (95% CI)	AOR (95% CI)	Α	OR (95	% CI)
esidence							
rban				1	1		
ural				3.75[1.33, 10.56]	4.	83[1.44	, 16.19]*
egion							
mhara				1	1		
gray				0.54[0.18, 1.63]		63[0.19	-
far				0.28[0.08, 0.94]		24[0.05	
romia				0.20[0.07, 0.55]		-	, 0.83]*
omali				0.84[0.32, 2.21]		98[0.27	_
enishangul (Gumuz			0.25[0.07, 0.92]		.37[0.09	
NNPR				0.21[0.06, 0.69]		56[0.14	-
ambella				0.26[0.06, 1.07]		.02[0.20	_
arari				0.71[0.19, 2.63]	0.	77[0.16	, 3.72]
eligion							
rthodox					1		1
luslim	1.		0.59[0.31, 1.12]			75[0.32	_
rotestant/cath			0.12[0.04, 0.35]		0.	11[0.03	, 0.37]**
ealth status	8		1 10[0 (0 0 11]		0	0750 45	1 (0)
00r			1.12[0.60, 2.11]			87[0.45	-
liddle ich			1.58[0.78, 3.19]			21[0.60	, 2.47]
	4 •		1		1		
Vomen's edu	Ication		1		1		
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						24	

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2				
³ Primary education		0.39[0.21, 0.75]		0.39[0.20, 0.74]**
⁴ ₅ Secondary and higher		0.49[0.18, 1.33]		0.63[0.23, 1.71]
6 education				
⁷ Birth order				
⁸ ₉ 1-3		1		1
104-5		0.49[0.24, 1.03]		0.50[0.24, 1.03]
¹ b and above		0.66[0.25, 1.75]		0.66[0.25, 1.73]
12 1 Parity				
100 nly one birth		1		1
¹ 2-4 birth		0.68[0.37, 1.28]		0.65[0.35, 1.22]
$16_{17} 5$ birth		0.45[0.16, 1.28]		0.42[0.15, 1.20]
18ANC visit				
¹ No ANC visit		2.85[1.76, 4.62]		2.77[1.70, 4.51]**
$^{20}_{21}$ -3 visit		1.22[0.68, 2.19]		1.11[0.62, 2.00]
2 ² and above visit		1		1
² Media exposure				
²⁴ ₂₅ Yes		1		1
28No		2.11[0.85, 5.24]		1.63[0.66, 4.04]
² Maternal height				
$^{28}_{29} \le 150 \text{ cm}$		2.66[1.47, 4.79]		2.73[1.50, 4.97]**
3∂2150 cm		1		1
³ Contraceptive use				
³² / ₃₃ Yes		0.74[0.43, 1.26]		0.72[0.41, 1.24]
34N0		1		1
³ Preceding birth interval				
³⁶ ₃₇ 24 month		1.92[1.19, 3.07]		1.93[1.20, 3.10]**
₃ ≩24 month		1		1
³ Mode of delivery				
⁴⁰ Vaginal delivery		1		1
4 Cesarean delivery		4.00[1.35, 11.85]		5.07[1.65, 15.58]**
4 C ommunity media				
44 exposure				
4 Jower community exposure			1	1
4Higher community exposure			0.96[0.51, 1.80]	1.02[0.51, 2.04]
⁴⁸ Community women's				
5&ducation				
5 Lower community education			1	1
⁵³ Higher community education ⁵³ ₅₄ Constant	0.00010.000.000.00	0.00250.001	1.28[0.61,2.71]	1.88[0.80, 4.42]
	0.003[0.002, 0.005]	0.003[0.001,	0.002[0.0005,0.0096]	0.001[0.0002, 0.01]
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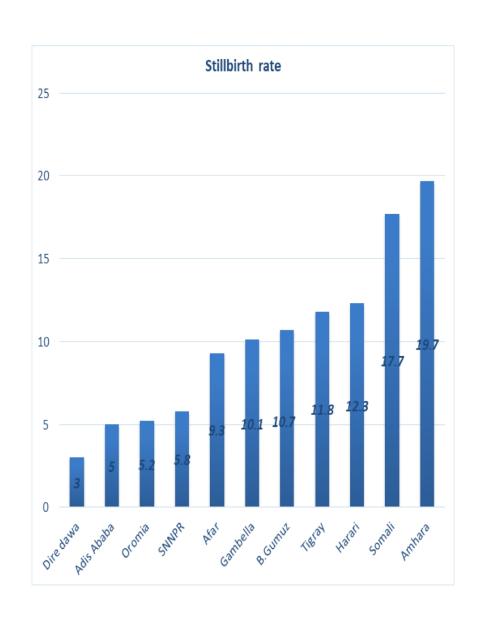
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³ Model comparison ₄ SRandom effects	and			
	0.47(0.25, 0.50)			
6 ICC 7 Lag likelihaad	0.47(0.35, 0.59)	551.0	594 26	540.50
⁷ Log-likelihood	-599.02	-551.2	-584.36	-540.50
⁹ Deviance 1 P CV	1198.04 Ref	1102.2 21.5	1168.72 9.3	1081 15.3
	5.03[3.19, 7.13]	5.91[3.44, 8.90]		5.69[3.31, 8.56]
$^{1}MOR_{12}_{13}$ 626 *AOR; Ad	justed Odds Ratio, CI; (
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	ds Ration, PCV; Proportion	nal Change in Variance) .	
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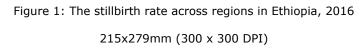
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3 4	629	Figure legends:
5	630	Figure 1: The stillbirth rates across regions in Ethiopia, 2016
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7 8	631	Figure 2: Global spatial autocorrelation of stillbirths in Ethiopia, 2016
9	051	rigure 2. Groour sputtur autocorrelation of stinion this in Europia, 2010
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11 12	632	Figure 3: Cluster and Outlier analysis of stillbirths in Ethiopia, 2016 (Source: Central Statistical
13	633	Agency (CSA), Ethiopia, 2013)
14	055	Agency (CSA), Europia, 2015)
15 16		
17	634	Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source:
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19 20	635	Central Statistical Agency (CSA), Ethiopia, 2013)
20 21		
22	636	Figure 5: Kriging Interpolation of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency
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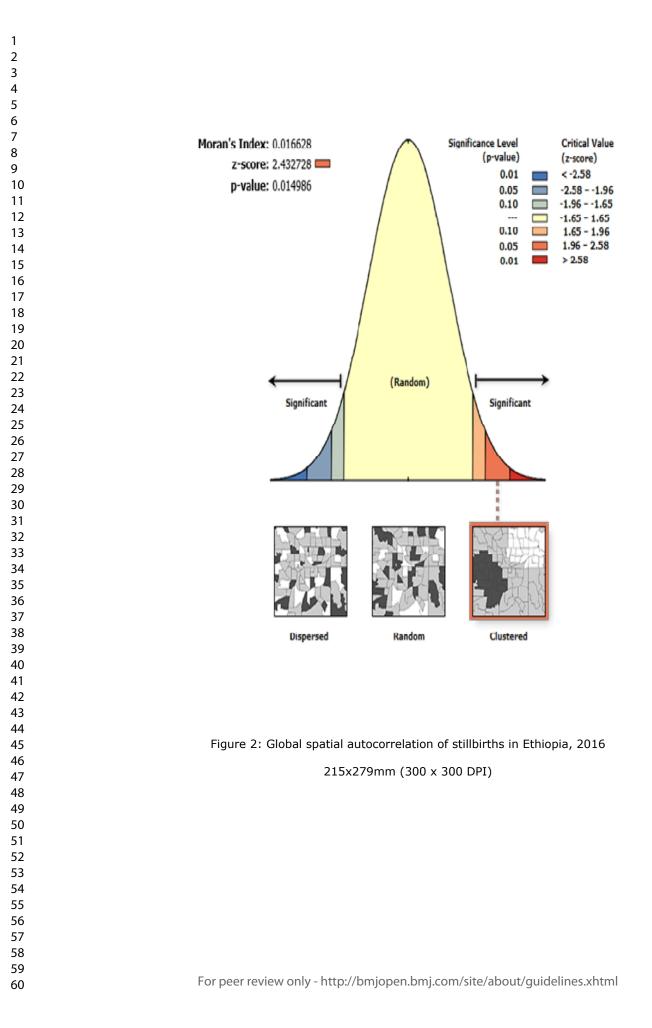


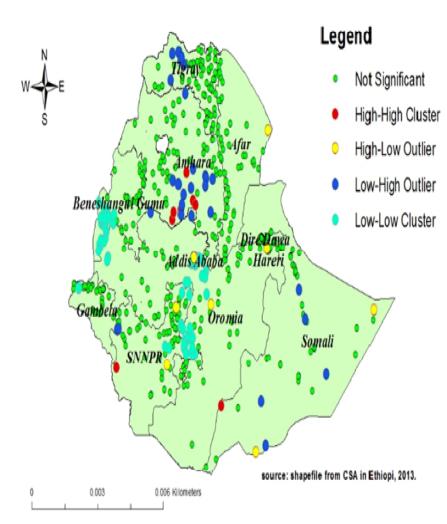












Cluster and Outlier analysis of stillbirth accross regions in Ethiopia, 2016



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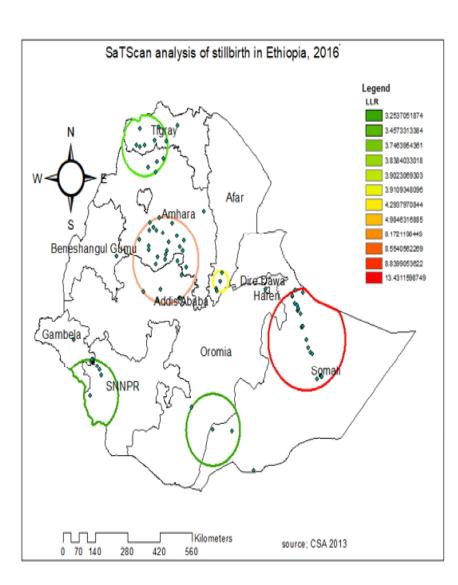
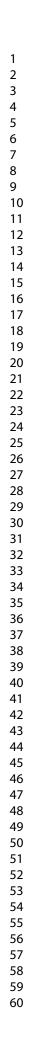
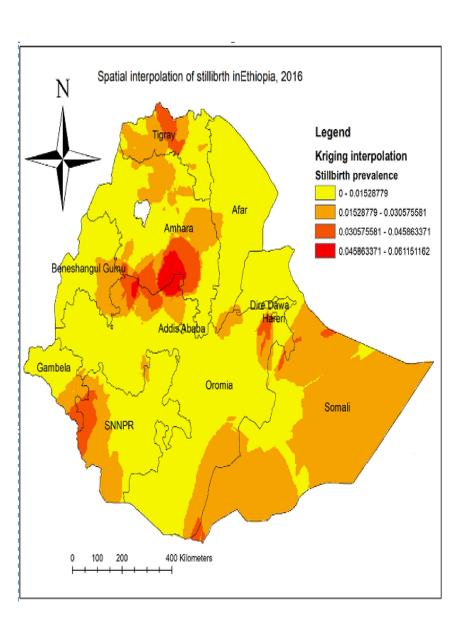
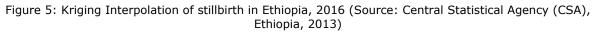


Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency (CSA), Ethiopia, 2013)

215x279mm (300 x 300 DPI)







215x279mm (300 x 300 DPI)

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	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2&3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4, 5 \$6
Objectives	3	State specific objectives, including any pre-specified 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, 7 \$8
Participants	6	(<i>a</i>) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	N/A
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	N/A
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6 &7
		(<i>b</i>) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	N/A
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7 & 8
Data	8*	For each variable of interest, give sources of data and details of methods of assessment	7&8
sources/measurement		(measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	8 & 9
Study size	10	Explain how the study size was arrived at	6&7

Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	, 8,9,10 &11
variables		groupings were chosen and why	
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8,9,10 &11
methods		(b) Describe any methods used to examine subgroups and interactions	N/A
		(c) Explain how missing data were addressed	10, 11
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	N/A
		Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	8,9 &10
		(<u>e</u>) Describe any sensitivity analyses	N/A
Results		6	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	N/A
1		for eligibility, 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	14
		exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	15
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	16 & 17
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous variables were categorized	14
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	N/A
		period	

Continued on next page

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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	21
		both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	18, 19, 20,
-		analyses, results from similar studies, and other relevant evidence	21& 22
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other informat	ion		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	23
6		original study on which the present article is based	
		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	

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Spatial distribution of stillbirth and associated factors in Ethiopia: Spatial and Multilevel Analysis

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Keywords:	Stillbirth, Ethiopia, Multilevel analysis, Spatial analysis





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Spatial distribution of stillbirth and associated factors in Ethiopia: a spatial and multilevel Analysis Getayeneh Antehunegn^{1*}, Lemma Derseh¹, Solomon Gedlu¹ ¹ Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia E-mail: (getayenehantehu..., lemmagezie@gmail.com) (sol.gondar@gmail.com) Corresponding author Getayeneh Antehunegn Tesema E-mail: getayenehantehunegn@gmail.com

16 Abstract

Objective: Even though the stillbirth rate has reduced globally, it is unacceptably high in developed countries. To date, only ten countries bear the burden of more than 65% of global stillbirth rates including Ethiopia in the seventh position. Exploring the spatial distribution of stillbirths is critical for monitoring and developing successful interventions for public health action, but there is no available national study on the spatial distribution and associated factors of stillbirth. Therefore, this study aimed to explore the spatial distribution, and associated factors of stillbirths.

Methods: Secondary data analysis was conducted based on the 2016 Ethiopian Demographic and Health Survey data. Total weighted samples of 11,375 women were included for analysis. The Bernoulli model was fitted using spatial scan statistics version 9.6 to identify hotspot areas and ArcGIS version 10.6 to explore the spatial distribution of stillbirths. For associated factors, a multilevel logistic regression model that accounts for the hierarchical structure of the data was fitted using STATA version 14 software. Variables with p-value<0.2 were considered for the multivariable multilevel analysis. In the multivariable multilevel analysis, the Adjusted Odds Ratio (AOR) with the 95% Confidence Interval (CI) were reported to declare factors significantly associated with stillbirth.

Result: The spatial analysis showed that stillbirth has significant spatial variation across regions
in Ethiopia. The SaTScan analysis identified significant primary clusters of stillbirth in the
Northeast Somali region (LLR=13.4, p<0.001) while the secondary cluster in the border area of
Oromia and Amhara regions (LLR=8.8, p<0.05). In the multilevel analysis; rural residence
(AOR=4.83, 95%CI:1.44-16.19), primary education (AOR=0.39, 95% CI:0.20-0.74), not having
ANC visit (AOR=2.77, 95% CI:1.70-4.51), caesarean delivery (AOR=5.07, 95% CI: 1.65-15.58),

39 birth interval <24 month (AOR=1.95, 95%CI: 1.20 - 3.10), and height <150 cm(AOR=2.73,

40 95%CI:1.45-4.97) were significantly associated with stillbirth.

41 Conclusion and recommendation: In Ethiopia, stillbirths had significant spatial variations across 42 the country. Residence, maternal stature, preceding birth interval, cesarean delivery, education, 43 and ANC visit were significantly associated with stillbirth. This could have public health 44 implications to target interventions to identified hotspot areas of stillbirth and the government 45 should scale up maternal health programs in rural areas.

46 Keywords: stillbirth, Ethiopia, multilevel logistic regression, spatial analysis

48 Strength and limitation of the study

• The study was based on the weighted EDHS to restore the representativeness of the data and to get a reliable estimate. Therefore, the study findings have the potential to inform policy-makers, planners and programmers, and to design appropriate intervention at national and regional levels

As a study was a cross-sectional study, the study was unable to show a temporal relationship.
 However, multilevel modeling was employed to take into account the clustering effect to get
 reliable estimates and standard error.

The EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or
 caregivers report. Besides, the study was based on self-reports of respondents. Therefore, it
 may have the possibility of social desirability and recall bias

• The SaTScan detect only circular clusters, irregularly shaped clusters were not detected

60 BACKGROUND

The World Health Organization (WHO) defines stillbirth as fetal death (death before the complete expulsion or extraction of a product of conception from its mother) in the third trimester (\geq 28 completed weeks of gestation) or birth weight \geq 1000 grams or length \geq 35 centimeters (1, 2). Stillbirth remains a global public health problem, particularly in Sub-Saharan Africa (SSA) and South Asia (SA) (3). Globally, 2.6 million stillbirths occurred annually, 98% of which were in developing countries (4).

Most of the stillbirths happen during the intrapartum period, which can be avoided by improving maternal health care services (5). More than half of the 2.6 million stillbirths occur during labor and delivery (6) and it is considered as an indicator of access to and quality of obstetric care (7). According to the most recent global estimate of WHO, the average global stillbirth rate was 18.4 per 1000 births (8), while developing countries have the stillbirth rates ten-fold higher than developed countries (9). SSA has the highest stillbirth rate of 28.3 per 1000 births (10).

Stillbirth rates have been varied across countries and remain a huge challenge to achieve Every Newborn Action Plan (ENAP) of the target of 12 or fewer stillbirths per 1000 births by 2030 (1). Even though many high-income and upper-middle-income countries have already met this target, developing countries particularly Africa will have to more than double present progress to reach this target (1). Despite the various international and national commitments on improving newborn and maternal health (11), stillbirth has been grossly under-reported and invisible in policies and programs worldwide (12). Like many countries in SSA, stillbirth is not routinely recorded and monitored in Ethiopia. It has reduced more slowly than maternal mortality and under 5 mortality, which remains invisible in the national policies (13).

The death of a fetus in utero or at birth is a devastating experience for the affected mothers and families (14). It has been associated with extensive psychosocial consequences for parents and family and has been linked to post-traumatic stress disorder, anxiety, depression, suicide, fear of the next pregnancy, and reduced relation with their partner (15, 16). In Ethiopia, a study conducted based on 2011 Ethiopian Demographic and Health Survey (EDHS) reported a stillbirth rate of 25.5 per 1000 births with significant variability across regions and the researchers recommended spatial analysis to investigate the spatial variability of experiencing stillbirth in Ethiopia (17). A study done at the Amhara region based on Ethiopian Mini Demographic and Health Survey 2014 reported that stillbirth rates of 85 per 1000 births (18). Previous studies on stillbirth showed that rural residence, parity, educational status, mode of delivery, Antenatal Care (ANC) utilization, and place of delivery, maternal nutritional status, and maternal obstetric factors were significantly associated with stillbirth (14, 19-21).

Stillbirth rates have been significantly varied across and within the country (17, 22). It is highly concentrated among rural, poor, and marginalized societies (12). Thus, the identification of geographic areas with a high rate of stillbirth using Geographic Information System (GIS) and Spatial Scan statistical analysis (SaTScan) has become fundamental to guide targeted public health interventions. However, previous studies in Ethiopia have been focused on the prevalence and associated factors of stillbirth (18, 23, 24) by using standard logistic regression models despite the hierarchical structure of EDHS data. These could result in a biased estimate since the data were nested within-cluster and violates the independent assumption (17). The findings of these studies are insufficient and limited to capture the spatial distribution of stillbirth and community-level factors associated with stillbirth. Therefore, this study aimed to investigate the spatial distribution and associated factors of stillbirth in Ethiopia using spatial and multilevel Analysis.

105 Method and materials

106 Study design, setting and period

Secondary data analysis was done based on the EDHS 2016 data. This survey is the fourth survey conducted in Ethiopia, situated in the Horn of Africa. Ethiopia is the13th in the world and 2nd in Africa's most populous country. It has 9 regional states (Afar, Amhara, Benishangul-Gumuz, Gambela, Harari, Oromia, Somali, Southern Nations, Nationalities, and People's Region (SNNP) and Tigray) and two Administrative Cities (Addis Ababa and Dire-Dawa). In Ethiopia, 84% of the population lives in rural areas and more than 80% of the country's total population lives in the regional states of Amhara, Oromia, and SNNP(25). The number of hospitals in Ethiopia varies across regions in response to differences in population size (26).

Sample and population

All births from reproductive age women within five years before the survey in Ethiopia were the source of population, whereas all births from reproductive-age women in the selected Enumeration Areas (EAs) within five years before the survey was the study population. In EDHS, a two-stage stratified cluster sampling technique selected in two stages using the 2007 Population and Housing Census (PHC) as a sampling frame. Stratification was achieved by separating each region into urban and rural areas. In total, 21 sampling strata have been created. In the first stage, 645 EAs (202 in urban areas) were chosen with probability sampling proportional to the size of the EAs with independent selection in each sampling stratum. In the second stage, on average 28 households were systematically selected. The detailed sampling procedure was presented in the full EDHS 2016 report (27).

Study variables

Outcome variables

The 2016 EDHS asked women to report any pregnancy loss that occurred in the five years preceding the survey. The duration of pregnancy was reported for every pregnancy which did not result in a live birth. Pregnancy losses occurring after seven completed months of gestation were considered as stillbirth (28). The response variable for this study was the occurrence of stillbirth among mothers of childbearing age. The response variable for the ith mother was represented by a random variable Y_i with two possible values coded as 1 and 0. So, the response variable of the i^{th} mother Y_i was measured as a dichotomous variable with possible values Y_i = 1, if i^{th} mother had experienced stillbirth and $Y_i = 0$ if mother had a live birth.

Independent variables

Consistent with the objective of the study and given the hierarchical structure of EDHS data where women were nested within the cluster/community, two levels of independent variables were considered. Level 1 contained individual socio-demographic and economic factors (age, marital status, religion, maternal education, paternal education, wealth index, maternal occupation, maternal working Status), pregnancy and pregnancy-related factors (mother's height, Body Mass Index (BMI), ANC visit, parity, preceding birth interval, contraceptive use, place of delivery, birth order, mode of delivery, wanted pregnancy, maternal anemia), and behavioral factors (smoking, and media exposure). The community-level factors; region, residence, community women education, community poverty, community media exposure, and community ANC utilization were considered as level 2 variables. In EDHS data, there is no variable collected at the cluster level except region and place of residence. Therefore, Individual-level variables were aggregated at the cluster level to generate community-level variables, to see whether cluster-level variables had an

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effect on stillbirth and were categorized as higher or lower based on national median value since it was not normally distributed. The community-level variables used in the analysis were from two sources; direct community-level variables that were used without any manipulation and aggregated community-level variables created by aggregating individual-level variables at the cluster level.

153 Data collection procedure

The study was conducted based on the 2016 EDHS data and geographic coordinate data by accessing these data from the DHS program official database<u>www.measuredhs.com</u> after permission was granted through an online request by explaining the objective of our study. We used the EDHS 2016 Birth Record data (BR) set for this study. Geographic coordinate data (longitude and latitude coordinates) were taken at the cluster level/ enumeration area level.

159 Data management and analysis

The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey and take into account the sampling design to get reliable statistical estimates. The sampling statisticians determine how many samples are needed in each region to get reliable estimates, in EDHS, some regions were oversampled, and some regions under sampled. To get statistics that are representative of Ethiopia, the distribution of women in the sample need to be weighted (mathematically adjusted) such that it resembles the true distribution in Ethiopia by using sampling weight (v005), primary sampling unit (v021) and strata (v022). Descriptive and summary statistics were conducted using STATA version 14 software.

169 In EDHS data, women are nested within a cluster and we expect that women within the same 170 cluster were more similar to each other than women in the rest of the country. It violates the

standard regression model assumptions, these are the independence of observations and equal variance across clusters assumptions. This implies that the need to take into account the between cluster variability by using an advanced model. Therefore, a multilevel random intercept logistic regression model was fitted to estimate the association between the individual and community level variables and the likelihood of experiencing stillbirth. Model comparison was done based on Deviance (The negative 2 log-likelihood (-2LL)) since the models were nested. Likelihood Ratio test (LR), Intra-cluster Correlation Coefficient (ICC), Median Odds Ratio (MOR), and Proportional Change in Variance (PCV) were computed to measure the variation between clusters. The ICC quantifies the degree of heterogeneity of stillbirth between clusters (the proportion of the total observed variation in stillbirth that is attributable to between cluster variations).

181 ICC=
$$\sigma^2/(\sigma^2 + \pi^2/3)(29)$$

MOR is used to quantify the variation or heterogeneity in stillbirth between clusters and is defined as the median value of the odds ratio between the cluster at high risk of stillbirth and cluster at lower risk when randomly picking out two clusters /EAs.

185 MOR= exp $(\sqrt{2*\partial 2*0.6745}) \sim MOR=exp (0.95*\partial)(30)$

 ∂^2 indicates that cluster variance

PCV measures the total variation of stillbirth attributed to individual-level factors and communitylevel factors in the multilevel model as compared to the null model.

189 PCV= <u>var (null model) - var full model</u>))

Var (null model)

191 Multilevel random intercept logistic regression was used to analyze factors associated with 192 stillbirth at two levels to take into account the hierarchical nature of the data, at individual and

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community levels. Four models were constructed for the multilevel logistic regression analysis. The first model (a multilevel random intercept logistic regression model without covariates) was the null model without any explanatory variables, to determine the extent of cluster variation on stillbirth. The second model (a multilevel model with level 1 independent variables) was adjusted with individual-level variables; the third model (a multilevel model with level 2 variables) was adjusted for community-level variables while the fourth model was fitted with both individual and community level variables simultaneously. The final model was the best-fitted model since it had the lowest deviance value.

Variables with p-value ≤0.2 in the bi-variable analysis for both individual and community-level
factors were fitted in the multivariable model. Adjusted Odds Ratio (AOR) with a 95% Confidence
Interval (CI) and p-value <0.05 in the multivariable model were used to declare significantly
associated factors of stillbirth. Multi-collinearity was checked using the Variance Inflation Factor
(VIF) which indicates that there is no multicollinearity because all variables have VIF<5 and
tolerance greater than 0.1.

207 Spatial analysis

For the spatial analysis, ArcGIS version 10.6 software and SaTScan version 9.6 software were used. Incremental spatial autocorrelation was done to get the maximum peak distance where stillbirth clustering is more pronounced. It measures spatial autocorrelation for a series of distances and creates a line graph of those distances and their corresponding Z-score. The maximum peak distance is the distance where maximum spatial autocorrelation occurs and this was used as a distance band for hotspot analysis. Totally 10 distance bands were detected by a beginning distance of 121,803 meters, the first peak of 136,586.06 meters, and the maximum peak

(clustering) was observed at 166152.17 meters. The maximum peak was used as the distance band for the hotspot analysis.

Spatial autocorrelation analysis

The spatial autocorrelation (Global Moran's I) was done to test whether there was significant spatial clustering of stillbirth or not. Moran's I is a statistic that measures whether stillbirth patterns were dispersed, clustered, or randomly distributed in the study area (31) by taking the entire data set and produce a single output value which ranges from -1 to +1. Moran's I values close to -1indicate spatial distribution of stillbirth was dispersed, whereas Moran's I close to +1 indicate spatial distribution of stillbirth was clustered and stillbirth distributed randomly if I value is 0. A statistically significant Moran's I (p-value < 0.05) leads to rejection of the null hypothesis (stillbirth is randomly distributed) and indicates the presence of significant spatial autocorrelation/spatial 24.0 dependence.

Hot spot analysis of stillbirth

Anselin Local Moran's I is used to investigate whether the local level cluster is positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high) regarding the prevalence of stillbirth. A positive Moran's I value indicated that a case had neighboring cases with similar values. A negative value of Moran's I indicated that a case was surrounded by cases with dissimilar values (32). Spatial scan statistical analysis (SaTScan) using the Bernoulli model was employed to test for the presence of statistically significant spatial clusters of stillbirth using Kuldorff's SaTS can version 9.6 software. The spatial scan statistic uses a circular scanning window that moves across the study area. Women who had stillbirth were taken as cases and those who had a live birth as controls to fit the Bernoulli model. The numbers of cases in each location had Bernoulli distribution and the model required data for cases, controls, and geographic

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coordinates. The default maximum spatial cluster size of <50% of the population was used, as an
upper limit, which allowed both small and large clusters to be detected and ignored clusters that
contained more than the maximum limit.

For each potential cluster, a likelihood ratio test statistic and the p-value was used to determine if the number of observed stillbirth within the potential cluster was significantly higher than expected or not. The scanning window with maximum likelihood was the most likely performing cluster, and the p-value was assigned to each cluster using Monte Carlo hypothesis testing by comparing the rank of the maximum likelihood from the real data with the maximum likelihood from the random datasets. The primary and secondary clusters were identified and assigned p-values and ranked based on their likelihood ratio test, based on 999 Monte Carlo replications(33).

248 Spatial interpolation

It is very expensive and laborious to collect reliable data in all areas of the country to know the burden of a certain event. Therefore, part of a certain area can be predicted by using observed data using a method called interpolation. The spatial interpolation technique was used to predict stillbirth on the un-sampled areas in the country based on sampled EAs measurements. There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best method since it incorporates the spatial autocorrelation and it statistically optimizes the weight (34). Ordinary Kriging spatial interpolation method was selected for this study for predictions of stillbirth in unobserved areas of Ethiopia since it had the smallest Root Mean Square Error (RMSE) value and residuals.

8 Patient and public involvement statement

259 Patients and public involvement were not involved in this study since we have conducted a 260 secondary data analysis based on already available DHS data which was collected to provide

estimates of common health and health-related indicators. For the original project from which data were obtained, patient and public involvement statements were essential since biomarker data such as anemia, HIV testing, and anthropometric measurements were collected (35).

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of Institute of Public Health, CMHS, and the University of Gondar. Permission for data access was obtained from major demographic and health survey through an online request from http://www.dhsprogram.com. The data used for this study were publicly available with no personal identifier. vere puo...

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1 2		
3 4 5	270	Result
6 7 8	271	Socio-demographic and economic characteristics of respondents
9 10	272	A total of 11,375 women who gave birth within five years preceding the survey were included for
11 12 13	273	the analysis. Of 11,375 of women, 10,149 (89.2%) were rural residents, and a half (49.2%) of the
14 15	274	respondent were aged 20-29 years. Regarding maternal education status, 7,606 (66.9%) had no
16 17	275	formal education (Table 1).
18 19 20	276	Pregnancy and maternal health service-related characteristics of respondents
21 22 23	277	Among 11375 women, two-third (65.7%) of the women were delivered at home and 194 (1.7%)
24 25	278	gave birth via cesarean section. About 2,602 (22.9 %) had no ANC visit during pregnancy (Table
26 27 28	279	2). The overall rate of stillbirth in Ethiopia was found to be 9.2 [95% CI; 7.9, 11.1] per 1000 births.
29 30 31	280	It was highest in the Amhara region and lowest in Diredawa (Figure 1).
32 33 34	281	Spatial analysis
35 36 37	282	Spatial Global autocorrelation
38 39	283	The spatial analysis revealed that the spatial distribution of stillbirth was significantly varied across
40 41 42	284	the country with Global Moran's I value of 0.017 (p< 0.05). The clustered patterns (on the right
42 43 44	285	sides) show high rates of stillbirth occurred over the study area. The outputs have automatically
45 46	286	generated keys on the right and left sides of each panel. Given the z-score of 2.4 indicated that
47 48	287	there is less than 1.5% likelihood that this clustered pattern could be the result of chance. The
49 50 51 52	288	bright red and blue colors to the end tails indicate an increased significance level (Figure 2).
53 54 55		
56 57		
58		14

Hotspot analysis of stillbirth

In the cluster and outlier analysis, the significant cluster was detected in Tigray, Amhara, Oromia, Addis Ababa, SNNPR, Benishangul-Gumuz, Somali, and Gambella regions. Hot spot areas for stillbirth were found in southwest Somali, southern Amhara, and west SNNPR, while the cold spot areas of stillbirth were found in the south and west Benishangul-Gumuz, Addis Ababa, southwest of Oromia region, west Gambella and Northeast SNNPR regions. The outliers were found in the central and southern parts of Amhara, north Tigray, southeast Gambella, and Somali regions (Figure 3).

In the Spatial scan statistical analysis, a total of 56 significant clusters of stillbirth were identified, of which 22 clusters were primary (most likely clusters) and 34 were secondary clusters. The primary cluster spatial window was located in the northeast Somali region centered at 7.829198 N, 43.706264 E of geographic location with a 166.48 km radius, a Relative Risk (RR) of 22.5 and Log-Likelihood ratio (LLR) of 13.4, at p < 0.001. It showed that women within the spatial window had 22.5 times higher risk of experiencing stillbirth than women outside the window. The secondary cluster scanning spatial window was located in the border area of the south Amhara region and the north Oromia region, and southern Afar region (Table 3). The red circular ring indicates that the most statistically significant spatial window contains the primary cluster of stillbirth. Women within the circular window had a higher likelihood of experiencing stillbirth than women outside the spatial window (Figure 4).

308 Interpolation of stillbirth

North West Tigray, northern and North West Oromia, east and south Amhara, east Benishangul,
East Gambella, Harari, and Northwest SNNPR were detected as predicted most risky areas of

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1 2		
3 4	311	stillbirth compared to other regions. The predicted low-risk areas of stillbirth were identified in
5 6	312	Oromia, Afar, and Gambella regions (Figure 5).
7 8 9 10	313	Factors associated with stillbirth
11 12	314	ICC and LR tests were checked, and the multilevel model was the best-fitted model for the data.
13 14	315	Therefore, the two-level multilevel logistic regression model was used to get an unbiased standard
15 16 17	316	error and to make a valid inference. Deviance was used for model comparison and the final model
18 19	317	was the best-fitted model with the lowest deviance value (Table 4).
20 21 22	318	The ICC-value was 47% in the null model, it showed that 47% of the total variability for stillbirth
23 24	319	was attributable to the between clusters/EA variability, with the remaining 53% attributable to the
25 26	320	individual differences. Moreover, in the null model, the MOR was 5.03 (95% CI: 3.19-7.13) and
27 28	321	PCV was 15.3%, it revealed that if we randomly select women from two different clusters, women
29 30 31	322	at the cluster with a higher risk of stillbirth had 5.03 times higher odds of experiencing stillbirth
32 33	323	as compared with women at cluster with a lower risk of stillbirth. About 15.3% of the variability
34 35 36	324	in stillbirth was explained by the full model (Table 4).
37 38	325	In the multivariable multilevel logistic regression model; residence, region, religion, preceding
39 40 41	326	birth interval, cesarean delivery, maternal height, ANC visit, and maternal education were
42 43	327	significantly associated with stillbirth. At the community level (level 2), two variables were
44 45	328	significantly associated with stillbirth. The odds of experiencing stillbirth among women residing
46 47	329	in rural areas were 4 .83 times (AOR= 4.83, 95% CI: 1.44-16.19) higher than women residing in
48 49 50	330	urban areas. The odds of experiencing stillbirth among women in Tigray, Afar, Somali, SNNPR,
51 52	331	Benishangul, Gambella, and Harari regions were not significantly different from that of
53 54 55 56 57	332	experiencing stillbirth in Amhara region. The odds of experiencing stillbirth among women who

live in the Oromia region were decreased by 75% (AOR= 0.25, 95% CI: 0.07- 0.83) compared to
women in the Amhara region.

At the individual level, six variables were significantly associated with stillbirth. Women who were protestant and catholic religious followers had 89% (AOR= 0.11, 95% CI: 0.03- 0.37) decreased odds of experiencing stillbirth than orthodox Christian religious followers. Women's educational level was significantly associated with stillbirth. Though women attained secondary education and higher had no significant difference in experiencing stillbirth, the odds of experiencing stillbirth among women who attained primary education were decreased by 61% (AOR= 0.39, 95% CI: 0.20 - 0.74) compared to women who didn't have formal education. Besides, women who had no ANC visits during pregnancy had 2.77 times (AOR= 2.77, 95% CI: 1.70 - 4.51) higher odds of experiencing stillbirth than women who had 4 and above ANC visits during pregnancy. Women who gave birth via cesarean delivery had 5.07 times (AOR= 5.07, 95%) CI: 1.65–15.58) higher odds of experiencing stillbirth than women who gave birth through vaginal delivery.

The preceding birth interval was a significant predictor of stillbirth. Women having preceding birth interval less than 24 months had 1.93 times (AOR= 1.93, 95% CI: 1.20 – 3.10) higher odds of experiencing stillbirth compared to women having preceding birth interval 24 months and above. Besides, mothers whose height less than 150 cm had 2.73 times (AOR= 2.73, 95% CI: 1.50 -4.97) higher odds of experiencing stillbirth compared to those mothers whose height greater than or equal to 150 cm (Table 4).

Discussion

The stillbirth rate in Ethiopia was 9.2 per 1000 births with marked spatial heterogeneity. The spatial distribution of stillbirth was significantly varied across the country. The SaTScan analysis detected a total of three statistically significant spatial windows with high stillbirth rates. The significant hotspot areas of stillbirth were identified in the northeast Somali, south Afar, south Amhara, and north Oromia regions. The possible explanation might be due to the reason that these areas are more of pastoralist areas where people did not have permanent residence, due to this relatively health facilities are not accessible and available in these areas compared to agrarian people and cities. Besides, these areas are more rural, which had a poor network of health facilities. Also, this could be attributed to the disparity in the distribution of maternal health service, and the inaccessibility of infrastructure in the border areas of regions (36). Whereas, the cold spot areas of stillbirth were found in south and west Benishangul-Gumuz, Addis Ababa, southwest of Oromia region, west Gambella and Northeast SNNPR. This could be due to these areas are relatively had better availability and accessibility of health services (Addis Ababa, Dire-Dawa) (37). Therefore, women are more likely to use ANC and institutional delivery services, this could contribute to the decrement of antepartum and intrapartum stillbirth. This result gives insight for public health planners and programmers for designing effective public health interventions to identified hotspot areas of stillbirth.

In the multilevel analysis, different individual and community factors were significantly associated with stillbirth. Among the community level variables, it was found that the odds of stillbirth women residing in the Oromia region were lower than in the Amhara region. This might be due to the availability and accessibility of maternal health facilities since Oromia regions are relatively around Addis Ababa and Dire-Dawa in which health facilities are accessible compared to other

regions. However, the high turnover of health professionals in the Amhara region, particularly physicians did not remain in the districts and choose to work in the capital city of Ethiopia (Addis Ababa), which may lead to the high intrapartum stillbirth rate in the districts due to the lack of trained health professionals (38). The study has shown that the odds of stillbirth were higher among women who lived in rural areas. This was consistent with previous study findings in South Africa (39), African Great lake Regions (12), Nigeria (19), Northern Ghana (14), and Ethiopia (17). This could be attributed to the disparity in the mother's health care access, availability, and accessibility of health facilities. Women in urban areas are relatively had improved health-seeking behavior than rural residents (36). Moreover, urban residents have better aware of maternal health services but in rural areas, health facilities may not be easily reachable and may end up with poor pregnancy outcomes during emergency cases (40).

Amongst the individual-level factors, catholic and protestant religious followers were significantly associated with lower odds of stillbirth compared to orthodox religious followers. This might be related to the miss-perception of religious followers and could shape their reproductive health decision making and practices, thereby govern the women's desire for using maternal health services (41). It could also be related to the feeding practice of women. Commonly orthodox religious followers may not eat animal products during pregnancy especially in the fasting period this could result in poor fetal outcomes (42). Animal products are the main source of micro and macronutrients like folate and iron. Orthodox religious followers considered giving birth at home are blessed, using contraceptive as sinning and not expose their body to health professionals during delivery this might be the possible reason which needs further qualitative study to explore the detailed reasons.

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This study noted lower odds of stillbirth among women who attained primary education compared to women who had no formal education. This finding was in line with previous studies done in Kenya (43) and Nigeria (19). It might be attributed to the reality that education can improve health care seeing behavior such as timely decision to seek health care during pregnancy, give better care for their health and their fetus, awareness of the danger sign of pregnancy, and maternal health service utilization (44).

The odds of stillbirth were higher among short stature women. A similar finding was reported in Pakistan (21). This might be because short stature women are prone to adverse pregnancy outcomes like Cephalo-Pelvic Disproportion (CPD), contracted pelvis, Intra-uterine Growth Restriction (IUGR), Intra-uterine Fetal Death (IUFD) and birth injury. Short stature reflects longstanding malnutrition or childhood infection that start in uretro or during early childhood, this kind of women may end up with poor pregnancy outcome unless we screen them as at-risk during ANC follow up (45).

Besides, having no ANC visit had a significant association with increased stillbirth. It was consistent with previous findings in low-middle income countries (46), Ghana (47), and Kenya (43). ANC follow up could help pregnant women to seek early treatment for her potential pregnancy-associated complications and early screening of underlying medical conditions, this could improve birth outcome (47, 48). On the other hand, women who did not have longer ANC follow up may not be benefited from basic ANC packages.

417 Consistent with studies done in Nigeria (19) and Gambia (49), caesarean deliveries in this study
418 showed higher odds of stillbirth when compared with normal vaginal delivery. This might be
419 because in developing countries including Ethiopia maternal health services were not available
420 and reachable, particularly caesarean section is done at tertiary hospitals. Though caesarean section

is applied to save the life of new-born in high-risk pregnancies, in Ethiopia, more than 84% of the population are rural residents and tertiary hospitals are not accessible due to transportation problems resulting in not to save the baby's life because the caesarean section is not done at the right time. Therefore, high-risk deliveries like birth asphyxia, malpresentation, fetal stress and Antepartum Haemorrhage (APH) that needs caesarean delivery are referred from health centers and health posts and may not reach at the right time to conduct caesarean section this could contribute for the increased risk of stillbirth (50, 51). Overall, in Ethiopia, since majority of the pregnant women are from rural areas caesarean sections are applied too late in hospitals since most women are referred to from distant health facilities.

In this study, having a short inter-pregnancy interval was associated with higher odds of stillbirth.
This was consistent study findings in SSA (52), Bangladesh (53), and Amhara Region (18). This
could be explained by women who had short preceding birth interval are less able to provide
nourishment for the fetus because her body had less time to recuperate from the previous
pregnancy, and the uterus had less time to recover. Furthermore, lactation will deplete maternal
nutrition and may end up with poor pregnancy outcomes (53).

The strength of this study was using weighted data to make it representativeness at national and regional levels: therefore, it can be generalized to all women who gave birth during the study period in Ethiopia. Moreover, the use of GIS and SaTScan statistical tests helped to detect similar and statistically significant hotspot areas of stillbirth and to design effective public health programs. However, the SaTScan detect only circular clusters, irregularly shaped clusters were not detected. Furthermore, the EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or caregivers report and might have the possibility of social desirability and recall bias since stillbirth (27).

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The findings of this study have valuable policy implications for health program design and interventions. Stillbirth high-risk areas can be easily identified to make effective local interventions. In general, these findings are of supreme importance for the minister of health, regional health bureaus, and NGO's to design intervention programs to reduce stillbirth in identified hotspot areas. To reduce the overall stillbirth rate in Ethiopia, Somali, Afar, Amhara, and Oromia regions should emphasize the identified SaTScan clusters through developing local interventional strategies like improving accessibility and availability of maternal health facility.

Conclusions

In Ethiopia, stillbirth had spatial variations across the country. Statistically significant hotspot areas of stillbirth were found in the central and southern parts of Amhara, west SNNPRs, south and north Tigray, and south West Somali region. Whereas, cold spot areas were found in Addis Ababa, central Oromia, and east SNNPRs. Short preceding birth interval, short maternal stature, ANC visit, rural residence, region, religion, maternal education, and cesarean delivery were significant predictors of stillbirth. This could have public health implications to target interventions to identified hotspot areas of stillbirth and the government should scale up maternal health programs in rural areas.

Abbreviations

ANC; Antenatal Care, AOR; Adjusted Odds Ratio, ARR; Annual Rate of Reduction, BMI; Body
Mass Index, CI; Confidence Interval, COR; Crude Odds Ratio, CSA; Central Statistical Agency,
DHS; Demographic Health Survey, EA; Enumeration Area, EDHS; Ethiopian Demographic
Health Survey, GIS; Geographic Information System, ICC; Intra-cluster Correlation Coefficient,
IUFD; Intra Uterine Fetal Death, IUGR; Intra Uterine Growth Restriction, LLR; log-

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466 likelihood Ratio, LR; Likelihood Ratio, MOR; Median Odds Ratio, PCV; Proportional Change in

Variance, PHC; Population and Housing census, SBR; Stillbirth Rate, SNNPRs; Southern Nations 467

and Nationality People Regional state, WHO; World Health Organization. 468

Declarations 469

470 Availability of data and materials

Data is available online and you can access it from www.measuredhs.com. 471

Competing Interests 472

Authors declare that they have no conflict of interest 473

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No funding was obtained for this study. 475

Authors' contribution 476

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- Data curation: Getayeneh Antehunegn Tesema 478
- Funding acquisition: Getayeneh Antehunegn Tesema 479
- 480 Investigation: Getaveneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu
- Methodology: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 481
- Project administration: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 482
- Resources: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 483
- Software: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 484
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24 25 26	494	References
27 28	495	1. Organization WH. Every newborn: an action plan to end preventable deaths. 2014.
29 30	496	2. Smith GC, Fretts RC. Stillbirth. The Lancet. 2007;370(9600):1715-25.
31 32 33 34	497 498 499	3. Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC pregnancy and childbirth. 2010;10(1):S1.
35 36	500 501	4. Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk factors, and acceleration towards 2030. The Lancet. 2016;387(10018):587-603.
37 38 39	502 503	5. Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When? Why? How to make the data count? The Lancet. 2011;377(9775):1448-63.
40 41 42	504 505	6. Temmerman M, Lawn JE. Stillbirths count, but it is now time to count them all. The Lancet. 2018;392(10158):1602-4.
43 44 45 46	506 507 508	7. Admasu K, Haile-Mariam A, Bailey P. Indicators for availability, utilization, and quality of emergency obstetric care in Ethiopia, 2008. International Journal of Gynecology & Obstetrics. 2011;115(1):101-5.
47 48 49 50	509 510 511	8. Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet Global Health. 2016;4(2):e98-e108.
50 51 52 53 54	512 513 514	9. Saleem S, Tikmani SS, McClure EM, Moore JL, Azam SI, Dhaded SM, et al. Trends and determinants of stillbirth in developing countries: results from the Global Network's Population-Based Birth Registry. Reproductive health. 2018;15(1):100.
55 56		
57 58		24
58 59		24

McClure EM, Pasha O, Goudar SS, Chomba E, Garces A, Tshefu A, et al. Epidemiology of stillbirth

10.

in low-middle income countries: a Global Network Study. Acta obstetricia et gynecologica Scandinavica. 2011;90(12):1379-85. 11. Bamford L. Maternal, newborn and child health: service delivery. South African health review. 2012;2012(2012/2013):49-66. 12. Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: A pooled analysis of Demographic and Health Surveys. PloS one. 2018;13(8):e0202603. 13. You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. The Lancet. 2015;386(10010):2275-86. 14. Badimsuguru AB, Nyarko KM, Afari EA, Sackey SO, Kubio C. Determinants of stillbirths in Northern Ghana: a case control study. The Pan African medical journal. 2016;25(Suppl 1). 15. Ogwulu CB, Jackson LJ, Heazell AE, Roberts TE. Exploring the intangible economic costs of stillbirth. BMC pregnancy and childbirth. 2015;15(1):188. Meaney S, Everard CM, Gallagher S, O'donoghue K. Parents' concerns about future pregnancy 16. after stillbirth: a qualitative study. Health Expectations. 2017;20(4):555-62. Berhie KA, Gebresilassie HG. Logistic regression analysis on the determinants of stillbirth in 17. Ethiopia. Maternal health, neonatology and perinatology. 2016;2(1):10. 18. Lakew D, Tesfaye D, Mekonnen H. Determinants of stillbirth among women deliveries at Amhara region, Ethiopia. BMC pregnancy and childbirth. 2017;17(1):375. Dahiru T, Aliyu AA. Stillbirth in Nigeria: rates and risk factors based on 2013 Nigeria DHS. Open 19. Access Library Journal. 2016;3(08):1. 20. Ali AAA, Adam I. Anaemia and stillbirth in Kassala hospital, eastern Sudan. Journal of tropical pediatrics. 2010;57(1):62-4. Badshah S, Mason L, Lisboa PJ. Risk Factors Associated with Stillbirths in Public-Hospitals in 21. Peshawar, Pakistan. The Journal of Humanities and Social Sciences. 2011;19(2):15. 22. Berhan Y, Berhan A. Perinatal mortality trends in Ethiopia. Ethiopian journal of health sciences. 2014;24:29-40. Welegebriel TK, Dadi TL, Mihrete KM. Determinants of stillbirth in Bonga General and Mizan Tepi 23. University Teaching Hospitals southwestern Ethiopia, 2016: a case-control study. BMC research notes. 2017;10(1):713. 24. Tilahun D, Assefa T. Incidence and determinants of stillbirth among women who gave birth in Jimma University specialized hospital, Ethiopia. Pan African Medical Journal. 2017;28(1). 25. Central statistical agency(CSA) I. Ethiopian Demographic and Health survey. Addis Abeba: Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF, 2016. 26. Adugna A. Health Institutions and Services. Addis Abeba: July 2014. 27. ICF CSACEa. Ethiopia Demographic and Health Survey 2016 Addis Ababa, Ethiopia, and Rockville, maryland, USA: CSA and ICF. 2016.

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- 554 28. Goldenberg RL, McClure EM, Bhutta ZA, Belizán JM, Reddy UM, Rubens CE, et al. Stillbirths: the 555 vision for 2020. The lancet. 2011;377(9779):1798-805.
- 556 29. Rodriguez G, Elo I. Intra-class correlation in random-effects models for binary data. The Stata 557 Journal. 2003;3(1):32-46.
- 558 30. Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic regression to investigate contextual phenomena. Journal of Epidemiology & Community Health. 2006;60(4):290-7.
- 561 31. Waldhör T. The spatial autocorrelation coefficient Moran's I under heteroscedasticity. Statistics in Medicine. 1996;15(7-9):887-92.
- 1556332.Tsai P-J, Lin M-L, Chu C-M, Perng C-H. Spatial autocorrelation analysis of health care hotspots in16564Taiwan in 2006. BMC Public Health. 2009;9(1):464.
- 18 565 33. Kulldorff M. SaTScanTM user guide. Boston; 2006.
- 566 34. Bhunia GS, Shit PK, Maiti R. Comparison of GIS-based interpolation methods for spatial distribution of soil organic carbon (SOC). Journal of the Saudi Society of Agricultural Sciences. 22 568 2018;17(2):114-26.
- 569 35. 2016. CSACEal. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF. 2016.
- ²⁶ 571 36. Adugna A. Health instituition and Services in Ethiopia. 2014.
- 2857237.Asefa A, Bekele D. Status of respectful and non-abusive care during facility-based childbirth in a29573hospital and health centers in Addis Ababa, Ethiopia. Reproductive health. 2015;12(1):33.
- 574 38. Assefa T, Mariam DH, Mekonnen W, Derbew M, Enbiale W. Physician distribution and attrition in the public health sector of Ethiopia. Risk management and healthcare policy. 2016;9:285.
- 55 576 39. Nfii FN. Levels, trends and household determinants of stillbirths and miscarriages in South Africa 577 (2010-2014) 2017.
- ³⁶ 578 40. Babalola S, Fatusi A. Determinants of use of maternal health services in Nigeria-looking beyond ³⁷ 579 individual and household factors. BMC pregnancy and childbirth. 2009;9(1):43.
- 580 41. Tarekegn SM, Lieberman LS, Giedraitis V. Determinants of maternal health service utilization in
 581 Ethiopia: analysis of the 2011 Ethiopian Demographic and Health Survey. BMC pregnancy and childbirth.
 582 2014;14(1):161.
- 4358342.Dugan B. Religion and food service. Cornell Hotel and Restaurant Administration Quarterly.445841994;35(6):80-5.
- 585 43. Cheptum JJ, Oyore JP, Okello Agina BM. Poor pregnancy outcomes in public health facilities in
 586 Kenya. African Journal of Midwifery and Women's Health. 2012;6(4):183-8.
- 48 587 44. Ahmed S, Creanga AA, Gillespie DG, Tsui AO. Economic status, education and empowerment:
 49 588 implications for maternal health service utilization in developing countries. PloS one. 2010;5(6):e11190.
- 589 45. Liselele HB, Boulvain M, Tshibangu KC, Meuris S. Maternal height and external pelvimetry to
 predict cephalopelvic disproportion in nulliparous African women: a cohort study. BJOG: An International
 Journal of Obstetrics & Gynaecology. 2000;107(8):947-52.

46. McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in low-middle income countries 2010-2013: a population-based, multi-country study from the Global Network. Reproductive health. 2015;12(2):S7.

47. Afulani PA. Determinants of stillbirths in Ghana: does quality of antenatal care matter? BMC pregnancy and childbirth. 2016;16(1):132.

48. Bhutta ZA, Darmstadt GL, Haws RA, Yakoob MY, Lawn JE. Delivering interventions to reduce the global burden of stillbirths: improving service supply and community demand. BMC pregnancy and childbirth. 2009;9(1):S7.

49. Jammeh A, Vangen S, Sundby J. Stillbirths in rural hospitals in the gambia: a cross-sectional retrospective study. Obstetrics and gynecology international. 2010;2010.

Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat 50. cesarean delivery at term and neonatal outcomes. New England Journal of Medicine. 2009;360(2):111-20.

51. Smith GC, Pell JP, Bobbie R. Caesarean section and risk of unexplained stillbirth in subsequent pregnancy. The Lancet. 2003;362(9398):1779-84.

Tolefac PN, Tamambang RF, Yeika E, Mbwagbaw LT, Egbe TO. Ten years analysis of stillbirth in a 52. tertiary hospital in sub-Sahara Africa: a case control study. BMC research notes. 2017;10(1):447.

53. DaVanzo J, Hale L, Razzaque A, Rahman M. 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.

	614	Table 1: Socio-demographic cha	aracteristics of women who	o gave birth within 5	years before the
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615 survey in Ethiopia, 2016.

Variables	Category	Unweighted frequency (%)	Weighted frequency (%)
Residence	Urban	1,994 (18.0)	1,226 (10.8)
	Rural	9,091 (82.0)	10,149 (89.2)
Region	Tigray	1,021 (9.2)	709 (6.2)
	Afar	1,102 (9.9)	119 (1.0)
	Amhara	1,004 (9.1)	2,122 (18.7)
	Oromia	2,617 (23.6)	5,280 (46.4)
	Somali	1,623 (14.6)	554 (4.9)
	Benishangul Gumuz	962 (8.7)	133 (1.2)
	SNNPR	1,334 (12.0)	2,402 (21.1)
	Gambella	789 (7.1)	29 (0.3)
	Harari	633 (5.7)	27 (0.2)
Religion	Orthodox	3,127 (28.2)	3,844 (33.8)
	Muslim	5,710 (51.5)	4,696 (41.3)
	Catholic and	2,248 (20.3)	2,835 (24.9)
	protestant	2	
Maternal	No education	7,241 (65.3)	7,606 (66.9)
education	Primary education	2,708 (24.4)	2,961 (26.0)
	Secondary and higher	1,136 (10.3)	808 (7.1)
	education		
Maternal age	<20 year	395 (3.6)	374 (3.3)
	20-29 year	5,556 (50.1)	5,599 (49.2)
	30-39 year	4,234 (38.2)	4,381 (38.5)
	≥40 year	900 (8.1)	1,021 (9.0)
Husband	No education	5,331 (51.2)	5,339 (49.6)
education	Primary education	3,260 (31.3)	4,139 (38.5)

	Secondary and higher	1,817 (17.5)	1,284 (11.9)
	education		
Maternal	Had occupation	6,584 (59.4)	6,352 (55.8)
occupation status	No occupation	4,501 (40.6)	5,023 (44.2)
Wealth status	Poor	6,081 (54.9)	5,360 (47.1)
	Middle	1,512 (13.6)	2,318 (20.4)
	Rich	3,492 (31.5)	3,697 (32.5)

Table 2: pregnancy and health service-related characteristics of women who gave birth within 5

618 years preceding the survey in Ethiopia, 2016.

Variable	Category	Unweighted frequency (%)	Weighted frequency (%)
Pregnancy and mater	rnal service-related fact	cors	
Place of delivery	Home	6,737 (60.8)	7,468 (65.7)
	Health facility	4,348 (39.2)	3,907 (34.3)
Parity	Only one birth	1,435 (13.0)	1,419 (12.5)
	2-4 birth	5,042 (45.5)	5,022 (44.1)
	≥5 birth	4,608 (41.5)	4,934 (43.4)
Birth order	1-3	5,806 (52.4)	5,703 (50.1)
	4-5	2,584 (23.3)	2,655 (23.4)
	≥6	2,695 (24.3)	3,017 (26.5)
BMI	Thin	2,981 (26.9)	2,483 (21.8)
	Normal	7,106 (64.1)	8,164 (71.8)
	Overweight	998 (9.0)	728 (6.4)
Maternal height	< 150 cm	1,018 (9.2)	1,228 (10.8)
	≥150 cm	10,067 (90.8)	10,147 (89.2)
ANC visit	No ANC visit	2,321 (20.9)	2,602 (22.9)
	1-3 ANC visit	1,917 (17.3)	2,145 (18.9)
	\geq 4 ANC visit	6,847 (61.8)	6,628 (58.2)

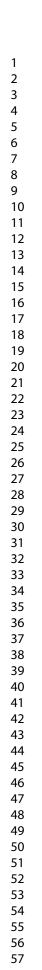
ſ	Preceding birth	< 24 month	2,347 (21.2)		2,145	5 (18.9)		
	interval	≥24 month	8,738 (78.8)		9,230	0 (81.1)		
-	Maternal anemia	Not anemic	6,696 (60.4)		7,590	0 (66.7)		
		Anemic	4,389 (39.6)		3,785	5 (33.3)		
	Ever use of	Yes	4,101 (37.0)		5,238	8 (46.0)		
	contraceptive	No	6,984 (63.0)		6,137	7 (54.0)		
	Mode of delivery	Vaginal delivery	/ 10,813 (97.5)		11, 1	81 (98	3)	
		Cesarean delive	ry 272 (2.5)		194 ((1.7)		
	Number of gestation	Single	10,798 (97.4)		11,07	72 (97.3	5)	
		Twin	287 (2.6)		303 ((2.7)		
	Behavioral and commun	nity-level factors						
-	Smoking cigarettes	Yes	10,976 (99.0)		11,28	36 (99.2	2)	
		No	109 (1.0)	109 (1.0)		.8)		
_	Media exposure	Yes 9,747 (87.9)		10,020 (88.1)				
		No	1,338 (12.1)	1,338 (12.1)		1,355 (11.9)		
	Community media	Lower	5,503 (49.6)		4,640	0 (40.8)		
	exposure	Higher	5,582 (50.4)		6,735	5 (59.2)		
	Community poverty	Lower	6,909 (62.3)	6,909 (62.3) 4,176 (37.7)	7,617 (67.0) 3,758 (33.0)			
		Higher	4,176 (37.7)					
-	Community ANC	Lower	5,387 (48.6)	0	6,665	5 (58.6)		
	utilization	Higher	5,698 (51.4)	5	4,710) (41.4)		
	Community women	Lower	6,909 (62.3)		7,617	7 (67.0)		
	education	Higher	4,176 (37.7)		3,758	8 (33.0)		
19 20	Table 3: SaTScan analys	is results of stillb	irth in Ethiopia, 2016	ó.				
ister	Enumeration area(clu	ster)identified	Coordinate/radius	Population	Case	RR	LLR	p-value
	497, 95, 198, 521, 58		(7.829198 N,	532	17	22.5	13.4	0.00069
	214, 251, 573, 239, 1		43.706264 E) /					
	492, 92, 568, 33, 277,	, 327	166.48 km					

2	350, 229, 482, 531, 218, 510, 206,	10, (10.195460 N,	384 14	3.6 8.84 0.04
	474, 267, 375, 423, 120, 176, 5	72, 38.150574 E) /		
	517, 460, 24, 403, 429, 38, 3, 4			
	456, 274, 167, 463, 112, 399, 532			
2	5(4, 20, 220, 51	(0.555410 N	50 4	
3	564, 39, 230, 51	(9.555410 N,	50 4	8.83 8.55 0.05
		40.326165 E) / 34.04 km		
621		54.04 KIII		
	Table 4: Multivariable multilevel logi			ial and
623	community-level factors associated w	ith stillbirth in Ethiopia, I	EDHS 2016	
ıdividual	and community- Null model	Model II	Model III	Model IV
	acteristics	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
esidence		~	-	
rban			1	1
ural			3.75[1.33, 10.56]	4.83[1.44, 16.19]*
egion			L / _	L
mhara			1	1
igray			0.54[0.18, 1.63]	0.63[0.19, 2.17]
far			0.28[0.08, 0.94]	0.24[0.05, 1.06]
romia			0.20[0.07, 0.55]	0.25[0.07, 0.83]*
omali			0.84[0.32, 2.21]	0.98[0.27, 3.56]
enishangı	ul Gumuz		0.25[0.07, 0.92]	0.37[0.09, 1.53]
NNPR			0.21[0.06, 0.69]	0.56[0.14, 2.18]
ambella			0.26[0.06, 1.07]	1.02[0.20, 5.22]
arari			0.71[0.19, 2.63]	0.77[0.16, 3.72]
eligion				
rthodox		1		1
luslim		0.59[0.31, 1.12]		0.75[0.32, 1.77]
rotestant/	catholic	0.12[0.04, 0.35]		0.11[0.03, 0.37]**
Vealth sta	atus			
oor		1.12[0.60, 2.11]		0.87[0.45, 1.69]
liddle		1.58[0.78, 3.19]		1.21[0.60, 2.47]
lich		1		1
	education			
lo educati	on	1		1
				21

1 2				
³ Primary education		0.39[0.21, 0.75]		0.39[0.20, 0.74]**
⁴ Secondary and higher		0.49[0.18, 1.33]		0.63[0.23, 1.71]
6 education		0.17[0110, 1000]		0.00[0.20, 1., 1]
⁷ Birth order				
8 1-3		1		1
104-5		0.49[0.24, 1.03]		0.50[0.24, 1.03]
¹¹ 6 and above		0.66[0.25, 1.75]		0.66[0.25, 1.73]
¹² 13 Parity				
14 Only one birth		1		1
¹⁵ 2-4 birth		0.68[0.37, 1.28]		0.65[0.35, 1.22]
$^{16}_{17} \ge 5$ birth		0.45[0.16, 1.28]		0.42[0.15, 1.20]
17-18 ANC visit				[,.]
¹⁹ No ANC visit		2.85[1.76, 4.62]		2.77[1.70, 4.51]**
$^{20}_{21}$ 1-3 visit		1.22[0.68, 2.19]		1.11[0.62, 2.00]
21 224 and above visit		1		1
²³ Media exposure				
²⁴ ₂₅ Yes		1		1
25 26 No		2.11[0.85, 5.24]		1.63[0.66, 4.04]
²⁷ Maternal height				
$\frac{28}{29} < 150 \text{ cm}$		2.66[1.47, 4.79]		2.73[1.50, 4.97]**
$_{30}^{29} \ge 150 \text{ cm}$		1		1
³¹ Contraceptive use				
³² ₃₃ Yes		0.74[0.43, 1.26]		0.72[0.41, 1.24]
33 34 No		1		1
³⁵ Preceding birth interval				
36 <24 month		1.92[1.19, 3.07]		1.93[1.20, 3.10]**
$_{38}^{37} \ge 24$ month		1		1
³⁹ Mode of delivery				
⁴⁰ Vaginal delivery		1		1
41 42 Cesarean delivery		4.00[1.35, 11.85]		5.07[1.65, 15.58]**
⁴³ Community media exposure				
⁴⁴ Lower community exposure			1	1
$^{45}_{46}$ Higher community exposure			0.96[0.51, 1.80]	1.02[0.51, 2.04]
47 Community women's				
⁴⁸ education				
$^{49}_{50}$ Lower community education			1	1
51 Higher community education			1.28[0.61,2.71]	1.88[0.80, 4.42]
⁵² Constant	0.003[0.002, 0.005]	0.003[0.001,	0.002[0.0005,0.0096]	0.001[0.0002, 0.01]
53 54		0.01]		
55				
56 57				
57 58				32
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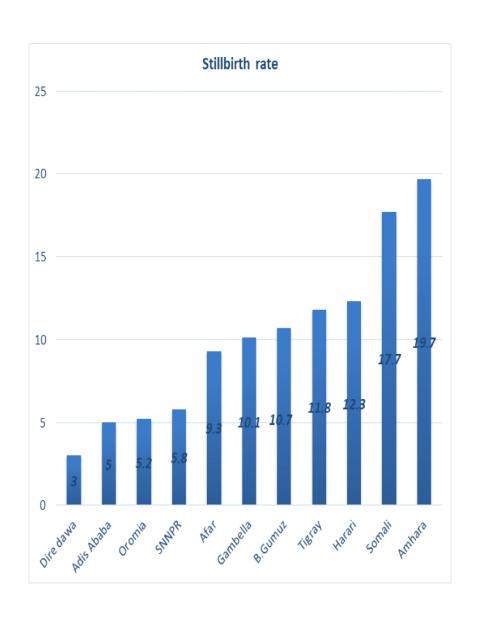
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4	andom	-				
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8 9 D	eviance		1198.04	1102.2	1168.72	1081
10 PC			Ref	21.5	9.3	15.3
¹¹ M 1 2	IOR		5.03[3.19, 7.13]	5.91[3.44, 8.90]	4.66[2.84, 6.69]	5.69[3.31, 8.56]
13 14	624	*AOR; Adjust	ed Odds Ratio, CI; Conf	fidence Interval, ICC	C; Intra-class Correld	ttion, MOR;
15 16	625	Median Odds	Ration, PCV; Proportional	-		
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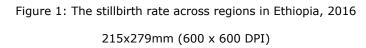
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3 4	627	Figure legends:
5	628	Figure 1: The stillbirth rates across regions in Ethiopia, 2016
6		
7 8	620	Figure 2: Clobal spatial autocorrelation of stillbirths in Ethiopia, 2016
8 9	629	Figure 2: Global spatial autocorrelation of stillbirths in Ethiopia, 2016
10		
11	630	Figure 3: Cluster and Outlier analysis of stillbirths in Ethiopia, 2016 (Source: Central Statistical
12 13		
14	631	Agency (CSA), Ethiopia, 2013)
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16	632	Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source:
17 18	052	
18 19	633	Central Statistical Agency (CSA), Ethiopia, 2013)
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22	634	Figure 5: Kriging Interpolation of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency
23 24		(CSA), Ethiopia, 2013)
24 25	635	(CSA), Ethiopia, 2013)
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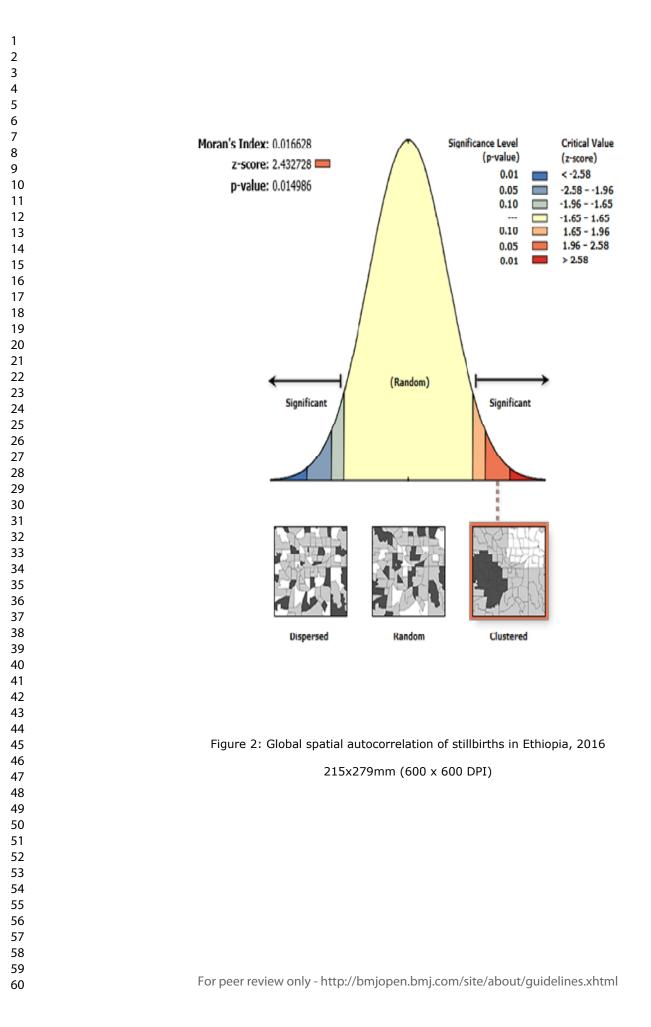


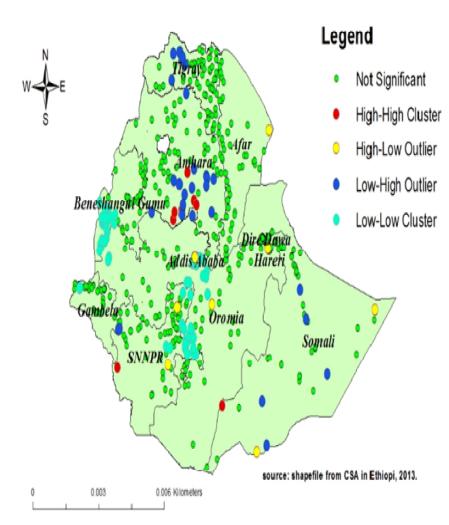


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Cluster and Outlier analysis of stillbirth accross regions in Ethiopia, 2016



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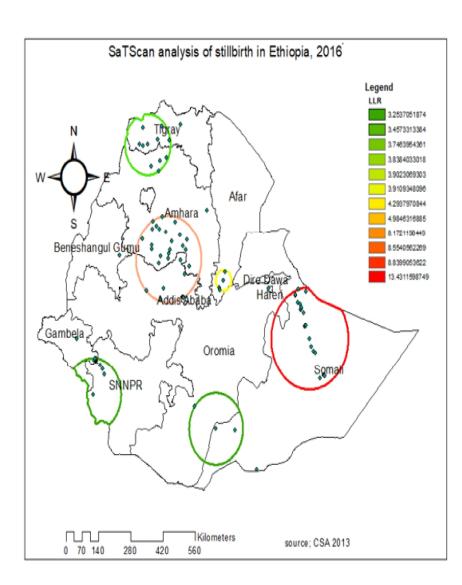
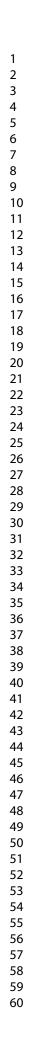
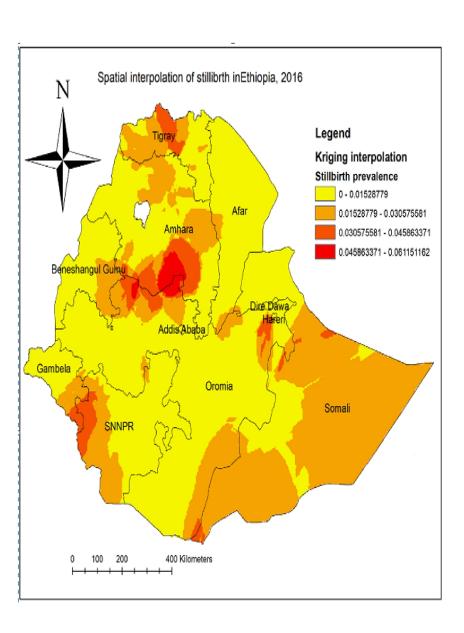
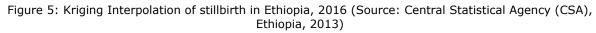


Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency (CSA), Ethiopia, 2013)

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	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2&3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4, 5 \$6
Objectives	3	State specific objectives, including any pre-specified 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, 7 \$8
Participants	6	(<i>a</i>) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	N/A
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	N/A
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6 &7
		(<i>b</i>) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	N/A
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7 & 8
Data	8*	For each variable of interest, give sources of data and details of methods of assessment	7&8
sources/measurement		(measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	8 & 9
Study size	10	Explain how the study size was arrived at	6&7

Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	, 8,9,10 &11
variables		groupings were chosen and why	
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8,9,10 &11
methods		(b) Describe any methods used to examine subgroups and interactions	N/A
		(c) Explain how missing data were addressed	10, 11
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	N/A
		Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	8,9 &10
		(<u>e</u>) Describe any sensitivity analyses	N/A
Results		6	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	N/A
		for eligibility, 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	14
		exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	15
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	16 & 17
Main results		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous variables were categorized	14
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	N/A
		period	

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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	21
		both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	18, 19, 20,
-		analyses, results from similar studies, and other relevant evidence	21& 22
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other informat	ion		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	23
6		original study on which the present article is based	
		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	

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Spatial distribution of stillbirth and associated factors in Ethiopia: Spatial and Multilevel Analysis

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Primary Subject Heading :	Obstetrics and gynaecology
Secondary Subject Heading:	Epidemiology, Health services research, Obstetrics and gynaecology
Keywords:	Stillbirth, Ethiopia, Multilevel analysis, Spatial analysis





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Spatial distribution of stillbirth and associated factors in Ethiopia: Spatial and **Multilevel Analysis** Getayeneh Antehunegn^{1*}, Lemma Derseh¹, Solomon Gedlu¹ ¹ Department of Epidemiology and Biostatistics, Institute of Public Health, College of Medicine and Health Sciences, University of Gondar, Gondar, Ethiopia E-mail: (getayenehantehu..., lemmagezie@gmail.com) (sol.gondar@gmail.com) Corresponding author Getayeneh Antehunegn Tesema E-mail: getayenehantehunegn@gmail.com

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16 Abstract

Objective: Despite the stillbirth rate has been reduced globally, it is still unacceptably high in developing countries. Today, only ten countries share the burden of more than 65% of global stillbirth rates including Ethiopia. Ethiopia ranks the seventh position concerning the stillbirth rate. Exploring the spatial distribution of stillbirth is critical for developing successful interventions and monitoring public health programs, but there is no study on the spatial distribution and associated factors of stillbirth in Ethiopia. Therefore, this study aimed to explore the spatial distribution and associated factors of stillbirth.

Methods: Secondary data analysis was conducted based on the 2016 Ethiopian Demographic and Health Survey (EDHS) data. A total weighted sample of 11,375 women was included for analysis. The Bernoulli model was fitted using SaTScan version 9.6 to identify hotspot areas and ArcGIS version 10.6 to explore the spatial distribution of stillbirth. For associated factors, a multilevel binary logistic regression model was fitted using STATA version 14 software. Variables with a p-value of less than 0.2 were considered for the multivariable multilevel analysis. In the multivariable multilevel analysis, the Adjusted Odds Ratio (AOR) with the 95% Confidence Interval (CI) were reported to declare significantly associated factors of stillbirth.

Result: The spatial analysis showed that stillbirth has significant spatial variation across the country. The SaTScan analysis identified significant primary clusters of stillbirth in the Northeast Somali region (LLR=13.4, p<0.001) while the secondary cluster in the border area of Oromia and Amhara regions (LLR=8.8, p<0.05). In the multilevel analysis; rural residence (AOR=4.83, 95%CI:1.44-16.19), primary education (AOR=0.39, 95% CI:0.20-0.74), not having ANC visit (AOR=2.77, 95% CI:1.70-4.51), caesarean delivery (AOR=5.07, 95% CI: 1.65-15.58), birth

interval <24 month (AOR=1.95, 95%CI: 1.20 - 3.10), and height <150 cm(AOR=2.73,

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95%CI:1.45-4.97) were significantly associated with stillbirth. 39 **Conclusion and recommendation:** In Ethiopia, stillbirth had significant spatial variations across 40 the country. Residence, maternal stature, preceding birth interval, cesarean delivery, education, 41 and ANC visit were significantly associated with stillbirth. Therefore, public health interventions 42 43 targeting the hotspot areas of stillbirth through enhancing maternal health care service utilization, and maternal education are crucial to reducing stillbirth in Ethiopia. 44 Keywords: Stillbirth, Ethiopia, Multilevel analysis, Spatial analysis 45 46 Strength and limitation of the study 47 The study was done based on the weighted EDHS data to secure the representativeness of the 48 data and to get a reliable estimate. Therefore, the study findings have the potential to inform 49 policy-makers and programmers, and also aid to design appropriate intervention at national 50 and regional levels 51 As the study was a cross-sectional study, it was unable to show a temporal relationship. 52 However, multilevel modeling was employed to take into account the clustering effect to get 53 54 reliable estimates and standard error. The EDHS survey did not incorporate clinically confirmed data rather it relied on mothers or 55 56 caregiver's verbal autopsy. Therefore, it may have the possibility of social desirability and recall bias 57

The SaTScan detected only circular clusters. However, irregularly shaped clusters were not
 detected.

60 BACKGROUND

The World Health Organization (WHO) defines stillbirth as fetal death (death before the complete expulsion or extraction of a product of conception from its mother) in the third trimester (\geq 28 completed weeks of gestation) or birth weight \geq 1000 grams or length \geq 35 centimeter(1, 2). Stillbirth remains a global public health problem, particularly in Sub-Saharan Africa (SSA) and South Asia (SA) (3). Globally, an estimated 2.6 million stillbirths occurred annually, 98% of which were in developing countries (4).

Most of the stillbirths happen during the intrapartum period, which can be avoided by improving maternal health care services (5). More than half of the 2.6 million stillbirths occur during labor and delivery (6), and it is considered as an indicator of poor access to and quality of obstetric care (7). According to the most recent global estimate of WHO, the average global stillbirth rate was 18.4 per 1000 births (8), while developing countries have the stillbirth rates ten-fold higher than developed countries (9). SSA has the stillbirth rates of 28.3 per 1000 births (10).

Stillbirth rates have been varied across countries and remain a huge challenge to achieve the Every Newborn Action Plan (ENAP) target of 12 or fewer stillbirths per 1000 births by 2030 (1). Even though many high-income and upper-middle-income countries have already met this target, developing countries particularly Africa will have to register more than double the present progress to reach this target (1). Despite the various international and national commitments on improving newborn and maternal health (11), stillbirth has been grossly under-reported and invisible in policies and programs worldwide (12). Like many countries in SSA, stillbirth is not routinely recorded and monitored in Ethiopia. It has reduced more slowly than maternal mortality and under 5 mortality, which remains invisible in the national policies (13).

The death of a fetus in utero or at birth is a devastating experience for the affected mothers and families (14). It has been associated with extensive psychosocial consequences for parents and family and has been linked to post-traumatic stress disorder, anxiety, depression, suicide, fear of the next pregnancy, and reduced relation with their partner (15, 16). In Ethiopia, a study conducted based on 2011 Ethiopian Demographic and Health Survey (EDHS) reported a stillbirth rate of 25.5 per 1000 births with significant variability across regions and researchers recommended spatial analysis to investigate the spatial variability of experiencing stillbirth in Ethiopia (17). A study done at the Amhara region based on the Ethiopian Mini Demographic and Health Survey 2014 reported that stillbirth rates of 85 per 1000 births (18). Previous studies on stillbirth showed that rural residence, parity, educational status, mode of delivery, Antenatal Care (ANC) utilization, place of delivery, maternal nutritional status, and maternal obstetric factors were significantly associated with stillbirth (14, 19-21).

Stillbirth rates have been significantly varied across and within the country (17, 22). It is highly concentrated among rural, poor, and marginalized societies (12). Thus, the identification of geographic areas with a high rate of stillbirth using Geographic Information System (GIS) and Spatial Scan statistical analysis (SaTScan) has become fundamental to guide targeted public health interventions. However, previous studies in Ethiopia have been focused on the prevalence and associated factors of stillbirth (18, 23, 24) by using standard logistic regression models despite the hierarchical structure of EDHS data. These could result in a biased estimate since the data were nested within-cluster and violates the independent assumption (17). The findings of these studies are insufficient and limited to capture the spatial distribution of stillbirth and community-level factors associated with stillbirth. Therefore, this study aimed to investigate the spatial distribution and associated factors of stillbirth in Ethiopia using spatial and multilevel Analysis.

105 Method and materials

106 Study design, setting and period

Secondary data analysis was done based on the EDHS 2016 data. This survey was the fourth survey conducted in the country. Ethiopia is situated in the Horn of Africa. It is the13th in the world and 2nd in Africa's most populous country. There are 9 regional states (Afar, Amhara, Benishangul-Gumuz, Gambela, Harari, Oromia, Somali, Southern Nations, Nationalities, and People's Region (SNNP) and Tigray) and two Administrative Cities (Addis Ababa and Dire-Dawa) in its territory. In Ethiopia, 84% of the population lives in rural areas and more than 80% of the country's total population lives in the regional states of Amhara, Oromia, and SNNP(25). The number of hospitals in Ethiopia varies across regions in response to differences in population size (26).

Sample and population

All births from reproductive age women within five years before the survey in Ethiopia were the source of population, whereas all births from reproductive-age women in the selected Enumeration Areas (EAs) within five years before the survey was the study population. In EDHS, a two-stage stratified cluster sampling technique was employed using the 2007 Population and Housing Census (PHC) as a sampling frame. Stratification was achieved by separating each region into urban and rural areas. In total, 21 sampling strata have been created. In the first stage, 645 EAs (202 in urban areas) were chosen with probability sampling proportional to the size of the EAs with independent selection in each sampling stratum. In the second stage, on average 28 households were systematically selected. The detailed sampling procedure was presented in the full EDHS 2016 report (27).

126 Study variables

Outcome variables

The 2016 EDHS asked women to report any pregnancy loss that occurred in the last five years preceding the survey. The duration of pregnancy was reported for every pregnancy separately which did not result in a live birth. Pregnancy losses occurring after seven completed months of gestation were considered as stillbirth (28). The response variable for this study was the occurrence of stillbirth among mothers of childbearing age (15-49 years). The response variable for the ith mother was represented by a random variable Y_i with two possible values coded as 1 and 0. So. the response variable of the ith mother Y_i was measured as a dichotomous variable with possible values $Y_i = 1$, if ith mother had experienced stillbirth and $Y_i = 0$ if the mother had a live birth.

136 Independent variables

Consistent with the objective of the study and given the hierarchical structure of EDHS data where women were nested within the cluster/community, two levels of independent variables were considered. Level 1 contained individual socio-demographic and economic factors (age, marital status, religion, maternal education, paternal education, wealth index, maternal occupation, maternal working Status), pregnancy and pregnancy-related factors (mother's height, Body Mass Index (BMI), ANC visit, parity, preceding birth interval, contraceptive use, place of delivery, birth order, mode of delivery, wanted pregnancy, maternal anemia), and behavioral factors (smoking, and media exposure). The community-level factors; region, residence, community women education, community poverty, community media exposure, and community ANC utilization were considered as level 2 variables. In EDHS data, there is no variable collected at the cluster level except region and place of residence. Therefore, Individual-level variables were aggregated at the cluster level to generate community-level variables, to see whether cluster-level variables had an

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effect on stillbirth and were categorized as higher or lower based on national median value since it was not normally distributed. The community-level variables used in the analysis were from two sources; direct community-level variables that were used without any manipulation (residence and region), and aggregated community-level variables (community media exposure, community poverty, community ANC utilization and community women education) created by aggregating individual-level variables at the cluster level.

Data collection procedure

The study was conducted based on the 2016 EDHS data and geographic coordinate data by accessing these data from the DHS program official database www.measuredhs.com after permission was granted through an online request by explaining the objective of our study. We used the EDHS 2016 Birth Record data (BR) set for this study. Geographic coordinate data (longitude and latitude coordinates) were taken at the cluster level/enumeration area level. During the period of data collection, there was no conflict across the country. A total of 645 enumeration areas were selected and the data was collected in all of the selected EAs but the geographic coordinate file of 21 enumeration areas was wrongly recorded (the latitude and longitude were recorded as 0) and when we locate these EAs the point was located out of Ethiopia and therefore we drop the 21 EAs for the spatial analysis but for the associated factors we have used all the 645 EAs. Regarding the spatial analysis, we have done Kriging interpolation technique to predict stillbirth on the unsampled areas since it optimizes the prediction level by considering the distance decline effect (inverse distance weighting) therefore, it predicts the stillbirth prevalence on the unsampled areas located between the sampled areas where the measurement was taken. If we have done extrapolation it may prone to bias because it predicts beyond the distance limit whereas for our study we have used interpolation to predict stillbirth on the unsampled areas.

Data management and analysis

The data were weighted using sampling weight, primary sampling unit, and strata before any statistical analysis to restore the representativeness of the survey and take into account the sampling design to get reliable statistical estimates. The sampling statisticians determined how many samples are needed in each region to get reliable estimates, in EDHS, some regions were oversampled, and some regions under sampled. To get statistics that are representative of Ethiopia, the distribution of women in the sample need to be weighted (mathematically adjusted) such that it resembles the true distribution in Ethiopia by using sampling weight (v005), primary sampling unit (v021), and strata (v022). Descriptive and summary statistics were conducted using STATA version 14 software.

Spatial analysis

For the spatial analysis, ArcGIS version 10.6 software and SaTScan version 9.6 software were used. Incremental spatial autocorrelation was done to get the maximum peak distance where stillbirth clustering is more pronounced. It measures spatial autocorrelation for a series of distances and creates a line graph of those distances and their corresponding Z-score. The maximum peak distance is the distance where maximum spatial autocorrelation occurs and this was used as a distance band for hotspot analysis. Totally 10 distance bands were detected by a beginning distance of 121,803 meters, the first peak of 136,586.06 meters, and the maximum peak (clustering) was observed at 166152.17 meters. The maximum peak was used as the distance band for the hotspot analysis.

Spatial autocorrelation analysis

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The spatial autocorrelation (Global Moran's I) was done to test whether there was significant spatial clustering of stillbirth or not. Moran's I is a statistic that measures whether stillbirth patterns were dispersed, clustered, or randomly distributed in the study area (29) by taking the entire data set and produce a single output value which ranges from -1 to +1. Moran's I values close to -1indicate spatial distribution of stillbirth was dispersed, whereas Moran's I close to +1 indicate spatial distribution of stillbirth was clustered and stillbirth distributed randomly if I value is 0. A statistically significant Moran's I (p-value < 0.05) leads to rejection of the null hypothesis (stillbirth is randomly distributed) and indicates the presence of significant spatial autocorrelation/spatial dependence.

202 Hot spot analysis of stillbirth

Anselin Local Moran's I is used to investigate whether the local level cluster is positively correlated (high-high and low-low) clusters or negatively correlated (high-low and low-high) regarding the prevalence of stillbirth. A positive Moran's I value indicated that a case had neighboring cases with similar values. A negative value of Moran's I indicated that a case was surrounded by cases with dissimilar values (30). Spatial scan statistical analysis (SaTScan) using the Bernoulli model was employed to test for the presence of statistically significant spatial clusters of stillbirth using Kuldorff's SaTS can version 9.6 software. The spatial scan statistic uses a circular scanning window that moves across the study area. Women who had a stillbirth were taken as cases and those who had a live birth as controls to fit the Bernoulli model. The numbers of cases in each location had Bernoulli distribution and the model required data for cases, controls, and geographic coordinates. The default maximum spatial cluster size of <50% of the population was used, as an upper limit, which allowed both small and large clusters to be detected and ignored clusters that contained more than the maximum limit.

For each potential cluster, a likelihood ratio test statistic and the p-value was used to determine if the number of observed stillbirth within the potential cluster was significantly higher than expected or not. The scanning window with maximum likelihood was the most likely performing cluster. and the p-value was assigned to each cluster using Monte Carlo hypothesis testing by comparing the rank of the maximum likelihood from the real data with the maximum likelihood from the random datasets. The primary and secondary clusters were identified and assigned p-values and ranked based on their likelihood ratio test, based on 999 Monte Carlo replications(31). In the Bernoulli model in the SaTScan analysis, we used the Monte Carlo hypothesis testing procedure for the statistical inference of the clusters detected. Under the null hypothesis, we generate a large number of data sets by randomly permuting the locations of observations. Then, we calculate the maximum values of test statistics for each data set. In that way, we obtain empirical null distributions of the proposed test statistics. The Monte Carlo-based p-value for the detected cluster is the rank of the maximum value of the test statistics from the real data set among all data sets divided by the number of all data sets. Just Monte Carlo testing to detect whether the identified clusters are significant or not.

231 Spatial interpolation

It is very expensive and laborious to collect reliable data in all areas of the country to know the burden of a certain event. Therefore, part of a certain area can be predicted by using observed data using a method called interpolation. The spatial interpolation technique was used to predict stillbirth on the un-sampled areas in the country based on sampled EAs measurements. There are various deterministic and geostatistical interpolation methods. Among all of the methods, ordinary Kriging and empirical Bayesian Kriging are considered the best method since it incorporates the spatial autocorrelation and it statistically optimizes the weight (32). Ordinary Kriging spatial

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interpolation method was selected for this study for predictions of stillbirth in unobserved areas of
Ethiopia since it had the smallest Root Mean Square Error (RMSE) value and residuals.

241 Associated factors of stillbirth

In EDHS data, women are nested within a cluster and we expect that women within the same 242 cluster were more similar to each other than women in the rest of the country. It violates the 243 standard regression model assumptions, these are the independence of observations and equal 244 variance across clusters assumptions. This implies that the need to take into account the between 245 cluster variability by using an advanced model. Therefore, a multilevel random intercept logistic 246 regression model was fitted to estimate the association between the individual and community 247 level variables and the likelihood of experiencing stillbirth. Model comparison was done based on 248 Deviance (The negative 2 log-likelihood (-2LL)) since the models were nested. Likelihood Ratio 249 test (LR), and Intra-cluster Correlation Coefficient (ICC) were computed to measure the variation 250 251 between clusters. The ICC quantifies the degree of heterogeneity of stillbirth between clusters (the proportion of the total observed variation in stillbirth that is attributable to between cluster 252 variations) (33). 253

Multilevel random intercept logistic regression was used to analyze factors associated with a 254 255 stillbirth at two levels to take into account the hierarchical nature of the data, at individual and 256 community levels. Four models were constructed for the multilevel logistic regression analysis. The first model (a multilevel random intercept logistic regression model without covariates) was 257 258 the null model without any explanatory variables, to determine the extent of cluster variation on stillbirth. The second model (a multilevel model with level 1 independent variables) was adjusted 259 with individual-level variables; the third model (a multilevel model with level 2 variables) was 260 261 adjusted for community-level variables while the fourth model was fitted with both individual and

262 community level variables simultaneously. The final model was the best-fitted model since it had263 the lowest deviance value.

Variables with p-value ≤ 0.2 in the bi-variable analysis for both individual and community-level factors were fitted in the multivariable model. Adjusted Odds Ratio (AOR) with a 95% Confidence Interval (CI) and p-value < 0.05 in the multivariable model were used to declare significantly associated factors of stillbirth. Multi-collinearity was checked using the Variance Inflation Factor (VIF) which indicates that there is no multicollinearity because all variables have VIF<5 and tolerance greater than 0.1.

270 Patient and public involvement statement

Patients and public involvement have not happened in this study since we have conducted a secondary data analysis based on already available DHS data which was collected to provide estimates of common health and health-related indicators. For the original project data were obtained by engaging patients and public involvement statements which were essential since biomarker data such as anemia, HIV testing, and anthropometric measurements were collected (34).

277 Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of Institute of Public Health, CMHS, and the University of Gondar. Permission for data access was obtained from major demographic and health survey through an online request from <u>http://www.dhsprogram.com</u>. The data used for this study were publicly available with no personal identifier. Result

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284 Socio-demographic and economic characteristics of respondents

A total of 11,375 women who gave birth within five years preceding the survey were included for the analysis. Of 11,375 of women, 10,149 (89.2%) were rural residents, and a half (49.2%) of the respondents were aged 20-29 years. Regarding maternal education status, 7,606 (66.9%) had no formal education (Table 1).

289 Pregnancy and maternal health service-related characteristics of respondents

Two-third (65.7%) of the women gave birth at home and 194 (1.7%) gave birth via cesarean
section. Two thousand six hundred two (22.9 %) women had no ANC visit during pregnancy
(Table 2). The overall rate of stillbirth in Ethiopia was found to be 9.2 [95% CI; 7.9, 11.1] per
1000 births. It was highest in the Amhara region and lowest in Diredawa (Figure 1).

294 Spatial analysis

295 Spatial Global autocorrelation

The spatial analysis revealed that the spatial distribution of stillbirth was significantly varied across the country with Global Moran's I value of 0.017 (p < 0.05). The z-score was 2.4 indicated that there is less than 1.5% likelihood that this clustered pattern could be the result of chance (Figure 2).

300 Hotspot analysis of stillbirth

In the cluster and outlier analysis; the significant cluster was detected in Tigray, Amhara, Oromia,
Addis Ababa, SNNPR, Benishangul-Gumuz, Somali, and Gambella regions. Hot spot areas of
stillbirth were found in Southwest Somali, Southern Amhara, and West SNNPR, while the cold

spot areas of stillbirth were found in the South and West Benishangul-Gumuz, Addis Ababa,
Southwest of Oromia region, West Gambella, and Northeast SNNPR regions. The outliers were
found in the central and southern parts of Amhara, North Tigray, Southeast Gambella, and Somali
regions (Figure 3).

In the Spatial scan statistical analysis, a total of 56 significant clusters of stillbirth were identified, of which 22 clusters were primary (most likely clusters) and 34 were secondary clusters. The primary cluster spatial window was located in the Northeast Somali region centered at 7.829198 N, 43.706264 E of geographic location with a 166.48 km radius, a Relative Risk (RR) of 22.5, and a Log-Likelihood Ratio (LLR) of 13.4, at p < 0.001. It showed that women within the spatial window had a 22.5 times higher risk of experiencing stillbirth than women outside the window. The secondary cluster scanning spatial window was located in the border area of the South Amhara region and the North Oromia region, and Southern Afar region (Table 3 and Figure 4). The red circular ring indicates that the most statistically significant spatial window contains the primary cluster of stillbirth. Women within the circular window had a higher likelihood of experiencing stillbirth than women outside the spatial window (Figure 4).

319 Interpolation of stillbirth

Northwest Tigray, Northern and Northwest Oromia, East and South Amhara, East Benishangul,
East Gambella, Harari, and Northwest SNNPR were predicted as the riskiest areas of stillbirth
compared to other regions. Whereas, the predicted low-risk areas of stillbirth were identified in
Oromia, Afar, and Gambella regions (Figure 5).

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Factors associated with stillbirth

325 ICC and LR tests were checked, and the multilevel model was the best-fitted model for the data.
326 Therefore, the two-level multilevel logistic regression model was used to get an unbiased standard
327 error and to make a valid inference. Deviance was used for model comparison and the final model
328 was the best-fitted model with the lowest deviance value (Table 4).

The ICC-value was 47% in the null model, it showed that 47% of the total variability for stillbirth was attributable to the between clusters/EA variability, with the remaining 53% attributable to the individual differences (Table 4).

In the multivariable multilevel logistic regression model; residence, region, religion, preceding 332 birth interval, cesarean delivery, maternal height, ANC visit, and maternal education were 333 significantly associated with stillbirth. At the community level (level 2), two variables were 334 significantly associated with stillbirth. The odds of experiencing stillbirth among women residing 335 in rural areas were 4.83 times (AOR= 4.83, 95% CI: 1.44-16.19) higher than women residing in 336 urban areas. The odds of experiencing stillbirth among women in Tigray, Afar, Somali, SNNPR, 337 Benishangul, Gambella, and Harari regions were not significantly different from that of 338 experiencing stillbirth in the Amhara region. The odds of experiencing stillbirth among women 339 who live in the Oromia region were decreased by 75% (AOR= 0.25, 95% CI: 0.07- 0.83) compared 340 to women in the Amhara region. 341

At the individual level, six variables were significantly associated with stillbirth. Women who were protestant and catholic religious followers had 89% (AOR= 0.11, 95% CI: 0.03- 0.37) decreased odds of experiencing stillbirth than orthodox Christian religious followers. Women's educational level was significantly associated with stillbirth. Though women attained secondary education and higher had no significant difference in experiencing stillbirth, the odds of

experiencing stillbirth among women who attained primary education were decreased by 61% (AOR= 0.39, 95% CI: 0.20 - 0.74) compared to women who didn't have formal education. Besides, women who had no ANC visits during pregnancy had 2.77 times (AOR= 2.77, 95% CI: 1.70 - 4.51) higher odds of experiencing stillbirth than women who had 4 and above ANC visits during pregnancy. Women who gave birth via cesarean delivery had 5.07 times (AOR= 5.07, 95%) CI: 1.65–15.58) higher odds of experiencing stillbirth than women who gave birth through vaginal delivery.

The preceding birth interval was a significant predictor of stillbirth. Women having preceding birth interval less than 24 months had 1.93 times (AOR= 1.93, 95% CI: 1.20 - 3.10) higher odds of experiencing stillbirth compared to women having preceding birth interval 24 months and above. Besides, mothers whose height less than 150 cm had 2.73 times (AOR= 2.73, 95% CI: 1.50 -4.97) higher odds of experiencing stillbirth compared to those mothers whose height greater than 1ezz or equal to 150 cm (Table 4).

Discussion

The stillbirth rate in Ethiopia was 9.2 per 1000 births with marked spatial heterogeneity. The spatial distribution of stillbirth was significantly varied across the country. The SaTScan analysis detected a total of three statistically significant spatial windows with high stillbirth rates. The significant hotspot areas of stillbirth were identified in the Northeast Somali, South Afar, South Amhara, and North Oromia regions. The possible explanation might be due to the reason that these areas are more of pastoralist areas where people did not have permanent residence, due to this relatively health facilities are not accessible and available in these areas compared to agrarian people and cities. Besides, these areas are more rural, which had a poor network of health facilities.

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Also, this could be attributed to the disparity in the distribution of maternal health service, and the inaccessibility of infrastructure in the border areas of regions (35). Whereas, the cold spot areas of stillbirth were found in South and West Benishangul-Gumuz, Addis Ababa, Southwest of Oromia region, West Gambella, and Northeast SNNPR. This could be due to these areas are relatively had better availability and accessibility of health services (Addis Ababa, Dire-Dawa) (36). Therefore, women are more likely to use ANC and institutional delivery services, this could contribute to the decrement of antepartum and intrapartum stillbirth. This result gives insight for public health planners and programmers for designing effective public health interventions to identified hotspot areas of stillbirth.

In the multilevel analysis, different individual and community factors were significantly associated with stillbirth. Among the community level variables, it was found that the odds of stillbirth among women residing in the Oromia region were lower than in the Amhara region. This might be due to the availability and accessibility of maternal health facilities since the Oromia region is relatively around Addis Ababa and Dire-Dawa in which health facilities are accessible compared to other regions. Besides, the high turnover of health professionals in the Amhara region, particularly physicians did not remain at the district level and choose to work in the capital city (Addis Ababa). These may lead to a high intrapartum stillbirth rate in the region due to the lack of trained health professionals (37). The study has shown that the odds of stillbirth was higher among women who lived in rural areas. This was consistent with previous study findings in South Africa (38), African Great lake Regions (12), Nigeria (19), Northern Ghana (14), and Ethiopia (17). This could be attributed to the disparity in the mother's health care access seek, availability, and accessibility of health facilities. Women in urban areas are relatively had improved health-seeking behavior than rural residents (35). Moreover, urban residents have better aware of maternal health services but

in rural areas, health facilities may not be easily reachable and may end up with poor pregnancyoutcomes during emergency cases (39).

Amongst the individual-level factors, catholic and protestant religious followers were significantly associated with lower odds of stillbirth compared to orthodox religious followers. This might be related to the miss-perception of religious followers towards maternal health care service utilization as religion shapes their reproductive health decision making and practices, thereby govern the women's desire for using maternal health services (40). It could also be related to the feeding practice of women. Commonly orthodox religious followers may not eat animal products during pregnancy especially in the fasting period this could result in poor fetal outcome(41). Animal products are the main source of micro and macronutrients like folate and iron. Orthodox religious followers considered giving birth at home are blessed, using contraceptive as sinning and not expose their body to health professionals during delivery this might be the possible reason which needs further qualitative study to explore the detailed reasons.

This study noted lower odds of stillbirth among women who attained primary education compared to women who had no formal education. This finding was in line with previous studies done in Kenya (42) and Nigeria (19). It might be attributed to the reality that education can improve health care seeing behavior such as timely decision to seek health care during pregnancy, give better care for their health and their fetus, awareness of the danger sign of pregnancy, and maternal health service utilization (43).

The odds of stillbirth were higher among short stature women. A similar finding was reported in
Pakistan (21). This might be because short stature women are prone to adverse pregnancy
outcomes like Cephalo-Pelvic Disproportion (CPD), contracted pelvis, Intra-uterine Growth
Restriction (IUGR), Intra-uterine Fetal Death (IUFD), and birth injury. Short stature reflects

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longstanding malnutrition or childhood infection that start in uretro or during early childhood, this
kind of women may end up with poor pregnancy outcome unless we screen them as at-risk during
ANC follow up (44).

Besides, having no ANC visit had a significant association with increased stillbirth. It was
consistent with previous findings in low-middle income countries (45), Ghana (46), and Kenya
(42). ANC follow up could help pregnant women to seek early treatment for her potential
pregnancy-associated complications and early screening of underlying medical conditions, this
could improve birth outcome (46, 47). On the other hand, women who did not have longer ANC
follow up may not be benefited from basic ANC packages.

Consistent with studies done in Nigeria (19) and Gambia (48), caesarean deliveries in this study showed higher odds of stillbirth when compared with normal vaginal delivery. This might be because in developing countries including Ethiopia maternal health services were not available and reachable, particularly caesarean section is done at tertiary hospitals. Though caesarean section is applied to save the life of new-born in high-risk pregnancies. In Ethiopia, more than 84% of the population are rural residents and tertiary hospitals are not accessible due to transportation problems which resulting not saving the fetus's life because the caesarean section is not done at the right time. Therefore, high-risk deliveries like birth asphyxia, malpresentation, fetal stress, and Antepartum Haemorrhage (APH) that needs caesarean delivery are referred from health centers and health posts and may not reach at the right time to conduct caesarean section. This could increase the risk of stillbirth (49, 50). Overall, in Ethiopia, since the majority of pregnant women are from rural areas caesarean sections are applied too late in hospitals since most women are referred from distant health facilities.

C-section delivery is mainly done to save the life of the baby as well as the mother when the C-section has done timely but in Ethiopia, more than 84% of the population are rural residents and health care facilities are not easily accessible and available. Only the health posts and the health centers are relatively accessible and they are too far to get services from hospitals where C-section has done. So, in the real scenario in developing countries including Ethiopia, the majority of the deliveries have happened at health centers and home, when the pregnancies are complicated like (birth asphyxia, fetal distress, and APH) they referred them to the hospitals but the hospitals are not easily reachable and transportation is not easily accessible. Therefore, even if the women reach at hospital and C-section done the newborns might die because the C-section was too late since they delay the decision or transportation.

In this study, having a short inter-pregnancy interval was associated with higher odds of stillbirth.
This was consistent study findings in SSA (51), Bangladesh (52), and Amhara Region (18). This
could be explained by women who had short preceding birth interval are less able to provide
nourishment for the fetus because her body had less time to recuperate from the previous
pregnancy, and the uterus had less time to recover. Furthermore, lactation will deplete maternal
nutrition and may end up with poor pregnancy outcomes (52).

The strength of this study was using weighted data to make it representativeness at national and regional levels. Therefore, it can be generalized to all women who gave birth during the study period in Ethiopia. Moreover, the use of GIS and SaTScan statistical tests helped to detect similar and statistically significant hotspot areas of stillbirth and will help to design effective public health programs. However, the SaTScan detect only circular clusters, irregularly shaped clusters were not detected. Furthermore, the EDHS survey did not incorporate clinically confirmed data rather it

relied on mothers or caregivers verbal autopsy and might have the possibility of social desirabilityand recall bias (27).

The findings of this study have valuable policy implications for health program design and interventions. Stillbirth high-risk areas can be easily identified to make effective local interventions. In general, these findings are of supreme importance for the minister of health, regional health bureaus, and NGO's to design intervention programs to reduce stillbirth in identified hotspot areas. To reduce the overall stillbirth rate in Ethiopia, Somali, Afar, Amhara, and Oromia regions should emphasize the identified SaTScan clusters through developing local interventional strategies like improving accessibility and availability of maternal health facility.

Conclusions

In Ethiopia, stillbirth had spatial variations across the country. Statistically significant hotspot areas of stillbirth were found in the Central and Southern parts of Amhara, West SNNPRs, South and North Tigray, and Southwest Somali region. Whereas, cold spot areas were found in Addis Ababa, Central Oromia, and East SNNPRs. Short preceding birth interval, short maternal stature, ANC visit, rural residence, region, religion, maternal education, and cesarean delivery were significant predictors of stillbirth. Therefore, public health programs should target the hotspot areas of stillbirth by enhancing maternal health care service utilization, and maternal education to reduce the incidence of stillbirth in the country.

477 Abbreviations

ANC; Antenatal Care, AOR; Adjusted Odds Ratio, ARR; Annual Rate of Reduction, BMI; Body
Mass Index, CI; Confidence Interval, COR; Crude Odds Ratio, CSA; Central Statistical Agency,
DHS; Demographic Health Survey, EA; Enumeration Area, EDHS; Ethiopian Demographic

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Health Survey, GIS; Geographic Information System, ICC; Intra-cluster Correlation Coefficient, IUFD; Intra Uterine Fetal Death, IUGR; Intra Uterine Growth Restriction, LLR; loglikelihood Ratio, LR; Likelihood Ratio, PHC; Population and Housing census, SBR; Stillbirth Rate, SNNPRs; Southern Nations and Nationality People Regional state, WHO; World Health Organization.

Declarations 486

- Availability of data and materials 487
- 488 Data is available online and you can access it from www.measuredhs.com.

Competing Interests 489

Authors declare that they have no conflict of interest 490

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493 Authors' contribution

- Conceptualization: Getayeneh Antehunegn Tesema 494
- Data curation: Getayeneh Antehunegn Tesema 495
- Funding acquisition: Getayeneh Antehunegn Tesema 496
- Investigation: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 497
- Methodology: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 498
- Project administration: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 499
- Resources: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu 500

Writing – review and editing: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu

Software: Getaveneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu

Supervision: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu

Validation: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu

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Smith GC, Fretts RC. Stillbirth. The Lancet. 2007;370(9600):1715-25.

factors, and acceleration towards 2030. The Lancet. 2016;387(10018):587-603.

Why? How to make the data count? The Lancet. 2011;377(9775):1448-63.

Organization WH. Every newborn: an action plan to end preventable deaths. 2014.

Lawn JE, Gravett MG, Nunes TM, Rubens CE, Stanton C. Global report on preterm birth and

Lawn JE, Blencowe H, Waiswa P, Amouzou A, Mathers C, Hogan D, et al. Stillbirths: rates, risk

Lawn JE, Blencowe H, Pattinson R, Cousens S, Kumar R, Ibiebele I, et al. Stillbirths: Where? When?

Temmerman M, Lawn JE. Stillbirths count, but it is now time to count them all. The Lancet.

Admasu K, Haile-Mariam A, Bailey P. Indicators for availability, utilization, and quality of

Blencowe H, Cousens S, Jassir FB, Say L, Chou D, Mathers C, et al. National, regional, and

24

emergency obstetric care in Ethiopia, 2008. International Journal of Gynecology & Obstetrics.

worldwide estimates of stillbirth rates in 2015, with trends from 2000: a systematic analysis. The Lancet

stillbirth (1 of 7): definitions, description of the burden and opportunities to improve data. BMC pregnancy

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Consent for publication

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and childbirth. 2010;10(1):S1.

2018;392(10158):1602-4.

Global Health. 2016;4(2):e98-e108.

2011;115(1):101-5.

Not applicable

References

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Visualization: Getayeneh Antehunegn Tesema, Lemma Derseh, Solomon Gedlu

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Saleem S, Tikmani SS, McClure EM, Moore JL, Azam SI, Dhaded SM, et al. Trends and determinants

9.

of stillbirth in developing countries: results from the Global Network's Population-Based Birth Registry. Reproductive health. 2018;15(1):100. 10. McClure EM, Pasha O, Goudar SS, Chomba E, Garces A, Tshefu A, et al. Epidemiology of stillbirth in low-middle income countries: A Global Network Study. Acta obstetricia et gynecologica Scandinavica. 2011;90(12):1379-85. 11. Bamford L. Maternal, newborn and child health: service delivery. South African health review. 2012;2012(2012/2013):49-66. Akombi BJ, Ghimire PR, Agho KE, Renzaho AM. Stillbirth in the African Great Lakes region: A 12. pooled analysis of Demographic and Health Surveys. PloS one. 2018;13(8):e0202603. You D, Hug L, Ejdemyr S, Idele P, Hogan D, Mathers C, et al. Global, regional, and national levels 13. and trends in under-5 mortality between 1990 and 2015, with scenario-based projections to 2030: a systematic analysis by the UN Inter-agency Group for Child Mortality Estimation. The Lancet. 2015;386(10010):2275-86. Badimsuguru AB, Nyarko KM, Afari EA, Sackey SO, Kubio C. Determinants of stillbirths in Northern 14. Ghana: a case control study. The Pan African medical journal. 2016;25(Suppl 1). 15. Ogwulu CB, Jackson LJ, Heazell AE, Roberts TE. Exploring the intangible economic costs of stillbirth. BMC pregnancy and childbirth. 2015;15(1):188. Meaney S, Everard CM, Gallagher S, O'donoghue K. Parents' concerns about future pregnancy 16. after stillbirth: a qualitative study. Health Expectations. 2017;20(4):555-62. Berhie KA, Gebresilassie HG. Logistic regression analysis on the determinants of stillbirth in 17. Ethiopia. Maternal health, neonatology and perinatology. 2016;2(1):10. 18. Lakew D, Tesfaye D, Mekonnen H. Determinants of stillbirth among women deliveries at Amhara region, Ethiopia. BMC pregnancy and childbirth. 2017;17(1):375. 19. Dahiru T, Aliyu AA. Stillbirth in Nigeria: rates and risk factors based on 2013 Nigeria DHS. Open Access Library Journal. 2016;3(08):1. Ali AAA, Adam I. Anaemia and stillbirth in Kassala hospital, eastern Sudan. Journal of tropical 20. pediatrics. 2010;57(1):62-4. Badshah S, Mason L, Lisboa PJ. Risk Factors Associated with Stillbirths in Public-Hospitals in 21. Peshawar, Pakistan. The Journal of Humanities and Social Sciences. 2011;19(2):15. 22. Berhan Y, Berhan A. Perinatal mortality trends in Ethiopia. Ethiopian journal of health sciences. 2014;24:29-40. 23. Welegebriel TK, Dadi TL, Mihrete KM. Determinants of stillbirth in Bonga General and Mizan Tepi University Teaching Hospitals southwestern Ethiopia, 2016: a case-control study. BMC research notes. 2017;10(1):713. 24. Tilahun D, Assefa T. Incidence and determinants of stillbirth among women who gave birth in Jimma University specialized hospital, Ethiopia. Pan African Medical Journal. 2017;28(1). 25. Central statistical agency(CSA) I. Ethiopian Demographic and Health survey. Addis Abeba: Addis Ababa, Ethiopia, and Rockville, Maryland, USA: CSA and ICF, 2016. 26. Adugna A. Health Institutions and Services. Addis Abeba: July 2014.

- 569 27. ICF CSACEa. Ethiopia Demographic and Health Survey 2016 Addis Ababa, Ethiopia, and Rockville,
 570 maryland, USA: CSA and ICF. 2016.
- 571 28. Goldenberg RL, McClure EM, Bhutta ZA, Belizán JM, Reddy UM, Rubens CE, et al. Stillbirths: the
 7 572 vision for 2020. The lancet. 2011;377(9779):1798-805.
- 8
 9 573 29. Waldhör T. The spatial autocorrelation coefficient Moran's I under heteroscedasticity. Statistics
 10 574 in Medicine. 1996;15(7-9):887-92.
- 575 30. Tsai P-J, Lin M-L, Chu C-M, Perng C-H. Spatial autocorrelation analysis of health care hotspots in
 576 Taiwan in 2006. BMC Public Health. 2009;9(1):464.
- 14 577 31. Kulldorff M. SaTScanTM user guide. Boston; 2006.
- 1657832.Bhunia GS, Shit PK, Maiti R. Comparison of GIS-based interpolation methods for spatial17579distribution of soil organic carbon (SOC). Journal of the Saudi Society of Agricultural Sciences.185802018;17(2):114-26.
- 19
 20 581 33. Rodriguez G, Elo I. Intra-class correlation in random-effects models for binary data. The Stata
 21 582 Journal. 2003;3(1):32-46.
- 583 34. 2016. CSACEaI. Ethiopia Demographic and Health Survey 2016. Addis Ababa, Ethiopia, and
 584 Rockville, Maryland, USA: CSA and ICF. 2016.
- 25 585 35. Adugna A. Health instituition and Services in Ethiopia. 2014.
 26
- 2758636.Asefa A, Bekele D. Status of respectful and non-abusive care during facility-based childbirth in a28587hospital and health centers in Addis Ababa, Ethiopia. Reproductive health. 2015;12(1):33.
- 588 37. Assefa T, Mariam DH, Mekonnen W, Derbew M, Enbiale W. Physician distribution and attrition in
 589 the public health sector of Ethiopia. Risk management and healthcare policy. 2016;9:285.
- 590 38. Nfii FN. Levels, trends and household determinants of stillbirths and miscarriages in South Africa
 591 (2010-2014) 2017.
- 35 592 39. Babalola S, Fatusi A. Determinants of use of maternal health services in Nigeria-looking beyond
 36 593 individual and household factors. BMC pregnancy and childbirth. 2009;9(1):43.
- 37
 38
 594
 40. Tarekegn SM, Lieberman LS, Giedraitis V. Determinants of maternal health service utilization in
 39
 595 Ethiopia: analysis of the 2011 Ethiopian Demographic and Health Survey. BMC pregnancy and childbirth.
 40
 596 2014;14(1):161.
- 41
 42 597 41. Dugan B. Religion and food service. Cornell Hotel and Restaurant Administration Quarterly.
 43 598 1994;35(6):80-5.
- 44 599 42. Cheptum JJ, Oyore JP, Okello Agina BM. Poor pregnancy outcomes in public health facilities in
 45 600 Kenya. African Journal of Midwifery and Women's Health. 2012;6(4):183-8.
- 47 601 43. Ahmed S, Creanga AA, Gillespie DG, Tsui AO. Economic status, education and empowerment:
 48 602 implications for maternal health service utilization in developing countries. PloS one. 2010;5(6):e11190.
 49
- 603 44. Liselele HB, Boulvain M, Tshibangu KC, Meuris S. Maternal height and external pelvimetry to
 604 predict cephalopelvic disproportion in nulliparous African women: a cohort study. BJOG: An International
 605 Journal of Obstetrics & Gynaecology. 2000;107(8):947-52.
- McClure EM, Saleem S, Goudar SS, Moore JL, Garces A, Esamai F, et al. Stillbirth rates in lowmiddle income countries 2010-2013: a population-based, multi-country study from the Global Network.
 Reproductive health. 2015;12(2):S7.

57

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

46. Afulani PA. Determinants of stillbirths in Ghana: does quality of antenatal care matter? BMC pregnancy and childbirth. 2016;16(1):132.

47. Bhutta ZA, Darmstadt GL, Haws RA, Yakoob MY, Lawn JE. Delivering interventions to reduce the global burden of stillbirths: improving service supply and community demand. BMC pregnancy and childbirth. 2009;9(1):S7.

48. Jammeh A, Vangen S, Sundby J. Stillbirths in rural hospitals in the gambia: a cross-sectional retrospective study. Obstetrics and gynecology international. 2010;2010.

- 49. Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW, et al. Timing of elective repeat cesarean delivery at term and neonatal outcomes. New England Journal of Medicine. 2009;360(2):111-20.
- 50. Smith GC, Pell JP, Bobbie R. Caesarean section and risk of unexplained stillbirth in subsequent pregnancy. The Lancet. 2003;362(9398):1779-84.
- 51. Tolefac PN, Tamambang RF, Yeika E, Mbwagbaw LT, Egbe TO. Ten years analysis of stillbirth in a tertiary hospital in sub-Sahara Africa: a case control study. BMC research notes. 2017;10(1):447.

52. DaVanzo J, Hale L, Razzaque A, Rahman M. 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.

628	Table 1: Socio-demographic characteristics of women who gave birth within 5 years before the	e
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629 survey in Ethiopia, 2016.

Variables	Category	Unweighted frequency (%)	Weighted frequency (%)
Residence	Urban	1,994 (18.0)	1,226 (10.8)
	Rural	9,091 (82.0)	10,149 (89.2)
Region	Tigray	1,021 (9.2)	709 (6.2)
	Afar	1,102 (9.9)	119 (1.0)
	Amhara	1,004 (9.1)	2,122 (18.7)
	Oromia	2,617 (23.6)	5,280 (46.4)
	Somali	1,623 (14.6)	554 (4.9)
	Benishangul Gumuz	962 (8.7)	133 (1.2)
	SNNPR	1,334 (12.0)	2,402 (21.1)
	Gambella	789 (7.1)	29 (0.3)
	Harari	633 (5.7)	27 (0.2)
Religion	Orthodox	3,127 (28.2)	3,844 (33.8)
	Muslim	5,710 (51.5)	4,696 (41.3)
	Catholic and	2,248 (20.3)	2,835 (24.9)
	protestant	2	
Maternal	No education	7,241 (65.3)	7,606 (66.9)
education	Primary education	2,708 (24.4)	2,961 (26.0)
	Secondary and higher	1,136 (10.3)	808 (7.1)
	education		
Maternal age	<20 year	395 (3.6)	374 (3.3)
	20-29 year	5,556 (50.1)	5,599 (49.2)
	30-39 year	4,234 (38.2)	4,381 (38.5)
	≥40 year	900 (8.1)	1,021 (9.0)
Husband	No education	5,331 (51.2)	5,339 (49.6)
education	Primary education	3,260 (31.3)	4,139 (38.5)

	Secondary and higher	1,817 (17.5)	1,284 (11.9)
	education		
Maternal	Had occupation	6,584 (59.4)	6,352 (55.8)
occupation status	No occupation	4,501 (40.6)	5,023 (44.2)
Wealth status	Poor	6,081 (54.9)	5,360 (47.1)
	Middle	1,512 (13.6)	2,318 (20.4)
	Rich	3,492 (31.5)	3,697 (32.5)

- Table 2: pregnancy and health service-related characteristics of women who gave birth within 5
- 632 years preceding the survey in Ethiopia, 2016.

Variable	Category	Unweighted frequency (%)	Weighted frequency (%)
Pregnancy and mater	rnal service-related fact	ors	1
Place of delivery	Home	6,737 (60.8)	7,468 (65.7)
	Health facility	4,348 (39.2)	3,907 (34.3)
Parity	Only one birth	1,435 (13.0)	1,419 (12.5)
	2-4 birth	5,042 (45.5)	5,022 (44.1)
	\geq 5 birth	4,608 (41.5)	4,934 (43.4)
Birth order	1-3	5,806 (52.4)	5,703 (50.1)
	4-5	2,584 (23.3)	2,655 (23.4)
	≥6	2,695 (24.3)	3,017 (26.5)
BMI	Thin	2,981 (26.9)	2,483 (21.8)
	Normal	7,106 (64.1)	8,164 (71.8)
	Overweight	998 (9.0)	728 (6.4)
Maternal height	< 150 cm	1,018 (9.2)	1,228 (10.8)
	≥150 cm	10,067 (90.8)	10,147 (89.2)
ANC visit	No ANC visit	2,321 (20.9)	2,602 (22.9)
	1-3 ANC visit	1,917 (17.3)	2,145 (18.9)
	\geq 4 ANC visit	6,847 (61.8)	6,628 (58.2)

Preceding birth	< 24 month	2,347 (21.2)		2,145	5 (18.9)		
interval	≥24 month	8,738 (78.8)		9,230) (81.1)		
Maternal anemia	Not anemic	6,696 (60.4)		7,590	0 (66.7)		
	Anemic	4,389 (39.6)		3,785	5 (33.3)		
Ever use of	Yes	4,101 (37.0)		5,238	3 (46.0)		
contraceptive	No	6,984 (63.0)		6,137	7 (54.0)		
Mode of delivery	Vaginal delivery	10,813 (97.5)		11, 1	81 (98.	3)	
	Cesarean delivery	272 (2.5)		194 (1.7)		
Number of gestation	Single	10,798 (97.4)		11,07	/2 (97.3)	
	Twin	287 (2.6)		303 (2.7)		
Behavioral and commu	nity-level factors						
Smoking cigarettes	Yes	10,976 (99.0)		11,28	36 (99.2	2)	
	No	109 (1.0)		89 (0	.8)		
Media exposure	Yes	9,747 (87.9)		10,02	20 (88.1)	
	No	1,338 (12.1)		1,355	5 (11.9)		
Community media	Lower	5,503 (49.6)		4,640 (40.8)			
exposure	Higher	5,582 (50.4)		6,735	5 (59.2)		
Community poverty	Lower	6,909 (62.3)		7,617	7 (67.0))	
	Higher	4,176 (37.7)		3,758	3 (33.0)		
Community ANC	Lower	5,387 (48.6)		6,665	5 (58.6)		
utilization	Higher	5,698 (51.4)	5	4,710	0 (41.4)		
Community women	Lower	6,909 (62.3)		7,617	7 (67.0)		
education	Higher	4,176 (37.7)		3,758	3 (33.0)		

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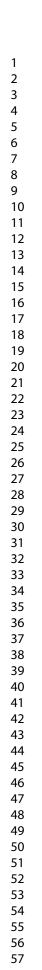
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	Fable 4: Multivariable multilevel logistic pammunity level factors approximated with			
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esidence				
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ural			3.75[1.33, 10.56]	4.83[1.44, 16.19]
egion				
mhara			1	1
igray			0.54[0.18, 1.63]	
far			0.28[0.08, 0.94]	0.24[0.05, 1.06]
romia			0.20[0.07, 0.55]	0.25[0.07, 0.83]*
omali			0.84[0.32, 2.21]	0.98[0.27, 3.56]
enishangu	ıl Gumuz		0.25[0.07, 0.92]	0.37[0.09, 1.53]
NNPR			0.21[0.06, 0.69]	0.56[0.14, 2.18]
ambella			0.26[0.06, 1.07]	1.02[0.20, 5.22]
arari			0.71[0.19, 2.63]	0.77[0.16, 3.72]
eligion				
rthodox				1
luslim	4 1	0.59[0.31, 1.12]		0.75[0.32, 1.77]
rotestant/c		0.12[0.04, 0.35]		0.11[0.03, 0.37]*
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oor		1.12[0.60, 2.11]		0.87[0.45, 1.69]
liddle		1.58[0.78, 3.19]		1.21[0.60, 2.47]
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³ Primary education		0.39[0.21, 0.75]		0.39[0.20, 0.74]**
⁴ Secondary and higher		0.49[0.18, 1.33]		0.63[0.23, 1.71]
6 education		0.17[0110, 1000]		0.00[0.20, 1., 1]
⁷ Birth order				
8 1-3		1		1
104-5		0.49[0.24, 1.03]		0.50[0.24, 1.03]
¹¹ 6 and above		0.66[0.25, 1.75]		0.66[0.25, 1.73]
¹² 13 Parity				
14 Only one birth		1		1
¹⁵ 2-4 birth		0.68[0.37, 1.28]		0.65[0.35, 1.22]
$^{16}_{17} \ge 5$ birth		0.45[0.16, 1.28]		0.42[0.15, 1.20]
17-18 ANC visit				[,.]
¹⁹ No ANC visit		2.85[1.76, 4.62]		2.77[1.70, 4.51]**
$^{20}_{21}$ 1-3 visit		1.22[0.68, 2.19]		1.11[0.62, 2.00]
21 224 and above visit		1		1
²³ Media exposure				
²⁴ ₂₅ Yes		1		1
25 26 No		2.11[0.85, 5.24]		1.63[0.66, 4.04]
²⁷ Maternal height				
$\frac{28}{29} < 150 \text{ cm}$		2.66[1.47, 4.79]		2.73[1.50, 4.97]**
$_{30}^{29} \ge 150 \text{ cm}$		1		1
³¹ Contraceptive use				
³² ₃₃ Yes		0.74[0.43, 1.26]		0.72[0.41, 1.24]
33 34 No		1		1
³⁵ Preceding birth interval				
36 <24 month		1.92[1.19, 3.07]		1.93[1.20, 3.10]**
$_{38}^{37} \ge 24$ month		1		1
³⁹ Mode of delivery				
⁴⁰ Vaginal delivery		1		1
41 42 Cesarean delivery		4.00[1.35, 11.85]		5.07[1.65, 15.58]**
⁴³ Community media exposure				
⁴⁴ Lower community exposure			1	1
$^{45}_{46}$ Higher community exposure			0.96[0.51, 1.80]	1.02[0.51, 2.04]
47 Community women's				
⁴⁸ education				
$^{49}_{50}$ Lower community education			1	1
51 Higher community education			1.28[0.61,2.71]	1.88[0.80, 4.42]
⁵² Constant	0.003[0.002, 0.005]	0.003[0.001,	0.002[0.0005,0.0096]	0.001[0.0002, 0.01]
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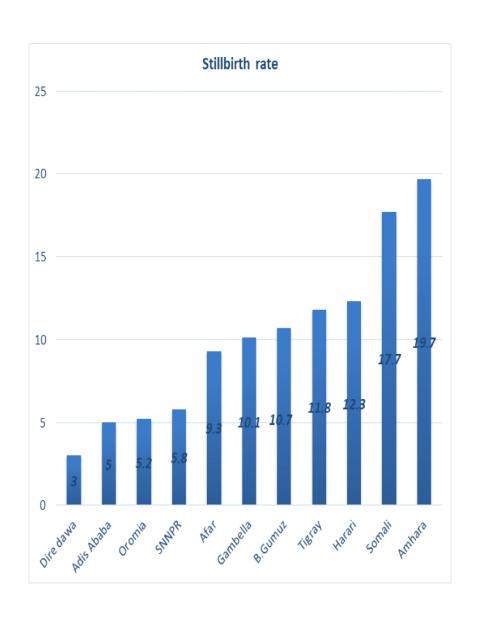
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³ Model comparison	and			
5 Random effects				
6 ICC	0.47(0.35, 0.59)			
⁷ Log-likelihood	-599.02	-551.2	-584.36	-540.50
9 Deviance	1198.04	1102.2	1168.72	1081
10 638 * <i>AOR; Adjt</i>	usted Odds Ratio, CI; Confid	dence Interval, ICO	C; Intra-class Correlat	ion
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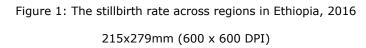
1 2		
3	640	Figure legends:
4 5 6 7	641	Figure 1: The stillbirth rates across regions in Ethiopia, 2016
7 8 9	642	Figure 2: Global spatial autocorrelation of stillbirths in Ethiopia, 2016
10 11 12	643	Figure 3: Cluster and Outlier analysis of stillbirths in Ethiopia, 2016 (Source: Central Statistical
13 14 15	644	Agency (CSA), Ethiopia, 2013)
16 17	645	Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source:
18 19 20	646	Central Statistical Agency (CSA), Ethiopia, 2013)
21 22 23	647	Figure 5: Kriging Interpolation of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency
24 25	648	(CSA), Ethiopia, 2013)
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59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

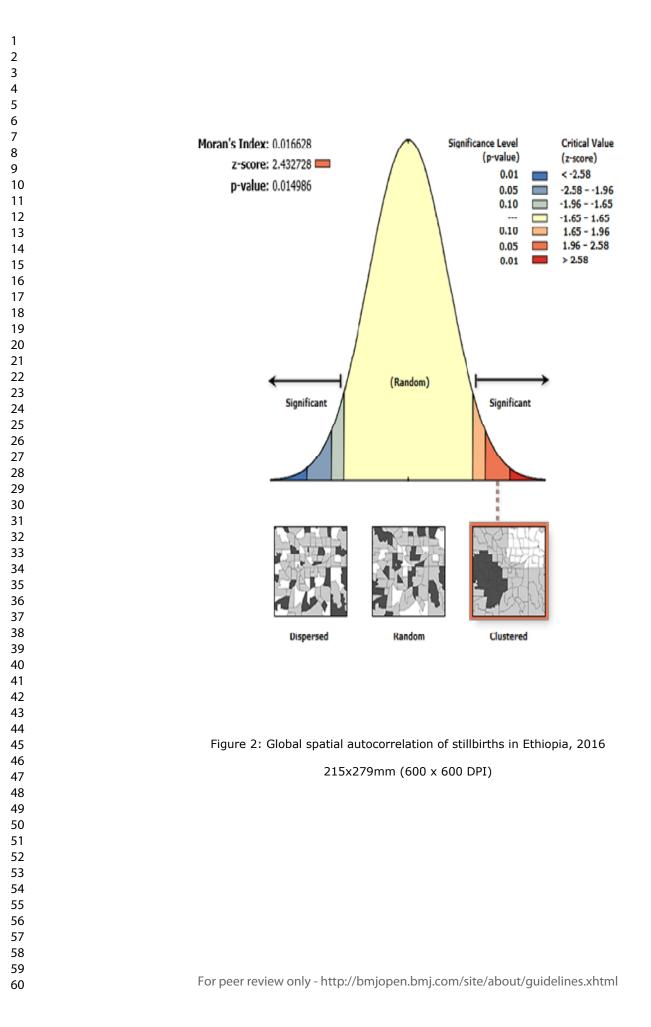


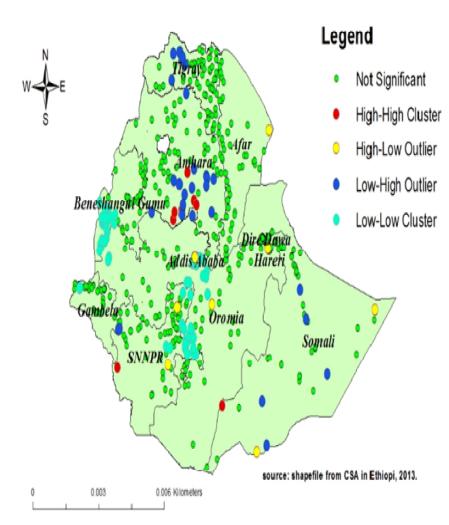


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Cluster and Outlier analysis of stillbirth accross regions in Ethiopia, 2016



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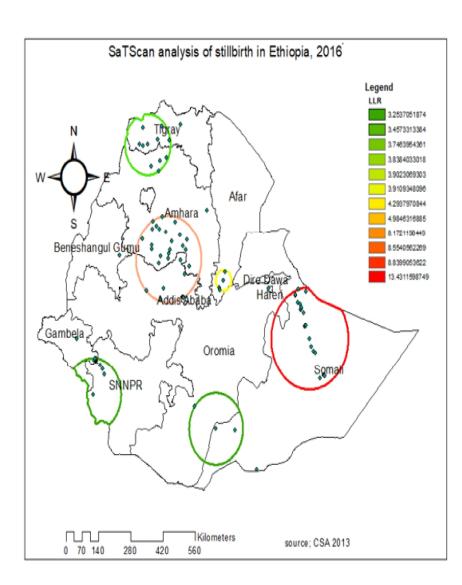
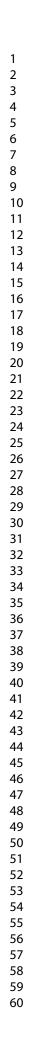
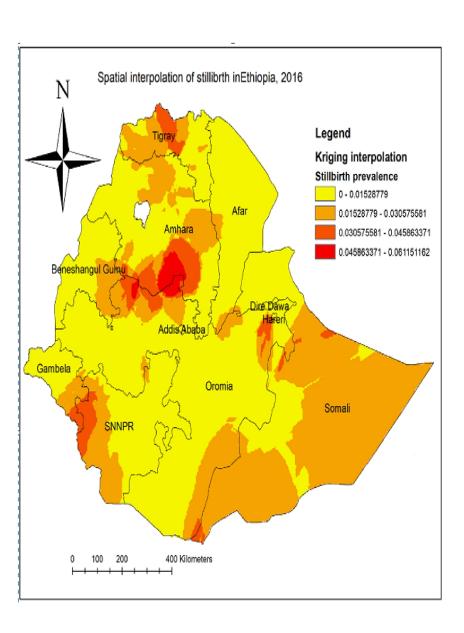
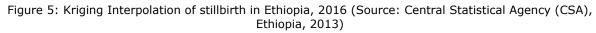


Figure 4: Spatial Scan Statistical analysis of hotspot areas of stillbirth in Ethiopia, 2016 (Source: Central Statistical Agency (CSA), Ethiopia, 2013)

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	Item No.	Recommendation	Page No.
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2&3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4, 5 \$6
Objectives	3	State specific objectives, including any pre-specified 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, 7 \$8
Participants	6	(<i>a</i>) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	N/A
		<i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls	N/A
		<i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	6 &7
		(<i>b</i>) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed	N/A
		<i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	7 & 8
Data	8*	For each variable of interest, give sources of data and details of methods of assessment	7&8
sources/measurement		(measurement). Describe comparability of assessment methods if there is more than one group	
Bias	9	Describe any efforts to address potential sources of bias	8 & 9
Study size	10	Explain how the study size was arrived at	6&7

Quantitative	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which	, 8,9,10 &11
variables		groupings were chosen and why	
Statistical	12	(a) Describe all statistical methods, including those used to control for confounding	8,9,10 &11
methods		(b) Describe any methods used to examine subgroups and interactions	N/A
		(c) Explain how missing data were addressed	10, 11
		(d) Cohort study—If applicable, explain how loss to follow-up was addressed	N/A
		Case-control study—If applicable, explain how matching of cases and controls was addressed	N/A
		<i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	8,9 &10
		(<u>e</u>) Describe any sensitivity analyses	N/A
Results		6	
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined	N/A
1		for eligibility, 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	14
		exposures and potential confounders	
		(b) Indicate number of participants with missing data for each variable of interest	15
		(c) Cohort study—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	Cohort study—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	14
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision	16 & 17
		(eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were	
		included	
		(b) Report category boundaries when continuous variables were categorized	14
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time	N/A
		period	

Continued on next page

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Other analyses	17	Report other analyses done-eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss	21
		both direction and magnitude of any potential bias	
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of	18, 19, 20,
-		analyses, results from similar studies, and other relevant evidence	21& 22
Generalisability	21	Discuss the generalisability (external validity) of the study results	21
Other informat	ion		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the	23
6		original study on which the present article is based	
		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	