

Tetanus toxoid immunization Coverage and associated factors in Ethiopia: A systematic review and meta-analysis.

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Systematic Review

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Abstract

Background: Tetanus is a bacterial disease caused by the bacterium Clostridium tetanus which is a highly fatal, non-communicable, and toxin-mediated disease. Globally, both maternal and neonatal tetanus is a public health problem due to low maternal tetanus toxoid vaccination. The main strategies for the prevention of maternal and neonatal tetanus at birth were vaccination of the mothers with a protective dose of tetanus toxoid and clean delivery. Ethiopia has the highest neonatal mortality and morbidity related to tetanus in the world due to low tetanus toxoid immunization coverage and a higher number of home-deliveries. The main aim of this systematic review and meta-analysis was to estimate the pooled tetanus toxoid immunization coverage and associated factors in Ethiopia.

Methods: The primary studies for this review were searched from PubMed/MEDLINE online, Science Direct, and Hinari databases. We retrieved 212 records; of these, 199 articles were excluded due to different reasons, and 13 studies were included in the systematic review and this meta-analysis. The data were extracted in Microsoft Excel format and exported to STATA Version 14.0 statistical software for analysis. Heterogeneity was evaluated by the I^2 test. A random-effect meta-analysis model was used to estimate the pooled coverage of two or more tetanus toxoid immunization and its associated factors. Egger's weighted regression and Begg's rank correlation test were used to assess publication bias at a 5% significance level.

Result: The pooled estimate of at least two dose of tetanus toxoid immunization coverage was 52.6% (95% CI 41.4%–63.8%). Ante-natal care (ANC) visits [OR = 7.8 (95% CI; 3.2, 19.2)], media exposure [OR = 8.3 (95% CI; 2.1, 33.3), distance from the health facility [OR = 2.635 (95% CI; 1.1, 6.6)], educational status of mothers [OR = 0.225 (95% CI; 0.105, 0.483) and husband educational status [OR = 0.184 (95% CI; 0.104, 0.323)] were significantly associated factors for tetanus toxoid immunization coverage in Ethiopia.

Conclusion: The tetanus toxoid immunization coverage among childbearing women was low in Ethiopia. Strengthening maternal health service utilization (ANC, institutional delivery) to the nearest health facility including in health posts and empowering education is recommended to increase tetanus toxoid immunization coverage. Additionally, awareness creation on the advantage of taking tetanus toxoid immunization should be emphasized.

Introduction

Tetanus is a bacterial disease caused by the bacterium Clostridium tetanus which is a highly fatal, non-communicable, and toxin-mediated disease [1, 2]. Due to unhygienic deliveries and low tetanus toxoid (TT) immunization, women and their newborns are at higher risk of acquiring tetanus [3-7]. Globally, both maternal and neonatal tetanus (MNT) is a public health problem due to low maternal TT immunization [8]. Annually, 3.3 million neonatal deaths occur, of which neonatal tetanus shares a high number particularly in developing countries where home delivery is common [9]. Every year 15,000–30, 000 maternal deaths occurred due to tetanus related to the delivery process [10]. The WHO report showed that 90% of maternal and neonatal tetanus occurred in South East Asian (SEA) and Sub-Saharan African (SSA) countries, and almost all cases ended with death [11].

The main strategies for the prevention of maternal and neonatal tetanus (MNT) at birth were vaccination of the mothers with a protective dose of tetanus toxoid (TT) immunization and clean delivery [3, 12, 13]. Nearly 94% of

neonatal mortality related tetanus can be reduced through the immunization of pregnant women or women of childbearing with at least two doses of tetanus toxoid immunization (TT²⁺) [14]. The World Health Organization (WHO) recommends 5 consecutive doses of tetanus toxoid (TT) vaccination for childbearing women (CBAW) per schedule to protect the birth against tetanus [1].

In many countries, at least two doses of the TT vaccination can be given to pregnant women during antenatal care (ANC) visits [15]. TT²⁺ immunization coverage among pregnant mothers ranges from India 27% [16] to Ghana 71% [17]. It could be concluded that most countries could not reach the WHO Global Immunization target of at least 90% of national TT vaccination coverage and at least 80% of TT vaccination coverage in every district [18, 19].

Previous studies identified factors such as age of the mothers, educational status, marital and occupational status, joint health decision with husband, distance from health facilities, wealth index, fear of side effects, fear of sterility, ANC follow-up, use of modern family planning, parity, information about TT vaccination, knowledge, attitude and awareness of mothers towards TT vaccination for low TT immunization coverage [14, 16, 18, 20-23]. TT immunization status also differs from urban to rural mothers as well as region to region in different countries [24, 25].

Despite the country's effort of interventional policy to meet the WHO goals towards Maternal and Neonatal Tetanus Elimination (MNTE) through extended immunizations and campaigning of Tetanus Toxoid, Ethiopia continues to have the highest neonatal tetanus mortality and morbidity in the world due to low TT immunization coverage and a higher number of home-deliveries [26, 27]. Although, the country was planned to reach 86% coverage of the national tetanus protective at birth (PAB) by 2015, only 49% of the pregnant mothers received at least two dose of tetanus toxoid vaccination as of the EDHS 2016 report [27, 28].

Different independent and fragmented studies have been conducted to assess TT immunization coverage in Ethiopia despite their reports showing great disproportion across the region in the country. Thus, reliable and summarized information is essential to refine government policies, strategies, and interventions. Hence, the main aim of this systematic review and meta-analysis was to estimate the pooled coverage of at least two dose of tetanus toxoid immunization and associated factors in Ethiopia. Therefore, this review can have vital importance to show summarized evidence and suggest possible applicable strategies for planning, decision making, and resource allocation in the health care system of Ethiopia.

Methods

Identification and selection of studies

Published and unpublished research reports describing tetanus toxoid immunization coverage and associated factors in Ethiopia were reviewed. Relevant studies were searched from PubMed/MEDLINE online, Science Direct, and Hinari databases. Gary literature was also identified from Google and Google Scholar. All searches were conducted from July 1st to August 25th/2020. The term 'tetanus toxoid' was searched in different variations such as tetanus toxoid immunization coverage/utilization/, protective dose of tetanus toxoid immunization, tetanus toxoid immunization status, tetanus toxoid vaccination uptake, and protection of last live birth against neonatal tetanus. The key terms used to retrieve primary studies were (Utilization OR coverage OR vaccination uptake OR immunization status AND (Tetanus toxoid) AND Ethiopia). We also used key terms of (Factors OR determinants

OR risk factors OR correlates) AND (Tetanus toxoid) AND Ethiopia to search literature regarding factors associated with the utilization of tetanus toxoid immunization in Ethiopia. Data were extracted from reports of articles. All literature available until August 25, 2020, was identified and evaluated for their eligibility to be included in the systematic review and meta-analysis using prepared eligibility assessment criteria. The systematic review and meta-analysis were carried out in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines [29].

Eligibility criteria

Observational studies with original data reporting the coverage of TT²⁺ immunization and its associated factors conducted in Ethiopia from 2010-2020 were included. In this review, we included articles published in English. Studies that had unclear outcomes and poor quality were excluded. Qualitative studies were not included in this meta-analysis. Regarding publication, both published and unpublished articles were included in this review.

Data extraction

We used a standardized data extraction format prepared in Microsoft Excel to extract all the necessary data. The extraction format contains different columns including the name of the first author, publication year, region of the country where the study was conducted, sample size, response rate, and coverage of TT²⁺ immunization for the first objective. For the second objective (factors associated with TT²⁺ immunization), the data extraction format was prepared in the form of a two -by- two table.

Outcome measurements

This study has two main objectives. The first objective was the pooled coverage of TT²⁺ immunization in Ethiopia. The second objective was the factors associated with TT²⁺ immunization. The utilization of TT²⁺ vaccination was calculated by dividing the number of mothers ever taking at least two dose of TT by the total number of mothers who were included in the study and multiplied by one hundred (100). For the second objective, the odds ratio was used to measure the level of the association between TT²⁺ immunization coverage and its associated factors. The odds ratio was calculated from primary studies using two by two tables.

Quality assessment

The qualities of primary studies were assessed using the Newcastle-Ottawa Scale [30]. The tool has three main parts. The first part has five components used to assess the methodological quality of each study. The second part assesses the comparability of primary studies, and the final part of the tool measures the quality of the original articles concerning their statistical analysis. Two authors independently evaluated the qualities of original articles by using quality assessment guidelines, and articles with high quality (a minimum score of 6 out of 10 scores) were included in this review. Any difference between the two authors during the quality assessment of primary studies was solved by taking the average of the two assessment scores.

Statistical procedure

The extracted data from the Microsoft Excel format were exported to STATA Version 14.0 (software) for analysis. The characteristics of the original articles were described using a table as well as a forest plot. Statistical heterogeneity was evaluated by the I² test, which shows the level of heterogeneity between studies [31]. The

percentage of variability due to heterogeneity rather than sampling error or chance in effect estimate was determined through the I^2 test. Basically, the I^2 test does not depend on the number of studies incorporated into the study. A random-effect meta-analysis model was used to estimate the pooled utilization of TT²⁺ immunization and its associated factors. The pooled effect size was conducted in the form of prevalence and odds ratio. Furthermore, we also employed a leave-one-out sensitivity analysis to identify the possible source of heterogeneity in the pooled meta-analysis. Subgroup analysis was also performed by a region where the study was conducted to minimize the random variations in the point estimates of the primary studies. Egger's weighted regression and Begg's rank correlation test were used to assess publication bias at a 5% significance level [32, 33]. P<0.05 was considered statistically significant publication bias.

Results

Search results

There were a total of 212 primary records retrieved during the literature search from the Midline/PubMed, Hinari, Science Direct, Google, and Goole Scholar databases. Approximately 79 articles were excluded due to duplication, and 102 studies were also excluded after reviewing their titles and abstracts as we found these articles as unrelated to our objective. Then, the remaining 31 articles were assessed by reading their full-text text based on the criteria. After the full-text review, 18 articles were further excluded due to the difference in the study population and outcome. Finally, 13 primary studies were included in this meta-analysis (**Fig.1**).

Characteristics of the included articles

In this review, 13 primary studies with a total of 13,731 study participants were included. The studies were conducted from 2010 to 2020 and were retrieved from five regions of the country: 4 from the southern region, 3 from Amahara, 3 from Oromia, 1 from Tigray, 1 from Somalia, and another study was based on EDHS data [34-46]. All of these studies included in this review were community-based cross-sectional studies with sample sizes ranging from 239 to 7193 participants as reported from studies done in Bahir Dar and studies from EDHS data respectively[34, 39]. Six studies were conducted in urban area and the other six were conducted in rural area. The highest coverage of TT²⁺ immunization was reported from Debre Tabor town in the Amhara region 79.0%[39], and the least was from the Meinit-Shasha district in the southern region 13.9%[41] (**Table 1**).

Table 1: Summary of included studies in the systematic review and meta-analysis of tetanus toxoid immunization status and factors associated in Ethiopia 2020

Author	publication year	place	region	Sample size	outcome	Response rate	Prevalence	prev	study desgin
Kalayu et al	2020	countrywide		7193	2990	100	0.416	41.6	multilevel analysis
Wolde Facha et al	2018	Duguna Fango	south	462	228	100	0.494	49.4	cross-sectional
Kenea A, et al.	2016	Ilu Aba Bora	oromia	779	310	100	0.398	39.8	cross-sectional
Mamoro et al	2018	kembata	south	837	607	99	0.725	72.5	cross-sectional
Gebremedhin et al	2020	Errer	somali	440	228	98	0.518	51.8	cross-sectional
Belihu KD et al.	2017	Debre birhan	Amhara	408	311	96.6	0.762	76.2	cross-sectional
Edossa Adugna	2011	Ambo	oromia	680	499	100	0.734	73.4	cross-sectional
Wolderuafael	2018	Meinit-Shasha	south	639	89	98.1	0.139	13.9	cross-sectional
Mihret et al	2018	DebreTabor	Amhara	511	377	100	0.79	79	cross-sectional
Anatea et al	2018	Dukem	oromia	416	163	98.6	0.392	39.2	cross-sectional
Mengesha et al.	2020	Hawzen	Tigray	515	207	100	0.402	40.2	cross-sectional
Zeine A. et al	2010	Hadiya	south	612	457	86.2	0.747	74.7	cross-sectional
Walle et al	213	Bahir Dar	Amhara	239	76	100	0.315	31.5	cross-sectional

Meta-analysis

The pooled estimate of at least two dose of tetanus immunization coverage in Ethiopia was 52.6% (95% CI 41.4%–63.8%). High heterogeneity was observed between studies ($I^2 = 99.1\%$ and $P \leq 0.01$) (**figure 2**). As a result, a random effect model was conducted to estimate the pooled coverage of TT²⁺ immunization among Ethiopian mothers. Publication bias was checked using Egger's test ($p = 0.271$), which showed that there was no significant publication bias. We also observed the symmetrical distribution of the funnel plot indicating the absence of publication bias (**figure 3**). Furthermore, we also conducted a leave-one-out sensitivity analysis to identify the possible source of heterogeneity in the pooled meta-analysis. The results of the test showed that the pooled coverage of TT²⁺ immunization ranges between 50.4% (39.2 – 61.5) and 54.4% (42.6 – 66.0). This indicates that the result of the review was strong and not dependent on the addition or removal of a single study from the analysis (**Table-2**). We also performed subgroup analysis by a region having more than two studies conducted. According to the results, the highest tetanus toxoid immunization coverage was in the Amhara region, 62.3% (95% CI: 37.1, 87.6), $I^2 = 99.0\%$ and the lowest was in the Oromia region 50.8% (95% CI: 27.3, 74.3), $I^2 = 89.2$ (**figure 4**). This meta-analysis also revealed that the pooled coverage of two or more TT immunization was

slightly higher in urban women (56.7 %, (95% CI; 40.2, 73.1)) than in rural urban women 49.0% (95% CI; 34.4, 63.7) (**Figure 5**).

Table 2:- Sensitivity analysis of tetanus toxoid immunization and associated factors in Ethiopia, 2020

	Utilization	95% confidence interval
Kalayu et al 2020	53.5	39.7- 67.2
Wolde Facha et al 2018	52.8	40.9 - 64.8
Kenea A, et al. 2016	53.7	41.5 - 65.7
Mamoro et al 2018	50.9	39.5 - 62.4
Gebremedhin et al 2020	52.6	40.7 - 64.6
Belihu KD et al. 2017	50.6	39.2 - 62.0
Edossa Adugna 2011	50.8	39.4 - 62.3
Wolderufael 2018	55.8	45.6 - 66.0
Mihret et al 2018	50.4	39.2 - 61.5
Anatea et al 2018	53.7	41.8 - 65.6
Mengesha et al. 2020	53.6	41.7 - 65.6
Zeine A. et al 2010	50.7	39.3 - 62.1
Walle et al 213	54.3	42.6 - 66. 0

Factors associated with tetanus toxoid immunization coverage

During the review, we identified numerous factors associated with tetanus toxoid immunization coverage among primary studies. Variables reported as a significant association in at least three primary studies were included in this meta-analysis. Accordingly, antenatal care (ANC) visits, media exposure, distance from the health facility, and educational status of mothers as well as their husbands were found to have a significant association with the coverage of tetanus toxoid immunization in Ethiopia.

Antenatal care (ANC) follow-up during pregnancy was identified as a factor for tetanus toxoid immunization among Ethiopian mothers among six primary studies included in the review [34, 38, 40, 42-44]. A total of 9755 study participants were included to analyze the association between ANC visits and tetanus toxoid immunization. Mothers having ANC visits during the last pregnancy were 7.8 times more likely to receive two or

more dose of tetanus toxoid immunization compared to their counterparts [OR = 7.8 (95% CI; 3.2, 19.2)] (**Figure 6**).

Three primary studies included in our meta-analysis reported that media exposure (TV, radio) was significantly associated with TT²⁺ immunization [34, 40, 43]. To see the association between media exposure and tetanus toxoid vaccination coverage, 8,289 study participants were included in the analysis. Accordingly, at least two dose of tetanus toxoid immunization among women having media exposure was 8.3 times higher than women having no media exposure [OR = 8.3 (95% CI; 2.1, 33.3)] (**Figure 7**).

Distance from home to health facility was identified as a factor associated with two or more tetanus toxoid immunization among three primary studies with a total of 1933 study participants [38, 43, 44]. Women who walked less than 1 hour to reach health facilities were 2.6 times more likely to take tetanus toxoid immunization than mothers who walked greater than or equal to 1 hour to reach the health facility [OR = **2.635** (95% CI; **1.1, 6.6**)] (**Figure 8**).

The educational status of the mothers was significantly associated with tetanus toxoid immunization coverage among five primary studies included in our analysis [37, 38, 40, 42, 43]. A total of 2884 mothers were included in the analysis to examine the association of the educational status of the mothers and tetanus toxoid immunization. Mothers who had never attended formal education were 77.5% less likely to receive two or more doses of TT injection than educated mothers [OR = 0.225 (95% CI; 0.105, 0.483)] (**Figure 9**).

Three primary studies reported that the husband's educational status was associated with receiving two or more dose of tetanus toxoid immunization with a total sample of 1957 mothers [37, 38, 40]. Accordingly, women whose husbands had no formal education were 81.6% less likely to receive two or more tetanus toxoid immunization as compared to women having educated husbands [OR = 0.184 (95% CI; 0.104, 0.323)] (**Figure 10**).

Discussion

Neonatal and maternal tetanus is still a major public health problem especially in developing countries, but can be easily prevented through immunization of childbearing women with at least two dose of tetanus toxoid immunization. This systematic review and meta-analysis was conducted to show the pooled coverage of two or more dose of tetanus toxoid immunization and associated factors in Ethiopia. To the best of our knowledge, this is the first systematic review and meta-analysis in Ethiopia.

In this meta-analysis, the pooled coverage of tetanus toxoid immunization at least two dose was 52.6% (95% CI 41.4, 63.8). This finding was consistent with a report from studies conducted in Kenya 52.0% and Pakistan 55.6% [18, 47]. It was low compared to studies conducted in different developing countries such as Ghana 71% [48], India 68% [16], and Sierra Leone 82.1% [49]. The possible explanation for this difference might be due to geographical differences, sociocultural variation and maternal and child health service utilization.

However, the pooled coverage of at least two dose of tetanus toxoid immunization in this meta-analysis was higher compared to reports of studies conducted in Rivers State, Nigeria 37.1% [50] and Nigeria 40.8% [51]. The reason for this difference might be due differences in sociocultural characteristics, knowledge, attitudes, and awareness of mothers toward immunization. The other explanation for this difference may be the difference in the educational status of the mothers and their husbands.

This meta-analysis also identified different associated factors for tetanus toxoid immunization. Accordingly, ANC visits, media exposure, distance of health facilities, educational status of mothers, and their husbands were significantly associated with tetanus toxoid immunization status among women in Ethiopia. Tetanus toxoid immunization coverage was 7.8 times higher among mothers attending ANC follow-up compared to their counterparts. This finding was supported by studies conducted in Kenya [21] and Pakistan [18]. Tetanus toxoid immunization was one component of ANC and counselling about the importance of TT immunization and other services during pregnancy.

Women who had media exposure were 8.3 times more likely to receive two or more dose of tetanus toxoid immunization than women who had no media exposure. A similar finding was reported from a study conducted in Indonesia [52]. The possible explanation for the association of media exposure with tetanus toxoid immunization might be that media may provide important information that can increase women's knowledge of the advantage of tetanus toxoid immunization. The odds of receiving two or more tetanus toxoid immunization was 2.6 times higher among women walking less than 1 hour to reach health facility than among women walking more than 1 hour to reach the nearest health facility. This might be because women in the household are responsible for multiple tasks that make them busy to receive tetanus toxoid immunization since TT vaccination requires repeated visits to health facilities.

Uneducated women in this meta-analysis were 77.5% less likely to immunize at least two dose of tetanus toxoid vaccine than educated women. This is consistent with studies conducted in Bangladesh [53] and France [54]. This could be because education increases women's knowledge, attitude, and awareness regarding the health benefit of tetanus toxoid immunization. Similarly, women having an educated husband were 81.6% more likely to receive two or more tetanus toxoid immunization than women having an illiterate husband. This might be because educated husbands have better knowledge and awareness of the advantage of TT immunization that could push their wives to take tetanus toxoid immunization. Furthermore, educated husbands may give more freedom to their wives to receive tetanus toxoid vaccination compared to non-educated husbands.

Limitation of the study

The limitation of this systematic review and meta-analysis was that all included primary studies were cross-sectional study designs which made it difficult to establish cause-effect relationships.

Conclusion

This systematic review and meta-analysis showed that tetanus toxoid immunization coverage among childbearing age women in Ethiopia was low compared to the WHO global immunization target. It was higher in urban than rural women. Absence of ANC visits, no media exposure, distant health facilities, and low educational status were factors for low coverage for tetanus toxoid immunization. Strengthening maternal health service utilization such as ANC to the nearest health facility including in health posts is recommended to increase the coverage of tetanus toxoid immunization. Great emphasis on awareness creation about the advantage of taking tetanus toxoid immunization through media and education should be given.

Declarations

Ethics approval

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The data used for this study are available here. It will be shared upon request and will be obtained by email to the corresponding author using “nigussiejemberu@gmail.com. Or jemberu2123@gmail.com”.

Competing interests

All authors declare that they have no competing interests.

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Authors' contributions

JN and BG conceived the idea, participated in data extraction, analysis, and draft writing. AM and MM participated in the analysis, manuscript preparation, and revision. All authors read and approved the final version of the manuscript to be considered for publication.

References

1. Organization WH: Weekly Epidemiological Record, 2006, vol. 81, 47 [full issue]. *Weekly Epidemiological Record Relevé épidémiologique hebdomadaire* 2006, 81(47):445-452.
2. Thwaites C, Farrar J: Preventing and treating tetanus: The challenge continues in the face of neglect and lack of research. In.: British Medical Journal Publishing Group; 2003.
3. World Health Organization: . Protection at birth (PAB) against tetanus. In: Global Health Observatory data; 2015. In.
4. UNICEF.: State of the World's Children: Celebrating 20 Years of the Convention on the Rights of the Child: Unicef; 2009.
5. WHO U: Review of national immunization coverage 1980-2002 (India). *New Delhi: WHO/UNICEF* 2003.
6. Roper MH, Vandelaer JH, Gasse FL: Maternal and neonatal tetanus. *The Lancet* 2007, 370(9603):1947-1959.
7. Rec WE, Organization WH: Tetanus vaccine. WHO Position Paper. 2006.
8. Demicheli V, Barale A, Rivetti A: Vaccines for women for preventing neonatal tetanus. *Cochrane Database of Systematic Reviews* 2015(7).
9. WHO: Maternal and Neonatal Tetanus Elimination the Initiative and Challenges Why Maternal and Neonatal Tetanus Elimination. 2017.
10. WHO U: World Bank. State of the world's vaccines and immunization. Geneva: World Health Organization; 2009. In.; 2017.

11. World Health Organization: Maternal and neonatal tetanus (MNT) elimination-the initiative and challenges. *Immun Vaccin Biol.* 2015;21:1–2. In.
12. Expanded Programme on immunization Ethiopia. Ethiopia Country Office; 2014. <http://www.who.int/countries/eth/> areas/immunization/en/. World Health Organization, .
13. Blencowe H, Lawn J, Vandelaer J, Roper M, Cousens S: Tetanus toxoid immunization to reduce mortality from neonatal tetanus. *International journal of epidemiology* 2010, 39(suppl_1):i102-i109.
14. Khan REA, Raza MA: Maternal health-care in India: The case of tetanus toxoid vaccination. *Asian Development Policy Review* 2013, 1(1):1-14.
15. Donken R, van der Maas N, Swaan C, Wiersma T, te Wierik M, Hahné S, de Melker H: The use of tetanus post-exposure prophylaxis guidelines by general practitioners and emergency departments in the Netherlands: a cross-sectional questionnaire study. *BMC Family Practice* 2014, 15(1):112.
16. Singh A, Pallikkadavath S, Ogollah R, Stones W: Maternal tetanus toxoid vaccination and neonatal mortality in rural north India. *PLoS one* 2012, 7(11):e48891.
17. S. K. Diamenu GB, F. Abotsi et al, : S. K. Diamenu, G. Bosnu, F. Abotsi et al., "Introducing protection at birth method of monitoring tetanus-diphtheria vaccination coverage of mothers in Ghana," *International Journal of Vaccines and Immunization*, vol. 1, no. 1, 2015.
18. Naeem M, Khan MZ-U-I, Abbas SH, Adil M, Khan A, Naz SM, Khan MU: Coverage and factors associated with tetanus toxoid vaccination among married women of reproductive age: a cross sectional study in Peshawar. *Journal of Ayub Medical College Abbottabad* 2010, 22(3):136-140.
19. WHO/FMOH: Vaccinators Guide for Maternal & Neonatal Tetanus Elimination Campaign in Ethiopia, 2002.
20. Hashmi FK, Islam M, Khan TA, Tipu MK: Vaccination coverage of mothers during pregnancy with tetanus toxoid and infants after Birth. *Pakistan J Pharmacy* 2011, 24(2):1-3.
21. Haile ZT, Chertok IRA, Teweldeberhan AK: Determinants of utilization of sufficient tetanus toxoid immunization during pregnancy: evidence from the Kenya demographic and health survey, 2008–2009. *Journal of community health* 2013, 38(3):492-499.
22. JSI: An Extended Programme on Immunization Coverage in Selected Ethiopia Zones a Baseline Survey for L10 kms Routine Immunization Improvement Initiative, JSI, Boston, MA, USA, 2015. .
23. Masuno K, Xaysomphoo D, Phengsavanh A, Douangmala S, Kuroiwa C: Scaling up interventions to eliminate neonatal tetanus: factors associated with the coverage of tetanus toxoid and clean deliveries among women in Vientiane, Lao PDR. *Vaccine* 2009, 27(32):4284-4288.
24. Tesfahun F, Worku W, Mazengiya F, Kifle M: Knowledge, perception and utilization of postnatal care of mothers in Gondar Zuria District, Ethiopia: a cross-sectional study. *Maternal and child health journal* 2014, 18(10):2341-2351.
25. Abdella A: Maternal mortality trend in Ethiopia. *Ethiopian Journal of Health Development* 2010, 24(1).
26. Maima W, Ephantus M, Kabiru E: Utilization of antenatal TT immunization services among women in Bahati division, Naku country Kenya. *International of innovative research and studies* 2014, 3(9).
27. ICF C: Ethiopian Demographic and Health Survey Addis Ababa. *Ethiopia, and Rockville, Maryland, USA* 2016.
28. Federal Democratic Republic of Ethiopia Ministry of Health: Health Sector Development Programme IV 2014. In.

29. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, Clarke M, Devereaux PJ, Kleijnen J, Moher D: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *Journal of clinical epidemiology* 2009, 62(10):e1-e34.
30. Peterson J, Welch V, Losos M, Tugwell P: The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. *Ottawa: Ottawa Hospital Research Institute* 2011.
31. Rücker G, Schwarzer G, Carpenter JR, Schumacher M: Undue reliance on I² in assessing heterogeneity may mislead. *BMC medical research methodology* 2008, 8(1):79.
32. Sterne JA, Egger M: Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. *Journal of clinical epidemiology* 2001, 54(10):1046-1055.
33. Egger M, Smith GD, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. *Bmj* 1997, 315(7109):629-634.
34. Kalayu G, Fisseha G, Shamie R, Berhe A, Embaye K: Factors Associated with Protection of Last Live Birth against Neonatal Tetanus among Mother Age 15-49 in Ethiopia: A Multilevel Analysis Using EDHS 2016. 2020.
35. Facha W, Yohannes B, Duressa G: Tetanus Toxoid Vaccination Coverage and Associated Factors among Pregnant Women in Duguna Fango District, Southern Ethiopia. *International Journal of Health Sciences and Research* 2018, 8(1):148-154.
36. Kenea A, Oljira D, Tesfa B, Abamecha A: Assessment of Protection at Birth of Tetanus Toxoid Immunization and Associated Risk Factors in Ilu Aba Bora Zone Southwest, Ethiopia. *Int J Vaccine Immunizat* 2016, 2(3).
37. Dubale Mamoro M, Kelbiso Hanfore L: Tetanus toxoid immunization status and associated factors among mothers in Damboya Woreda, Kembata Tembaro zone, SNNP, Ethiopia. *Journal of nutrition and metabolism* 2018, 2018.
38. Gebremedhin TS, Welay FT, Mengesha MB, Assefa NE, Werid WM: Tetanus Toxoid Vaccination Uptake and Associated Factors among Mothers Who Gave Birth in the Last 12 Months in Errer District, Somali Regional State, Eastern Ethiopia. *BioMed Research International* 2020, 2020.
39. Belihu K, Tesso F, Woldetsadik T: Dropout Rate of Tetanus Toxoid Immunization and Associated Factors among Reproductive Age Group of Women in Debrebirhan Town, Amhara Region, Northern Ethiopia. *J Women's Health Care* 2017, 6(390):2167-0420.1000390.
40. Adugna E: factors influencing tetanus toxoid immunization and protection at birth coverage among child bearing age women of Ambo town and its surrounding area. *Ethiopia: Oromia regional state* 2011.
41. Wolderuafel TS: Factors Influencing Antenatal Care Service Utilization Among Pregnant Women in Pastoralist Community in Menit-Shasha District, Ethiopia. *International Journal of Medical Research & Health Sciences* 2018, 7(5):143-154.
42. Mihret MS, Limenih MA, Gudayu TW: The role of timely initiation of antenatal care on protective dose tetanus toxoid immunization: the case of northern Ethiopia post natal mothers. *BMC pregnancy and childbirth* 2018, 18(1):235.
43. Anatea MD, Mekonnen TH, Dachew BA: Determinants and perceptions of the utilization of tetanus toxoid immunization among reproductive-age women in Dukem Town, Eastern Ethiopia: a community-based cross-sectional study. *BMC international health and human rights* 2018, 18(1):27.

44. Mengesha MB, Weldegeorges DA, Assefa NE, Gebremeskel SG, Hidru HD, Teame H, Hailesilassie Y: Tetanus Toxoid Immunization Status and Associated Factors among Mothers in Hawzen, Eastern Zone of Tigray, Ethiopia, 2019. *The Open Public Health Journal* 2020, 13(1).
45. Walle1 F, and Mekibib Kassa: Coverage and factors associated with tetanus toxoid vaccination among private college students, Bahirdar, Ethiopia, July 29-31, 2013 Embassy Suites Las Vegas, NV, USA 2013.
46. Abosse Z, Woldie M, Ololo S: Factors influencing antenatal care service utilization in hadiya zone. *Ethiopian Journal of Health Sciences* 2010, 20(2).
47. Kilowua LM, Otieno KO: Health System Factors Affecting Uptake of Antenatal Care by Women of Reproductive Age in Kisumu County, Kenya. *International Journal of Public Health* 2019, 5(2):119-124.
48. S. K. Diamenu GB, F. Abotsi et al, : "Introducing protection at birth method of monitoring tetanus-diphtheria vaccination coverage of mothers in Ghana," International Journal of Vaccines and Immunization, vol. 1, no. 1, 2015.
49. Yaya S, Kota K, Buh A, Bishwajit G: Prevalence and predictors of taking tetanus toxoid vaccine in pregnancy: a cross-sectional study of 8,722 women in Sierra Leone. *BMC Public Health* 2020, 20:1-9.
50. Gabriel-Job N, Ide LY: Tetanus Toxoid Status and Determinants of Uptake among Women in Etche Local Government Area, Rivers State, Nigeria: A Community Based Study. *Asian Journal of Medicine and Health* 2019:1-7.
51. Adeiga A, Omilabu S, Audu R, Sanni F, Lakehinde G, Balogun O, Olagbaju O: Tetanus toxoid immunization coverage among mothers of below one year of age in difficult-to-reach area of Lagos Metropolis. *African Journal of Clinical and Experimental Microbiology* 2005, 6(3):233-237.
52. Roosihermiatie B, Nishiyama M, Nakae K: Factors associated with TT (tetanus toxoid) immunization among pregnant women, in Saparua, Maluku, Indonesia. *Southeast Asian journal of tropical medicine and public health* 2000, 31(1):91-95.
53. Mohammad M: Determinants of the utilization of the tetanus toxoid (TT) vaccination coverage in Bangladesh: evidence from a Bangladesh demographic health survey 2004. *The Internet Journal of Health* 2008, 8.
54. Guthmann J, Fonteneau L, Antona D, Lévy-Bruhl D: Factors associated with tetanus vaccination coverage in adults in France and with knowledge of vaccination status. *Medecine et maladies infectieuses* 2010, 40(10):560-567.

Figures

212 Records identified through searching PubMed, science direct, Google and Google scholar published in English from 2010 to 2020

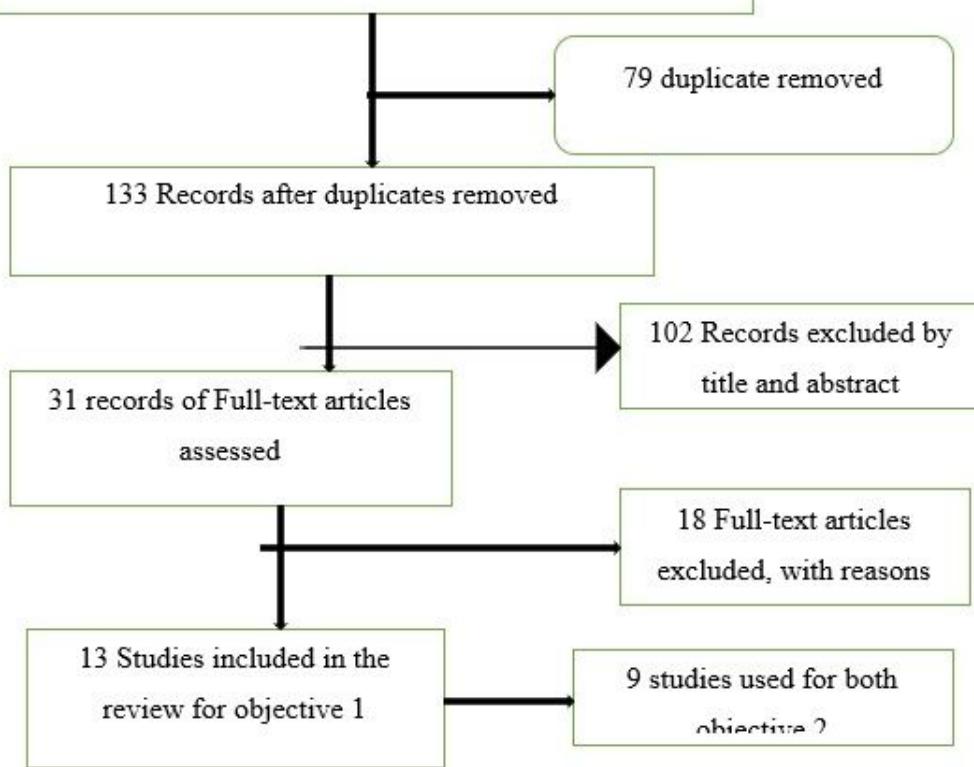


Figure 1

Flow chart of the selection process for the studies included in the analysis.

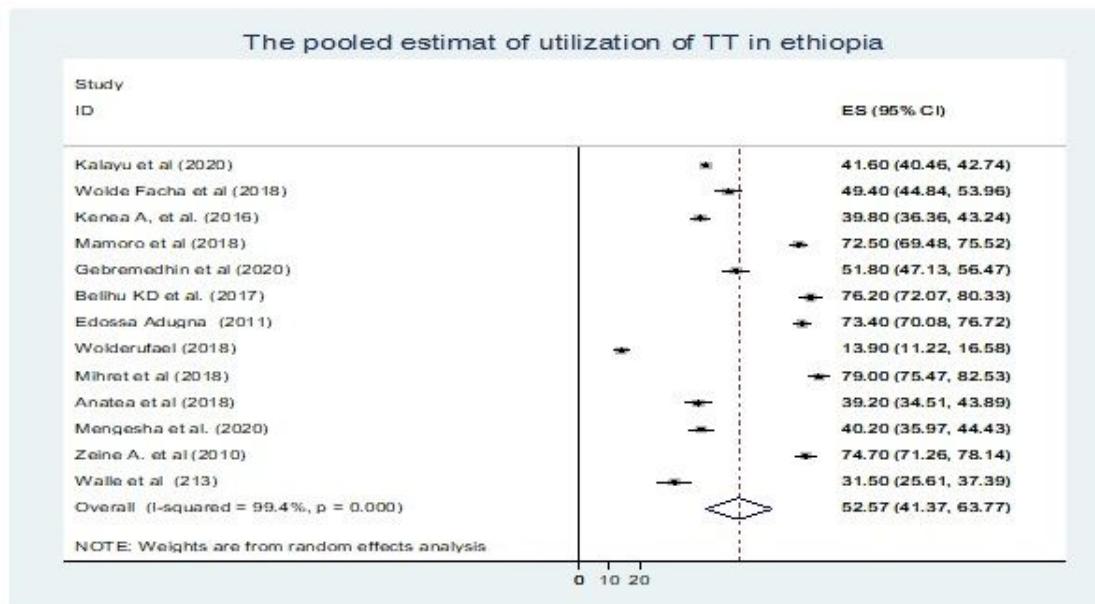


Figure 2

Forest plot for the pooled coverage of tetanus toxoid immunization in Ethiopia, 2020.

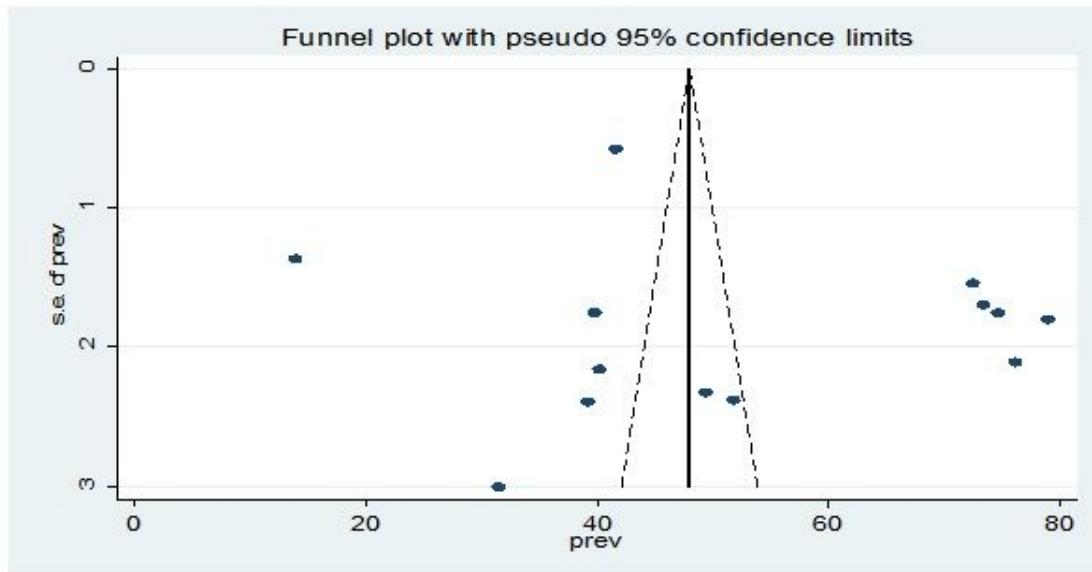


Figure 3

Funnel plot showing symmetric distribution of articles of tetanus toxoid immunization in Ethiopia, 2020.

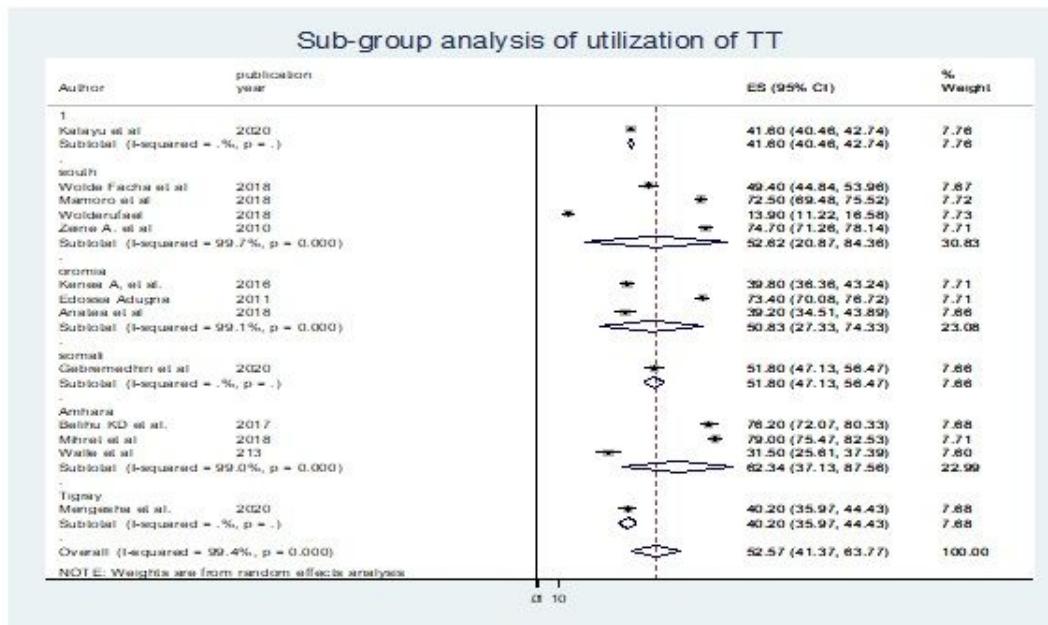


Figure 4

sub-group analysis of tetanus toxoid immunization coverage in Ethiopia, 2020

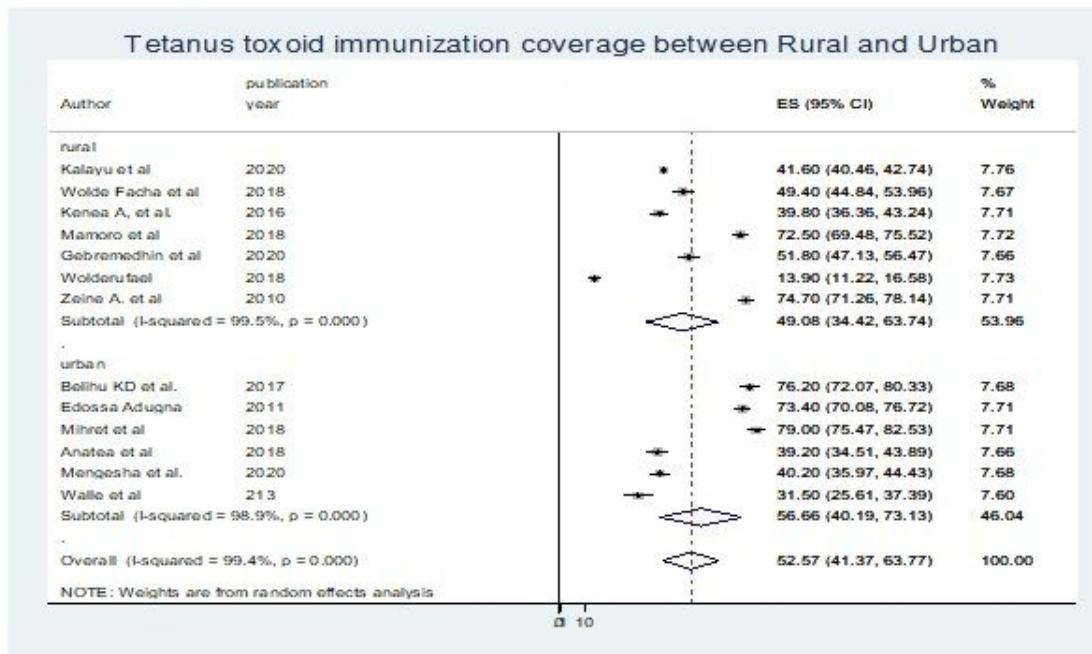


Figure 5

Tetanus toxoid immunization coverage between rural and urban women in Ethiopia, 2020.

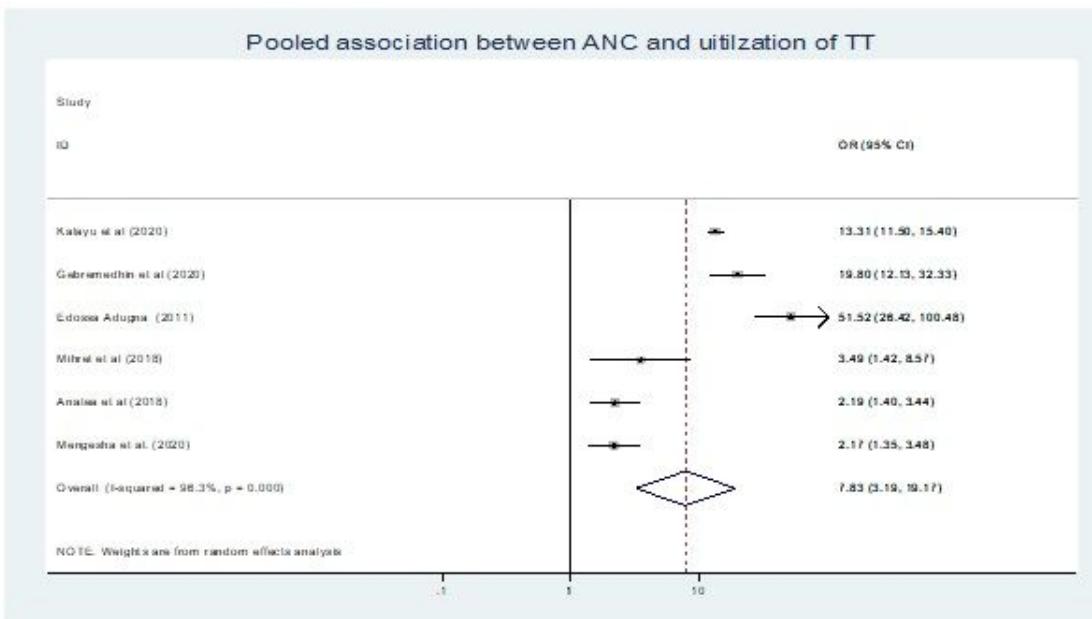


Figure 6

Association of anti-natal care visit with tetanus toxoid immunization coverage in Ethiopia, 2020.

Pooled association between media exposure and TT immunization

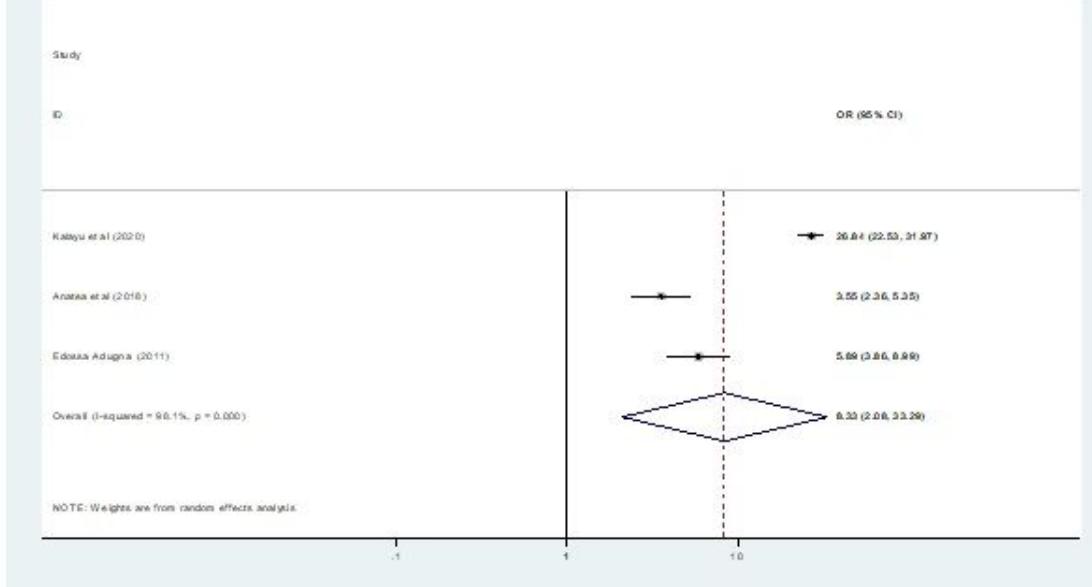


Figure 7

Association of media exposure with tetanus toxoid immunization coverage in Ethiopia, 2020.

Pooled association between distance from health facility and TT immunization

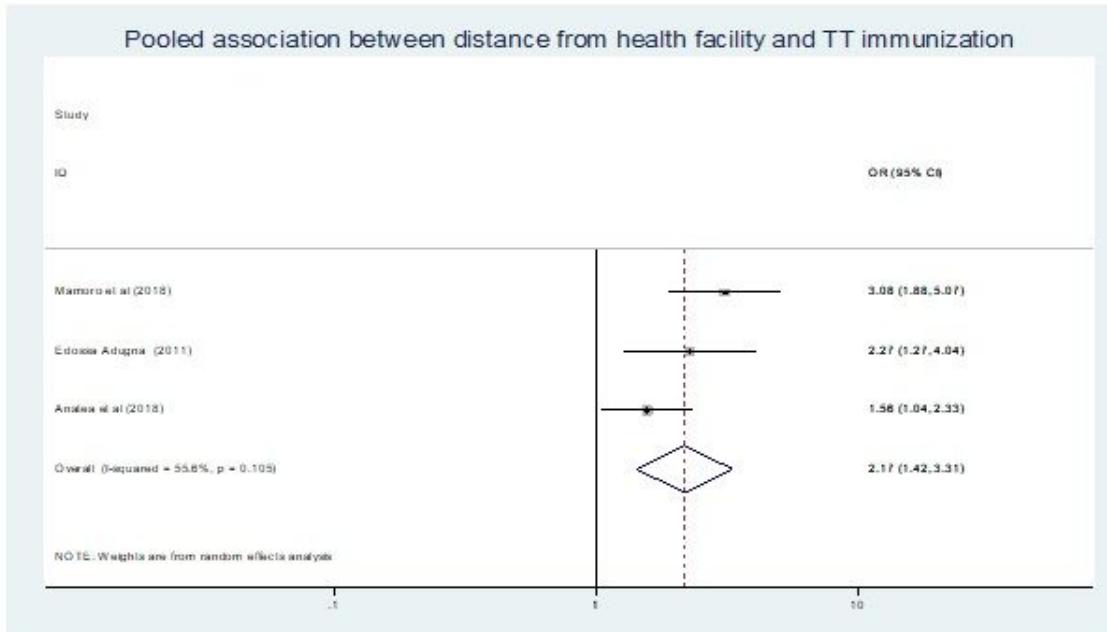


Figure 8

Association of distance of health facility with tetanus toxoid immunization coverage in Ethiopia, 2020.

Pooled association between distance from health facility and TT immunization

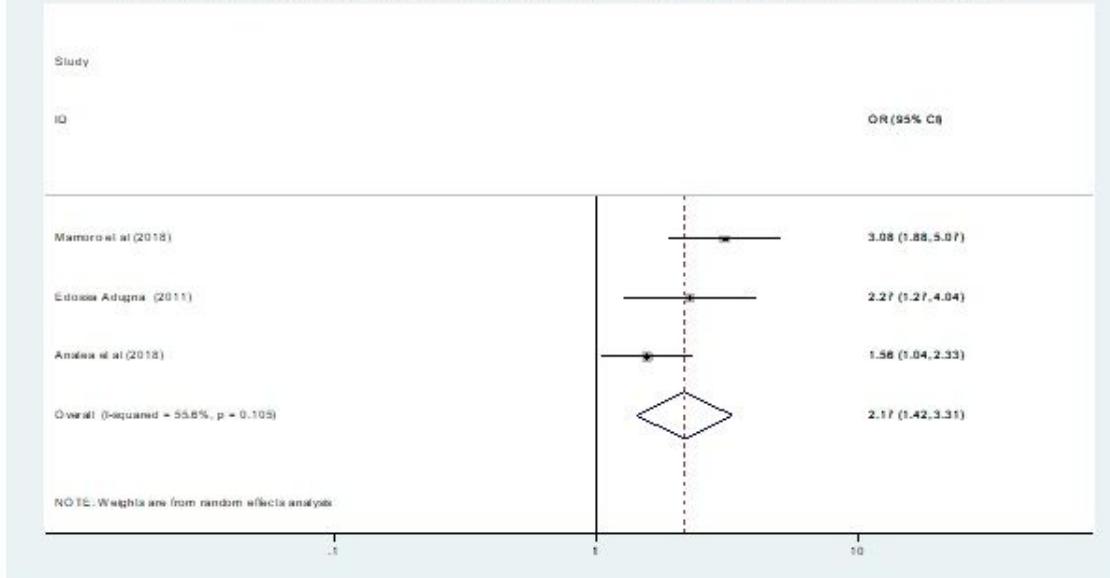


Figure 9

Association of mothers' educational status with tetanus toxoid immunization coverage in Ethiopia, 2020.

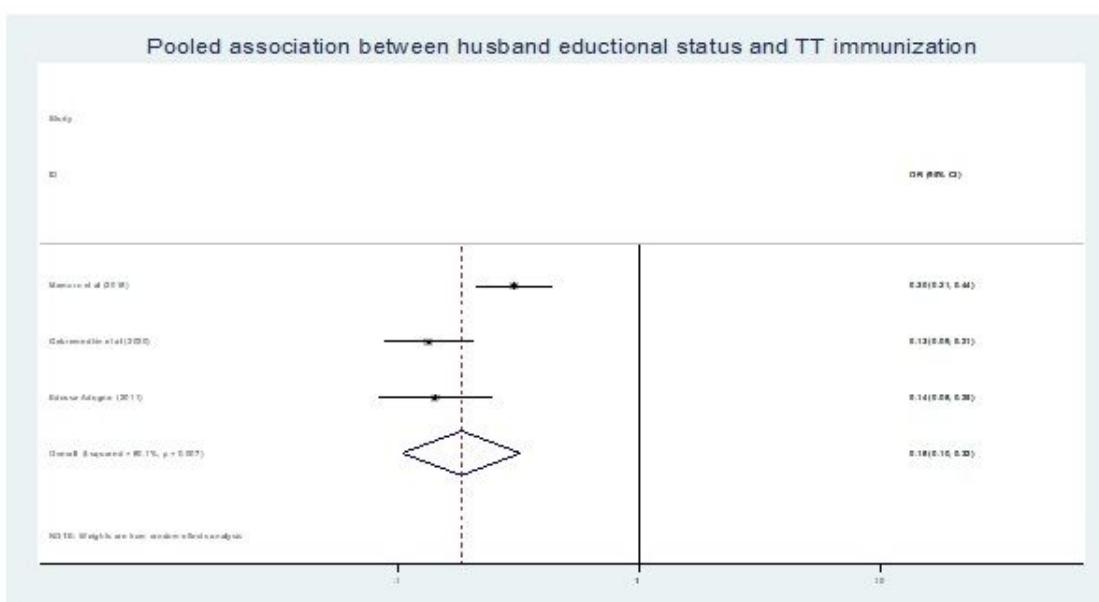


Figure 10

Association of husband educational status with maternal tetanus toxoid immunization coverage in Ethiopia, 2020.