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Health system delay in the treatment of tuberculosis patients in Ethiopia: a systematic review and meta-analysis

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Abstract

Background: Delay in diagnosis and initiation of effective treatment associated with increase in morbidity, mortality and on-going person-to-person transmission in the community at large. In Ethiopia, several studies have been conducted regarding health system delay among tuberculosis patients. However, studies assessing the health system delay in treatment of tuberculosis patients in Ethiopia had inconsistent and inconclusive findings. Therefore, this systematic review and meta-analysis aimed to determine the pooled median time of the health system delay in the treatment of tuberculosis and its determinants in Ethiopia.

Methods: We systematically searched from different databases: Google Scholar, Science Direct, PubMed, Embase, Scopus and Springer link databases for studies published from June 6, 1997 up to December 20, 2020. The quality of the studies was assessed using the Newcastle-Ottawa scale adapted for observational studies. Heterogeneity was evaluated using I squared statistic. We conducted a meta-analysis for the pooled median time of health system delay and its determinants using random-effects model in R version 4.0.3 software(for median estimation) and Stata version 14 (for metan). The pooled estimates with 95% confidence intervals (CI) were presented using forest plots.

Results: A total of 14 studies which comprising 6161 patients satisfying a priori set criteria were included. Our meta-analysis showed that, the estimated pooled median time of the health system delay was 15.29(95%CI: 9.94–20.64) days. In the subgroup analysis, studies conducted from 1997 to 2015 the pooled median health system delay was 21.63(95% CI: 14.38-28.88) days, whereas studies conducted after 2015 the pooled median time of 9.33(95% CI: 3.95-14.70) days. Living in rural area (pooled OR: 2.42, 95%CI: 1.16-5.02) was significantly associated with health system delay.

Conclusions: In Ethiopia, patients are delayed more-than two weeks in the treatment of tuberculosis. Being from rural residence was more likely to lead prolonged health system delay. Implementing efforts by targeting rural residence may help to shorten the health system delay and important implications for the success of tuberculosis control.

Keywords: Patients, Health system Delay, Median, Meta-analysis, Tuberculosis, Ethiopia.

Background

Despite a remarkable progress in TB control has been achieved over the past years; it remains a global public health challenge. About a quarter of the world's population are affected by Latent Tuberculosis(TB) and TB is the leading infectious disease killer(1). In 2019,there were an estimated 1.2 million individuals died due to TB, including 208 000 deaths among HIV-positive people(2). It kills more than five thousand children, women and men each day (3, 4). In addition, globally an estimated 3.3% of new TB cases and 17.7% of previously treated cases are believed to harbor drug resistant-TB(2). According to 2020 Global tuberculosis report, Ethiopia is among the 30 High TB, HIV and MDR-TB burden Countries, with annual estimated TB incidence of 140/100,000 populations and HIV negative TB mortality rate of 19 per 100,000 populations(2). Despite this, with a timely diagnosis and appropriate treatment, most people who develop TB can be cured and averts millions of deaths each year, but there are still enormous gaps notably in detection and treatment of tuberculosis(5, 6).

Delay can be categorized as patient delay, health system delay (diagnostic and treatment delay) and total delay as the sum of patient delay and health system delay(7). Majority of Ethiopian studies on health system delay(8-11) and a country assessment in 2016 done, as well as according to WHO 2006 report defined, health system delay as the interval from the first visit to the health care provider to initiation of effective treatment and usually used median value to categorize TB patients into delayed and not delayed(12, 13). Delay in diagnosis and treatment cause patients more likely to have advanced disease, complications, mortality and increase on-going person-to-person transmission in the community at large (14-18). It has been estimated that a patient with untreated smear-positive pulmonary TB may infect on average more than 10 patients annually and over 20 during the natural course of untreated disease until death(4). This means that, rapid diagnosis and early treatment initiation are fundamental to reducing transmission, morbidity and mortality of tuberculosis patients(6). Thus, determining the extent of delay and identifying the factors that correlate with different types of delay can aid tuberculosis control programs and help medical providers improve diagnosis and treatment efforts(19).

The health system delay is a larger problem than patient delay and still it remains a major challenge against TB control(20, 21). Delay in diagnosis and treatment initiation of TB has remained unacceptably high especially among high burden countries(22, 23). A systematic

review and meta-analysis showed that the median health system delay ranged from 2–87 days for low income countries(24). In high income countries [HICs], it ranged from a shortest of 7.2 days in Japan(25) to a longest of 33 days in Norway(19). In low- and middle- income countries [LMICs], it varied from 7 days in Vietnam(26) to 128.5 days in Afghanistan(27). Among Sub-Saharan countries median health system delay ranged from the lowest of 2 days in Zimbabwe(28) to 77 days in Uganda(29).

According to WHO, factors related to delayed in TB diagnosis and treatment can be divided into three levels: socio-economic, clinical, and health system factors(30). The main factors associated with health system delay included human immunodeficiency Virus, extra pulmonary TB, rural residence, visit private practitioner or traditional healer, old age, poverty, alcoholism and substance abuse(23, 31, 32).Health care facilities related factors such as lack of diagnostic modalities, availability of trained staff and lack of effective supervision were significantly associated with health system delay (20, 33, 34). In addition, unemployment, labor migration, the number of providers that patients visit and low income were also reported as factors of health system delay(21, 35, 36). A systematic review and meta-analysis conducted in Sub-Saharan African countries and Middle East Asia showed that travel time for the return visit and being female was associated with health system delay(37, 38).

Massive efforts were implemented during the era of Stop TB Strategy to substantially reduce the global burden of TB by 2015 through universal access to diagnosis and treatment regardless of socio-economic barriers. But, Health system delay remains a major challenge against achieving effective TB prevention and control(39). There are different studies that reported health system delays and its associated factors among TB patients in Ethiopia; however, these studies had varied or had inconsistent and inconclusive findings on health system delay. With these variations of reports and as far as in our search we could not find any study conducted on systematic review and meta- analysis on the extent and associated factors of health system delay in Ethiopia. Therefore, this systematic review and meta-analysis aimed to provide a pooled national estimate of the median time of health system delay and to identify its associated factors in Ethiopia. This evidence will be helpful for healthcare professionals, health-policy makers and program managers to apply efficient interventions, and to improve effective tuberculosis control program.

Methods

Reporting

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline(40) was used to report the result of this systematic review and meta-analyses. This systematic review and Meta-analysis was registered with PROSPERO Registration number **CRD42020220820.**

Study design and setting

We systematically reviewed studies conducted from Ethiopia aimed to estimate the pooled median time and to identify factors contributing health system delay in the treatment of tuberculosis. The country Ethiopia subdivided into ten national regional states: namely Amhara, Tigray, Oromia, Afar, Benishangul-Gumuz, Somali, Southern Nations Nationalities and People Region (SNNPR), Sidama, Gambella, Harari, and two city administrative states (Dire Dawa city council and Addis Ababa city administration)(41).

Inclusion and exclusion criteria

Inclusion criteria:

The studies were included if they met the following inclusion criteria:

Study design: All observational studies (cohort, case-control, and cross-sectional studies)

Study setting: Studies conducted in Ethiopia.

Study participants: All tuberculosis patients above 15 years old.

Outcome: The outcome of interest was the median time of health system delay for TB treatment.

Publication status: Published and unpublished studies in English language

Publication date: The authors included articles published from June 6, 1997 until December 20th, 2020

Exclusion criteria: Despite the above-mentioned eligibility criteria, articles which we were unable to access the full-text after two email contacts of the principal investigator of the particular study were excluded from the analysis.

Studies done before 1997 were excluded from the review since Ethiopia launched Directly Observed Treatment, Short-Course (DOTs) strategy in 1997 as part of National Tuberculosis and Leprosy Control Program (TLCP) to treat TB patients(3). WHO developed DOTS strategies to address major constraints to the achievement of global TB control targets. One of the strategy was expanding access to diagnosis and treatment through community TB care and public–private mix approaches aimed at engaging all care providers in DOTS implementation(39), this might have impact on reducing the number of days in the initiation of tuberculosis treatment.

Databases and Search strategy

The comprehensive search for potential studies was conducted by two of the authors (KT and FW), studies published in English from June 6 1997 up to December 20 2020. We exhaustively searched the following databases: Google Scholar, Science Direct, PubMed, Embase, Scopus and Springer link databases for all available studies using the search strategy by combining the keywords; Medical Subject Heading (MeSH) and free text terms described in **(S1 Table).** In addition, the manual search of reference list of included studies were also reviewed to retrieve further studies. The titles and abstracts of the identified reports were used to exclude studies that did not meet the inclusion criteria at the first step. In the next step, for studies potentially eligible for inclusion, both authors (KT and FW) selected full text studies based on eligibility criteria independently. The full articles of selected studies were screened to confirm eligibility and the reviewers discussed whether the studies should be included until a consensus was reached. If not, the disagreement was resolved by the decision of the third coauthor (DE).To identify unpublished and ongoing studies, we contacted researchers and experts in the TB field. We also requested unpublished data from organizations such as Federal Ministry of Health, Government of Ethiopia) and Non-governmental organizations (NGOs) working on tuberculosis, but no one responds.

Outcome measures and data extraction

The outcome of interest of this study was health system delay in the treatment of TB defined from the first visit of health care provider to treatment initiation(12, 42). Therefore, included studies define operationally health system delay from first visit to the health care facility to the initiation of treatment and report the median health system delay with the inter quartile range(IQR).All observational studies of patients receiving treatment for TB that recorded at least

the median health system delay were included. We converted all time measures to days for studies that did not report delay measures in days, delay reported in weeks were transformed into days by a multiple of 7; months by a multiple of 30. We used median and interquartile range from studies as primary measure for meta-analysis because all included studies reported by median number of days with interquartile range. Eligible studies were selected using the pre-specified inclusion/ exclusion criteria. All relevant information from the included studies were extracted independently by two (KT and FW) of authors after data extraction checklist development. Two authors (KT, FW) screened titles and abstracts obtained from the database search, and decided on eligibility. Following identification of potential studies, KT and FW made the final selection through review of full articles including the study design, participants, outcome variable and publication year. Co-authors (DE and YAB) closely supervised the selection process. Finally, potentially eligible full text articles that fulfilled the inclusion criteria were included in the review. We extracted data from each included studies on Microsoft excel spreadsheet: first authors, publication year, the region of the study conducted, data collection period, study participants, sample size and median with IQR of health system delay. We also extracted the predictor variables from the included studies for health system delay**.** Further data were also extracted on the health system delay among exposure categories and odds ratio for meta- analysis.

Quality assessment tool

Two reviewers (KT and FW) independently assessed the quality of articles before including in the analysis. The Newcastle-Ottawa Scale(NOS) adapted for cross sectional studies was used to assess quality of included studies(43, 44). The quality of each study was assessed in three sections using the following criteria: participant selection, comparability of the groups and description of outcome assessment with a maximum of ten score. Star was assigned for each point of the scale to categorize the studies into good, fair and poor quality based on the NOS criteria. The first section scored a maximum of five stars and focuses on the representativeness of the sample. The second section concerned on how the confounding variables controlled with a maximum of two stars. The third section is focused with the outcomes and statistical analysis of study with a possibility of three stars to be gained **(S2 Table).** Finally, the average score provided by two reviewers was taken. Disagreement of their assessment results were resolved by

involving third author (DE). Articles scored seven and above were considered as high quality. This cut-off point was considered after referring previous literature(45).

Data processing and analysis

Data were extracted from each of original studies using Microsoft excel and then exported to STATA version 14 and R software version 4.0.3 for analysis. The pooled estimates with 95% confidence intervals (CI) were presented using forest plots. Random effect model was employed to estimate pooled median health system delay (in days). The heterogeneity among included studies was evaluated using I squared statistic(46)**.** In this study, a significant heterogeneity was observed among the included studies (I^2 = 99.88%, $p < 0.0001$). As a result, a random-effects meta-analysis model was used. Potential publication bias was assessed by funnel plot by using median value or odds ratio. The median time of health system delay from different studies was pooled in meta-analysis using R software. We also conducted a meta-analysis on factors of health system delay in the treatment of TB using STATA version 14 statistical software. The overall effect of factors related to delays was estimated from studies by conducting a meta-analysis based on ORs and 95% CIs. Sub-group analysis was performed to identify potential factors that can explain the inconsistencies between effect sizes across the primary studies based on different variables (i.e., year of study, region of study conducted, sample size and types of TB).

Results

Search results

A total of 1031 articles were identified during our initial search from databases and all retrieved studies were exported to Endnote version 9 (Clarivate, Thomson Reuters, George Mason university) reference manager and then 477 articles were excluded due to duplication. We excluded 692 articles after examining the titles and abstracts, primarily because they did not have a relationship with the outcome of interest. Full-text evaluations were performed on 48 studies; of which 34 studies excluded after reading the full text with reason **(S3 Table).** Finally a total of 14 studies that satisfied the eligibility criteria were included in this systematic review and meta-analysis **(fig.1).**

Characteristics of original studies

The included articles covered 9 regions with two city administration; majority of the studies were conducted in Amhara region (7, 11, 47-50). Five studies (35, 50-53) enrolled pulmonary tuberculosis, 3 studies(7, 8, 47) were smear positive PTB and the remaining six studies(9-11, 48, 49, 54) include both form of tuberculosis patients. All articles were cross sectional studies and the sample size of the individual studies included in our meta-analysis ranged from 129(35) to 875(51) with total study participants of 6161 patients. The included studies were published between 2003 and 2019**(Table 1).**

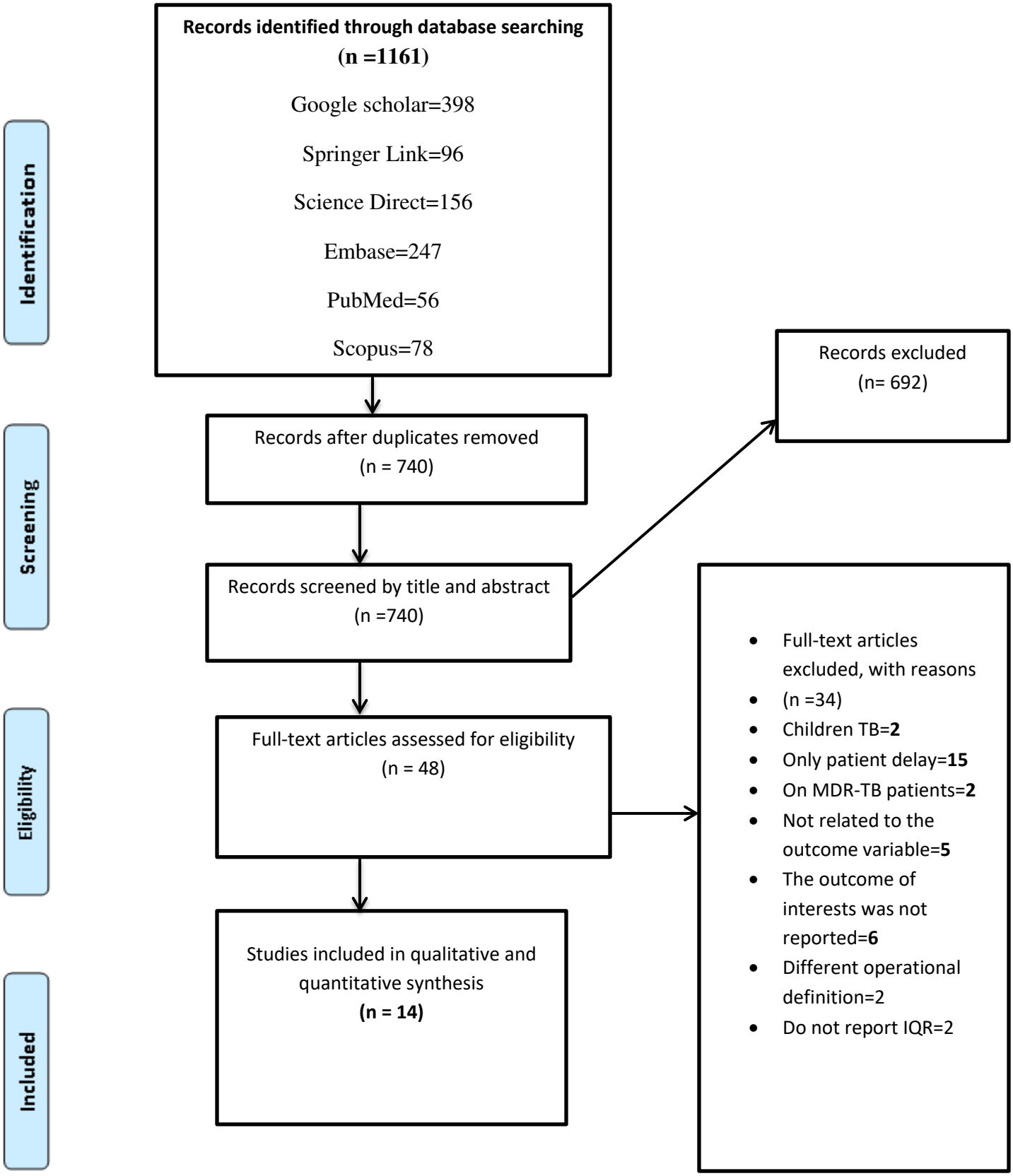

Fig.1 Flow diagram describing the selection of studies included in the systematic review and meta-analysis of health system delay among tuberculosis patients in Ethiopia.

Table 1. Characteristics of included studies conducted in Ethiopia on health system delay in Tuberculosis patients (n=14)

Author	Year of study	region	Study area	Study design	Sample size	HS delay [Median with IQR]	Participants	Study quality
Ayalew et al	2018	Amhara	both	CS	300	4 [3-5]	EPTB &PTB	high
Belay et al	2010	Afar	both	CS	216	33.5	EPTB &PTB	high
Gebregizaber et al	2014	Amhara	both	CS	706	22[4-88]	PTB	low
Yimer et la	2010	Amhara	hospital	CS	201	27[8-60]	EPTB &PTB	high
Asefa et la	2012	SNNPR	HC	CS	328	11[7-18]	Smear +ve PTB	high
Hussen et al	2011	Oromia	both	CS	129	34[8-105]	PTB	high
Adenager et al	2012	AA	both	CS	425	9[3-29]	PTB	high
Seid et al	2017	Amhara	both	CS	382	6[4-8]	EPTB&PTB	high
Tedla et al	2019	Tigray	both	CS	875	18[2-72]	PTB	low
Haboro et al	2017	SNNPR	both	CS	340	5[4-85]	PTB	high
Asres et al	2016	SNNPR	both	CS	735	22[9-48]	EPTB&PTB	high
yimer et al	2003	Amhara	both	CS	384	21[7-60]	Smear +ve PTB	high
Datiko et al	2017	All regions	HC	CS	844	6 (3–15)	EPTB &PTB	low
Bogale et al	2016	Amhara	both	CS	296	5[4-7]	Smear +ve PTB	high

HS=health system, IQR=Inter quartile range, EPTB=Extra pulmonary tuberculosis, PTB=pulmonary tuberculosis, HC=health center, both=both hospital and health center, CS=Cross sectional study

SNNPR=Southern nations nationalities and peoples´ region, AA=Addis Ababa

Meta-analysis

The smallest median health system delay among studies included in the analysis was 4 days(11) and the longest was 34 days (35). The overall estimated pooled median health system delay was 15.29 (95% CI: 9.94–20.64) days. We used random effect model because the overall results of I squared statistic shown high heterogeneity among included studies (I^2 = 99.88%) for median health system delay estimation. Therefore, we conducted subgroup analysis through sample size, year of study, region the study conducted and type of tuberculosis in order to explore possible causes of heterogeneity.

Subgroup analysis

In subgroup analyses, studies conducted with sample size less than 350 report a pooled median health system delay of 16.34(95% CI: 6.33-26.34), Whereas, studies conducted with a sample size of more than 350 with a pooled median health system delay was 14.65(95% CI: 9.03-20.28) days. By type of TB subgroup analysis, enrolling PTB patients had the highest pooled median health system delay 16.63 (95% CI: 16.63(7.46-25.81) days, followed by all form of TB 16.01(95% CI: 6.02-26.01) days and smear positive pulmonary tuberculosis 12.14(95% CI: 3.13-21.15). Similarly studies conducted from 1997 to 2015 reported the highest pooled median health system delay of 21.63(95% CI: 14.38-28.88) days compared to studies conducted after 2015 with a pooled median time of 9.33(95% CI: 3.95-14.70) days **(Table 2).**

Factors associated with health system delay

The data for each of the five associated factors were exported to Stata SE version 14 after extracting data on excel spreadsheet. Ten studies (7, 9, 10, 35, 48-53) assessed associated factors including patients socio-demographic characteristics, clinical characteristics, and diagnostic modalities. Six studies analyzed the relationship between sex and health system delay; four studies assess distance to the health facility with health system delay. HIV sero status was mentioned in three articles; from this one article mention that being HIV positive decrease health system delay as compared to HIV negative patients(48). Type of TB or form of TB mentioned in three articles and from this two articles showed that those who are smear negative and EPTB patients had prolonged health system delay(10, 50) **(S4 Table).** Three studies reported association between residence and health system delay; one article revealed that patients living in the rural area had prolonged health system delay as compared to patients living in urban residence(35)**.**

Our meta-analysis also showed that patients from rural area were more likely to have a prolonged delay with pooled OR of the studies (OR: 2.42, 95%CI: 1.16-5.02). However, in our meta-analysis, there was no significant relationship between health system delay and distance from the health facility [OR: 1.36 (0.72-2.55)], form of TB [OR: 1.39(0.99-1.95)], HIV sero status [OR: 1.07(0.82-1.39)] and sex [0.96(0.80-1.15)] **(S5 Fig 3).** Other socio demographic and clinical as well as diagnostic modality factors was not evaluated due to the lack of data in the individual studies.

Table 2. Subgroup Analysis of studies included in meta-analysis on health system delay in the treatment of tuberculosis patients (n=14)

subgroup	Number of included studies	Random effects(95% CI)	Test of Heterogeneity(I^2)	P-value
By year of study				
1997-2015	7	21.63(14.38-28.88)	97.35%	<0.0001
After 2015	7	9.33(3.95-14.70)	99.89%	<0.0001
By Region				
Amhara	6	13.84(5.69-21.98)	99.94%	<0.0001
SNNP	3	12.68(2.98-22.37)	98.38%	<0.0001
others	5	19.27(7.92-30.62)	99.06%	<0.0001
By type of TB				
All form of TB	6	16.01(6.02-26.01)	99.94%	<0.0001
PTB	5	16.63(7.46-25.81)	97.09%	<0.0001
Smear +ve PTB	3	12.14(3.13-21.15)	99.51%	<0.0001
by sample size				
Less than 350	7	16.34(6.33-26.34)	99.94%	<0.0001
Greater than 350	7	14.65(9.03-20.28)	99.35%	<0.0001

Others: Afar, Oromia, Addis Ababa, Tigray [only one study reported from each region]

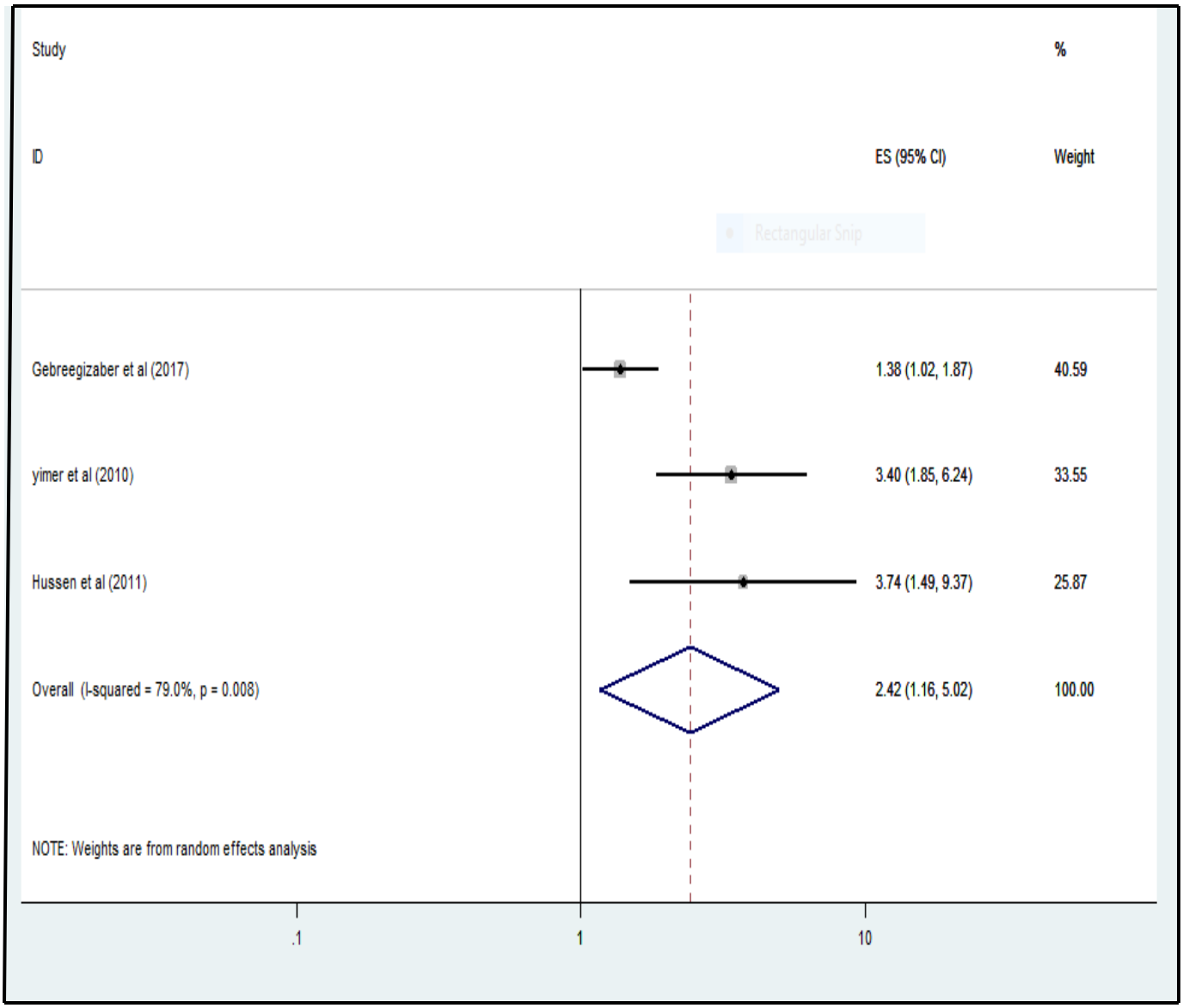

Fig 2: The pooled odds ratio of the association between residence and health system delay in the treatment of TB in Ethiopia.

Discussion

A meta-analysis regarding health system delays in Ethiopia was not previously conducted. Thus this meta-analysis attempted to estimate the pooled median health system delay and identifying the factors that are closely associated with health system delay. The findings could contribute to TB prevention and controlling programs; to effectively reducing delays for seeking prompt diagnosis and treatment.

Our finding showed that the pooled median health system delay in treatment of tuberculosis patients was 15.29 (95% CI: 9.94–20.64) days. These results suggest that even when patients seek care in a timely manner, significant time can be lost after their first contact with the healthcare provider. Our pooled analysis also indicated that residence was significantly associated with health system delay. Patients from rural residence were more likely to delay in the treatment of tuberculosis compared to those patients from urban areas (pooled OR = 2.42**;** 95% CI = 1.16–5.02). This may be due to the fact that access to health services is particularly low in rural areas of Ethiopia where the majority of the population lives. Together with an uneven distribution of health workers, results in little availability and poor quality of health services in rural areas(55).

We found to be shorter duration of health system delay compared to the previous systematic review and meta-analysis done in LMIC estimated average health system delay was 28.4 days(24), India the pooled median health system delay was 31 days(22) and another systematic review done in 78 countries, the pooled health system delay was 39.3 days(56). This finding also lower than primary studies done Vietnam 42 days(26) , Taiwan 29 days (57) ,china 26 days(58) and Turkey 64.1 days(59). The possible reasons for such discrepancy might be related to difference in accessibility of health care service or variation of the infrastructure from country to country and it could be also due to improvements in the diagnostic capacities like the introduction of rapid molecular diagnostic test especially Gene Xpert technology which are effectively shortened the health facility delays(34, 60). Our finding is in line with studies conducted Hong Kong 20 days (61) and Nepal 18 days(33). However, the pooled estimate median health system delay was higher than studies done in Vietnam 7days (26) , china 4 days (62) and Uzbekistan 7 days(63). This might be due to the high costs variation especially for the diagnosis of EPTB patients for pathological and x-ray diagnoses which are not free of charge

globally unlike the rest of TB services. Secondly, it may be due to difference in our inclusion criterion regarding dates of publication, study participants and types of TB. Our systematic review and meta-analysis include both PTB and EPTB but the above studies only include smear positive PTB patients. Since smear negative PTB and EPTB patients would likely increase the number of investigations that would be requested before confirming the diagnosis which would increase health system delay (32, 64).The other possible explanation may be due to having poor access and low health service coverage, a study done in Ethiopia showed that, the overall TB health service coverage was 23%(65)**.**

Our findings**,** in the subgroup analysis suggested that; studies conducted from 1997 to 2015 had the highest pooled median health system delay of 21.63(95% CI: 14.38-28.88) days as compared to studies conducted after 2015 with a pooled median health system delay of 9.33(95% CI: 3.95-14.70) days. This might be due to the establishment of End TB Strategy, since it starts after 2015 and the main targets was a 90% reduction in TB deaths and minimize TB incidence by 80% in 2030. To achieve this goal WHO sets as one of the main strategy through early diagnosis and prompt treatment(5). Therefore, to reduce the time delay for diagnosis and treatment of tuberculosis patients, WHO recommended rapid molecular diagnostic tests such as Xpert® MTB/RIF assay; it can provide results within 2 hours; this leads to a significant impact on reducing health system delay(5). Furthermore, the national TB program of Ethiopia has also re-prioritized the key strategic interventions in the five-year National TB strategic plan that paves towards achieving to reach 90% of all people with tuberculosis diagnosed and treated(3). The program is committed to improve access and equitable TB services to vulnerable and marginalized population groups where TB burden concentrates and most delays happen. In addition, the program also considered that the strategies can only be achieved if TB diagnosis, treatment and prevention services are provided within the context of progress towards universal health coverage(30). This program related considerations might be the contributing factor for the reduction of a pooled median health system delay for studies conducted after 2015 in Ethiopia.

In this systematic review and meta-analysis, we found that rural residence had positive association with health system delay; being from rural residence were nearly two and half times more likely to delay in the treatment of tuberculosis compared to those patients from urban residence with a pooled OR of 2.42(95% CI: 1.16-5.02). The findings of this review was

consistent with a systematic review and meta-analysis done in 40 countries(23). Similarly this finding was supported by primary studies conducted in Tajikistan(66), India(67),Indonesia(68) and China(62). The possible plausible reason for the situation could be patients living in rural areas had low access to health facilities or as a result of the absence of better access to anti-tuberculosis drugs and diagnostic modalities(69). For instance, most patients in rural areas of Ethiopia have primary access to the health post (first level of the health system) where there are no TB diagnostic services(48) and patients might have to walk for some hours to access hospitals or health centers(70). The other possible explanation might be, 85% of the rural population of Ethiopia not having access to health care and lack of physicians available in the public sectors as well as appropriate, affordable TB services is still problematic in some rural areas of Ethiopia (71-73) that could lead to prolonged health system delay. In addition to this, those patients come from rural residence repeatedly visited traditional healers first before diagnosis and treatment(74) and many patients from rural areas do not arrive to the health facility on time unless they are seriously sick(70). Since, the presence of traditional healers, which are prominent in rural areas across developing countries, have been suggested that seeing traditional healers influence tuberculosis treatment initiation(75). A study conducted in rural area of China, Tanzania and South Africa showed that visiting traditional healers were significantly associated with health system delay(58, 75, 76). Therefore, this may lead to longer health system delay.

In this systematic review and meta-analysis, distance from the health facility, HIV status, sex and type of TB were not associated with the health system delay. Even though a number of included studies reported that distance from the health facility more likely to lead prolonged health system delay, the pooled analysis indicated that distance from the health facility was not associated with health system delay. The possible explanation may be, since health system delay starts from, when the patients reach at the health care provider, factors which are related to the health system delay are mainly connected to health system related factors or factors which drive within the health system like lack of availability of trained man power and diagnosis services that might be lead to prolonged health system delay(33).

Limitations

Our search strategy was rigorous and multiple sources were searched and we obtain studies from all regions of Ethiopia, this allows the study to represent the burden of health system delay at the national level. Despite these, our systematic review and meta-analysis was not free from limitations that arose from either individual studies or the review process. The review was limited to only articles published in the English language. All included studies were cross-sectional studies. Since cross-sectional studies have a number of inherent limitations that potentially bias the results and lack the ability to determine causality as do other observational studies. The other limitation was, for the reason that; WHO as well as Ethiopia, had no cut off point available to say tuberculosis patients delayed or not delayed. Due to this, each included studies had different cut of point and they were not directly suited for a meta-analysis. Rather than excluding studies that failed to meet strict criteria, we tried to extract all the studies to arrive on a more national understanding of factors contributing to the health system delay.

Conclusion

In Ethiopia, patients are delayed more-than two weeks in the treatment of tuberculosis. Being from rural residence, increased health system delay. This finding sound that, patients living in rural areas need support to overcome the barriers to health system delay. For successful TB control, implementing efforts that could improve to shorten the health system delay could have important implications. Decentralization and scaling up of rapid molecular diagnostic test such as Gene expert and improving access to DOTS services through trained health care worker on tuberculosis in rural areas is vital.

Abbreviations

AIDS: Acquired Immunodeficiency Syndrome

CI: Confidence Interval

DOTs: Directly Observed Treatment, Short-Course

EPTB: Extra Pulmonary Tuberculosis

HIV: Human Immunodeficiency Virus;

IQR: Inter Quartile Range

MDR TB: Multi Drug Resistance Tuberculosis

MTB: Mycobacterium Tuberculosis

OR: Odds Ratio

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analysis

PTB: Pulmonary Tuberculosis

TB: Tuberculosis

WHO: World health Organization

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KT and FW: originated the research idea, literature review, data extraction, data analysis, interpretation and drafting the manuscript. **YAB, DE and DB:** contribute on data extraction, quality assessment, data analysis and manuscript review, edition & validation. All authors have read and approved the manuscript.

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Figures

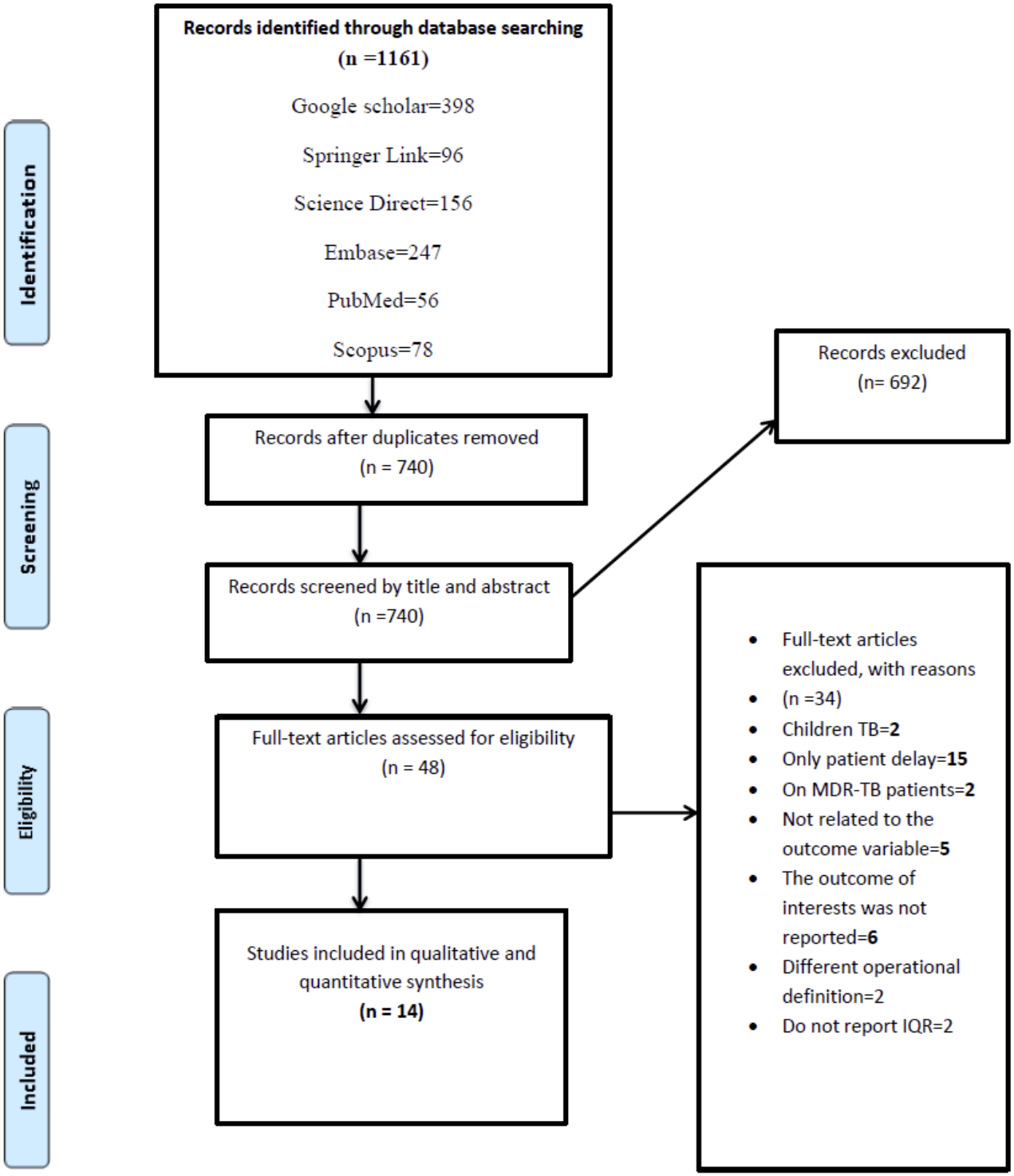

Figure 1

Flow diagram describing the selection of studies included in the systematic review and meta-analysis of health system delay among tuberculosis patients in Ethiopia.

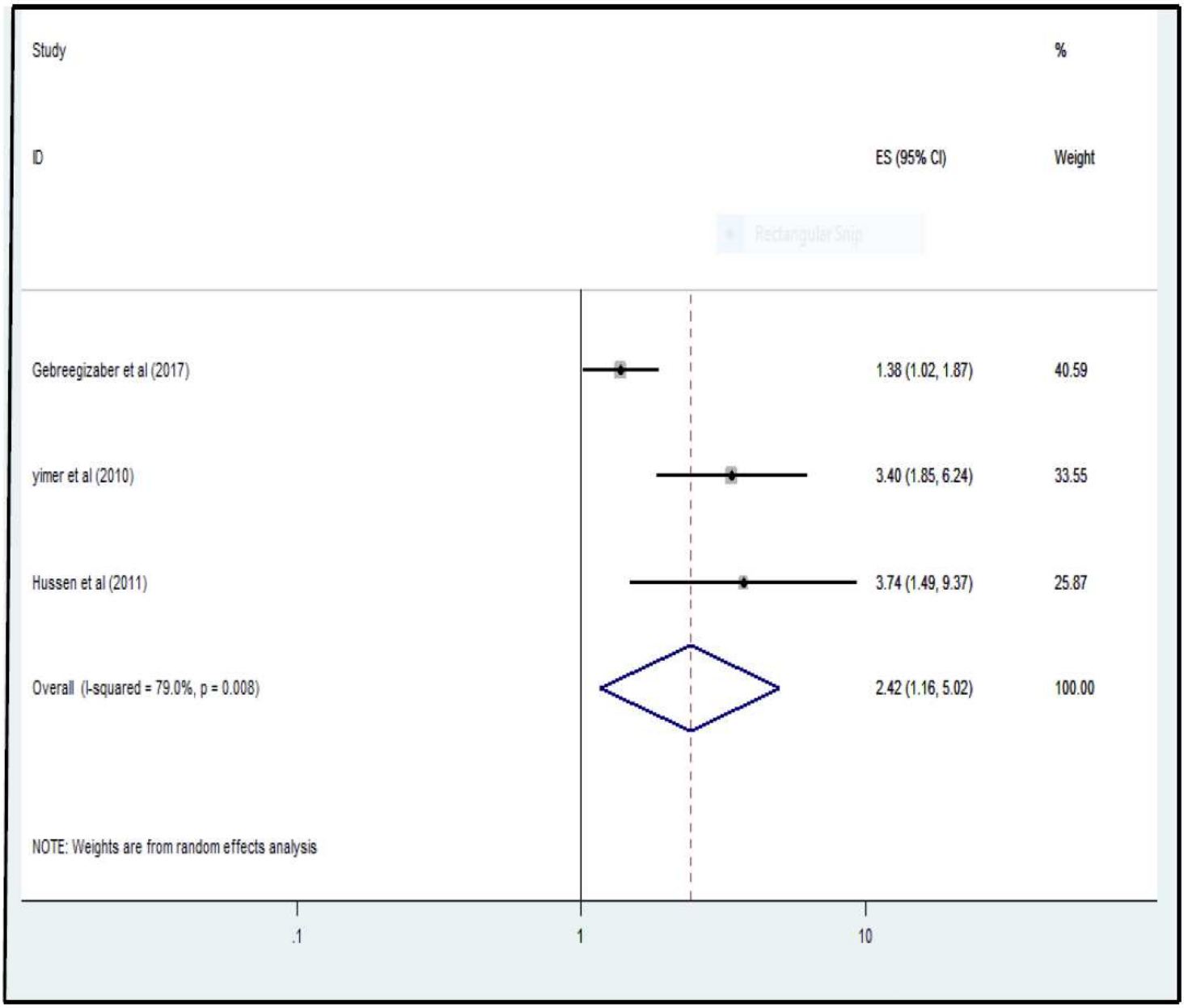

Figure 2

The pooled odds ratio of the association between residence and health system delay in the treatment of TB in Ethiopia.

Supplementary Files

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- Supplementarymaterial.pdf