Prevalence of Dog-Mediated Rabies in Ethiopia: A Systematic Review and Meta-Analysis From 2010-2020

Shiret Belete
Woldia University

Melke Meseret
Woldia University

Haileyesus Dejene
University of Gondar

Ayalew Assefa (hayall2020@gmail.com)
Woldia University https://orcid.org/0000-0002-6287-5318

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Abstract

Background: Rabies is a lethal zoonotic viral disease mostly transmitted by dog-bite. Ethiopia accommodates the second largest number of human rabies deaths in Africa. The total number of animal rabies cases in Ethiopia is not known. This systematic review and meta-analysis aimed to summarize and pool estimates of dog-mediated rabies' status in Ethiopia.

Methods: Published researches between the years 2010 to 2020 were comprehensively searched and the required information was extracted. The prevalence was estimated using the random-effects meta-analysis because higher heterogeneity between studies was expected.

Results: The pooled estimate of rabies was 32% (95% CI: 19% - 46%), with individual study prevalence estimates ranged from 1% - 78%. Studies were approximately weighted equally with individual weight ranging from 5.19% - 5.28%. Subgroup analysis indicated that the random pooled prevalence of rabies based upon hosts affected was 28% (95% CI: 0% – 81%) in animals and 33% (95% CI: 20% - 47%) in humans. Furthermore, a subgroup analysis across regions indicated that the pooled prevalence in Amhara and Tigray regional states was 5% (CI: 3% - 8%) and 55% (CI: 21% - 86%), respectively. No single study was reported from the country's Eastern and Southern parts which might be due to the religious aspect that most Muslims do not keep dogs in this region. Thus, the regional differences in data availability may have led to an overestimation of some regions' estimates.

Conclusion: The estimated pooled rabies prevalence was found high and showed varying among study regions. Therefore, focusing on mass dog vaccination campaigns and public awareness should be implemented to control the disease.

1. Introduction

Rabies is a life-threatening, zoonotic viral disease that can cause fatal encephalomyelitis (Jibat, Mourits, & Hogeveen, 2016). According to WHO (WHO, 2013), canine rabies causes an estimated 61,000 deaths per year within the wider international community, of which 56% and 44% of the deaths occurred in Asia and Africa, respectively (Deribe et al., 2012). This disease is mostly transmitted by dog-bite and causes significant morbidity and mortality among humans and animals, with high incidence in rural areas each year (WHO, 2013).

As Yimer *et al*. (Yimer et al., 2002) reported and Deressa *et al*. (H. A. Deressa et al., 2010), dogs are the primary cause for fatal human rabies cases and responsible for maintaining and disseminating rabies in Ethiopia. The country accommodates the second largest number of rabies deaths of all African countries (Coetzer et al., 2016). The first rabies epidemic in Ethiopia was recorded in the capital city of Addis Ababa in 1903 (Pankhurst, 1970). A retrospective study done between 2001 and 2009 by the Ethiopian Public Health Institute (EPHI) showed that approximately 1000 to1600 patients were exposed each year in Addis Ababa (H. A. Deressa et al., 2010; Reta, T., Teshale, S., Deresa, A., Ali, A., Mengistu, F., Sifer, D. and Freuling, 2014). The total number of animal rabies cases in Ethiopia is unknown, but with a rural and farming

population of more than 80%, annual livestock losses caused by rabies place a large societal and economic burden (Pieracci et al., 2016).

In recent data reported by Beyene *et al*. (Beyene, Mourits, Kidane, & Hogeveen, 2018), more than 2.9 thousand human rabies deaths occurred every year. The annual rabid dog exposures in some selected urban and rural districts were estimated to be 135,101 and 86 bites per 100,000 inhabitants, respectively (Beyene, Mourits, & Hogeveen, 2017). Quiet, the virus has long been a significant public health threat in Ethiopia (A. Deressa et al., 2010). This is considering with limited information on the true Ethiopian dog populations (i.e., owned dog and free-roaming dog populations (Ali, 2012; A. Deressa et al., 2010; Jemberu, Molla, Almaw, & Alemu, 2013; Yimer et al., 2002).

Dog-derived rabies in rural seating has also been reported as a potential problem for animal production sectors as dogs are kept in close contact with them for safeguarding purposes, which might provide an opportunity to transmit the virus (Jibat et al., 2016; Yizengaw et al., 2018). Researchers like Coetzer *et al*. (Coetzer et al., 2016) raise the question why the control and elimination of rabies is a daunting undertaking and why it is going as further challenged in Ethiopia. Every case of rabies in the country is confirmed by the only one National Rabies Laboratory (EPHI's), poor surveillance, irregular reporting and discrepancies in official data are the contributing factors for the underestimated burden of rabies Ethiopia (Coetzer et al., 2016; Reta, T., Teshale, S., Deresa, A., Ali, A., Mengistu, F., Sifer, D. and Freuling, 2014). Most importantly, limited vaccine availability in the regions is an extra headache where vaccine production is truncated. Thus, an increasing stray dog population, lack of rabies vaccines, poor rabies surveillance, low level of public awareness, poor attention and resource allocation by the government are major significant problems that hinder the control of rabies in Ethiopia (Coetzer et al., 2016).

Rabies has been reported as a significant public health threat in Ethiopia (A. Deressa et al., 2010) and the control and elimination of rabies is a daunting undertaking and going as further challenged in Ethiopia. Due to an increasing stray dog population, lack of rabies vaccines, poor rabies surveillance, low level of public awareness, poor attention and resource allocation by the government are major important problems facing forward (Coetzer et al., 2016). Scientific researches based on observational studies on viral isolation and identification is limited, except survey studies focused on knowledge assessment using questionnaire data. Furthermore, no data on systematic review and meta-analysis was done on rabies in Ethiopia. Hence, this systematic review and meta-analysis summarize and pool estimates of rabies' status in Ethiopia, which indicates necessary practical measures for the government and policymakers for appropriate control strategies at the national level.

2. Methods

The study was conducted based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) group checklist guideline (Moher D, Liberati A, 2009). The checklist was used to ensure the inclusion of relevant information (Additional file 1). The outcome of interest was the incidence

of rabies in Ethiopia. Mendeley version 1.19.4 was used to catalog the initial literature search results and to manage citations.

2.1 Literature Search Strategy and Eligibility criteria

Literature was searched in PubMed, Science Direct and Google Scholar databases. A Boolean operator "and/or" was used during online search by combining topic-related keywords. Key-words/MeSH terms used when searching the principal database were: rabies, dog bite, prevalence, incidence, and Ethiopia. The reference lists of all available studies on Rabies in Ethiopia were checked to obtain additional literature. All searched articles were downloaded and added to Mendeley reference manager. First titles and abstracts were assessed, and respective papers were examined in detail.

2.2. Inclusion/Exclusion criteria

Cross-sectional, prospective cohort and retrospective (conducted for not more than 5 years) studies, regarding the incidence of dog bite exposure of rabies during covering all dates in range of 2010 to 2020, published in a reputable journal, written in English, and conducted in Ethiopia articles were included. Infected animals and/human, number infected, study localities, study population size, and study method were considered an inclusion criterion. Survey and case studies were not included in this review. Titles were checked twice in both excluded and included databases of the Mendeley reference manager before starting the data extraction process. Duplicates were checked and removed.

2.3. Data extraction procedure

Data were extracted using standardized Microsoft Excel tables (Microsoft Office 2010, version 14.0). The following data were recorded in the extraction tables: paper identification (ID, first author, year of publication, title, journal, volume, page numbers), study type (Cross-sectional, Prospective cohort and Case-control study), Year of study, Geographic area, Region). Two independent researchers extracted data, and the consensus was resolved by consensus based on the standardized extraction forms to guarantee consistency and accuracy. Detailed evaluation was done on articles meeting the inclusion criteria.

2.4. Statistical analysis method

Mean prevalence and standard errors were initially calculated by considering numbers of events over total studied samples. Pooled prevalence estimates were calculated using the random-effects model meta-analysis at 95% CI as substantial heterogeneity was expected (DerSimonian & Laird, 1986). Cochran's Q test and inverse variance index (I^2), Heterogeneity between studies was evaluated, which describes the percentage of observed total variation between studies that are due to heterogeneity rather than chance. The I^2 values of 25, 50, and 75% were considered low, moderate and high heterogeneity (Higgins & Thompson, 2002). The I^2 values, 0%, indicate no observed heterogeneity. Q is weighted of squares on a standardized scale. Low p-values were reported as the presence of heterogeneity (Higgins &

Thompson, 2002). Subgroup analysis was conducted according to regional distribution, study methods, sample size, and hosts (human and/ animals). Publication bias was assessed using the Begg and Egger's test (Egger, Davey Smith, Schneider, & Minder, 1997), and by visual inspection of the funnel plot (Fig. 2). Potentially contributing factors for between-study heterogeneity was evaluated using Meta-regression. Univariable and final multivariant analysis was done for variables like study location, affected host, study type and sample size. Statistical analyses were then computed using Stata software version 13 (Stata Corporation, College Station, USA).

3. Results

From the total of 1075 records identified in the mentioned electronic databases depicted in Fig. 1, ten articles with 20 different observations were met inclusion criteria. The study characteristics indicated that the total sample size throughout the study years was 33,232 (2,161 animals and 31,071 humans), of which 5,640 were found positive for the rabies virus. The most extensive study regarding sample size employed was 6,874, while the smallest was 278 in humans. The overall apparent prevalence in all studies estimated was 32%. The disease was reported in 5 regions, including Addis Ababa city administration and was highly prevalent in northern parts of the country, such as Amhara and Tigray regional state. Detailed characteristics of the include studies and enrolled pooled Meta-analysis are summarized in Table 1.

Table 1
Descriptive Meta data of rabies from 2010–2020 in Ethiopia

Study regions	Host affected	Study type	Sample size	Event	Rate	Reference
Oromia	Human	Prospective	694	23	0.03	Beyene *et al.*, 2017
Amhara	Human	Cross-sectional	532	83	0.15	Jemberu *et al.*, 2013
Amhara	Animal	Retrospective	803	288	0.35	Jemberu *et al.*, 2013
Oromia	Animal	Retrospective	817	515	0.63	Jibat *et al.*, 2016
Tigray	Human	Retrospective	832	747	0.89	Teklu *et al.*, 2017
Tigray	Human	Retrospective	861	630	0.73	Teklu *et al.*, 2017
Tigray	Human	Retrospective	3,042	140	0.04	Teklu *et al.*, 2017
Tigray	Human	Retrospective	3,101	81	0.02	Teklu *et al.*, 2017
Amhara	Human	Retrospective	3,161	40	0.01	Yibrah and Damtie (2014)
Amhara	Human	Retrospective	6,527	423	0.06	Yibrah and Damtie (2014)
Amhara	Human	Retrospective	6,874	501	0.07	Yibrah and Damtie (2014)
Amhara	Human	Retrospective	278	206	0.74	Yizengaw *et al.*, 2018
Amhara	Human	Retrospective	336	255	0.75	Yizengaw *et al.*, 2018
Nationwide	Human	Retrospective	278	83	0.29	Beyene *et al.*, 2017
Nationwide	Human	Retrospective	336	34	0.10	Beyene *et al.*, 2017
Nationwide	Human	Prospective	3,042	368	0.12	OIE, 2017
Nationwide	Human	Retrospective	935	726	0.77	OIE, 2017
Tigray	Human	Prospective	694	23	0.03	Gebru *et al.*, 2019
Adiss Ababa	Animal	Cross-sectional	532	83	0.15	Reta *et al.*, 2014

3.1. Meta-analysis and meta-regression

Pooled prevalence estimates for ten studies included in the meta-analysis are presented in Table 2. The pooled estimate of rabies across studies for the entire period was 32 % (95 % CI: 0.19–0.46), with individual study prevalence estimates ranged from 1–78%. Studies were approximately equal with an

individual weight ranging from 5.19 % to 5.28 %. The Forest plot for the pooled prevalence of rabies derived from the meta-analysis is depicted in Fig. 2. Variables such as study region, study type, sample size and host affected were used in meta-regression. However, except for study regions, none of the variables were significantly associated with rabies' event in the final multivariate meta-regression. The analysis indicated that many studies were derived from the Amhara and Tigray region, both in the country's northern part. Study variability was observed in two locations and thus, results in such locations were omitted due to an insufficient number of observations. The subtotal pooled prevalence for Amhara and Tigray regional state was 5% (CI: 0.03; 0.08%) and 55% (CI: 0.21; 0.86%), respectively. Despite this, one and two studies performed in Addis Ababa and Oromia regional state showed 78% and 45% pooled prevalence, respectively. The results of the final meta-regression analysis have been summarized in Table 3.

Table 2
Subgroup Meta-statistics

Characteristics	No of observations	Pooled rabies prevalence				Heterogeneity	
		Sample size	Event	Event rate	95% CI	I^2 %	P-value
Overall prevalence	20	33,232	5,640	0.32	0.19;0.46	99.85	0.000
Region						99.85	0.00
Addis Ababa	1	935	726	0.78	0.75;0.80	0	
Amhara	7	23,527	1,240	0.05	0.03;0.08	98.3	
Nationwide	4	1,228	578	0.47	0.14;0.80	99.4	
Oromia	2	1,187	548	0.46	0.42;0.48	0	
Tigray	5	6,355	2,548	0.40	0.21;0.86	99.9	
Host affected							
Animal	3	2,161	832	0.39	0.81;15.8	0	0.00
Human	17	31,071	4,808	0.34	0.20;0.47	99.8	0.06
Study type							0.00
Prospective	3	3,864	423	0.12	0.04;0.22	0	
Retrospective	15	27,845	4,669	0.35	0.20;0.53	99.9	
Cross sectional	2	1,187	548	0.45	0.42;0.48	0	
Sample size							0.001
< 385	5	1,356	610	0.45	0.21;0.65	99.3	
385–1000	8	6.129	3,477	0.57	0.18;0.39	99.8	
> 1000	6	25,747	1,553	0.06	0.02;0.08	99.4	

Table 3
Multivariate meta-regression analysis

Variables	Coefficient	p-value	95%CI
Regions			
Addis Ababa	*		
Amhara	-0.75	0.06	-1.35; -0.14
Oromia	-0.62	0.15	-1.47; -0.23
Tigray	-0.67	0.08	-1.43; 0.08
Nationwide	-0.24	0.54	-1.03; 0.54
Host			
Animal	*		
Human	0.55	0.06	-0.04; 1.14
Study type			
Prospective	*		
Retrospective	-0.01	0.98	-0,44; 0.44
Cross sectional	**		
Sample size			
<385	*		
385–1000	0.34	0.43	-0.50; 1.17
>1000	-0.20	0.52	-0.81; 0.41

*Reference

** Omitted due to collinearity

3.2 Subgroup meta-analysis

Substantial heterogeneity was observed in the pooled estimate. A subgroup meta-analysis was computed for host affected, location, study type and sample size Table 2. Hence, sub-total random pooled prevalence of rabies was estimated at 28% (95% CI: 0.00 - 0.81) in animals and 33% (95% CI: 0.20 - 0.47) in human. Furthermore, subgroup analysis was computed for study location by clustering into regions. The Forest plot indicating host-affected subgroup analysis is illustrated in Fig. 3 and the forest plot showed that study region subgrouping is illustrated in Fig. 4.

3.3 Publication bias and small study effect assessment

The funnel plots (Fig. 5) and the Egger's regression asymmetry coefficient [b: 13.4] (CI: 5.43; 21.38: $p<0.05$) suggest the presence of publication bias (Table 5). This might be due to excluding all survey and case study data on our literature search strategy and eligibility criteria.

Table 5

Egger's test for small-study effects

	Standard effect	Coefficient	Std err	P-value	95% CI
slope	-0.11	0.09	-1.19	0.250	-0.29; 0.08
bias	13.41	3.78	3.55	0.002	5.43; 21.38

4. Discussion

This is the first systematic review and meta-analyses on the incidence of rabies in Ethiopia to the best of our knowledge. The results presented in this report were from the analysis of data obtained through a systematic review of scientific publications of the prevalence of rabies at the country level between the years 2010 to 2020. Literature was heterogeneous, had inappropriate study designs, unrepresentative sample size and diagnostic methods. This diversity, together with the lack of data on other required variables, reduced our dataset substantially. The final quantitative and meta-analysis of the prevalence were done only with ten articles that have 20 observations. Among them, 15 were on humans, three on animals and two records on both hosts. Datasets show relatively more studies implemented in humans than animal through a retrospective method among patients emanated from hospitals. This indicates no active surveillances are undertaken. On the other hand, studies conducted in animals are very few even though the disease's primary source is animals. An increasing number of stray dogs in Ethiopia and lack of dog vaccination practice and low public awareness level create difficulty in controlling the disease. In Ethiopia, almost all animals are kept extensively and whether an animal develops rabies via a bite by own keeper dogs or others are usually not visibly known. Most importantly absence of a post-exposure vaccine for animals made the condition worsen. As the prime source of the disease is animals, rabies in animals should be well studied through active surveillance.

The random effect meta-analysis result showed high variability with Higgin's I^2, which indicates that the variability between studies was not by chance alone. Because of the considerable variability between studies, the random effects meta-analysis weight of studies was nearly equal. The sample size was a highly significant predictor, indicating a substantial portion of the variability between sample sizes. However, other variables in the final meta-regression remained statistically insignificant in explaining the study variability.

This review demonstrated that there is still a significantly higher prevalence of rabies in Ethiopia. A pooled prevalence of 32% at the country level needs critical attention from the country's responsible

bodies. The pooled prevalence estimate varies significantly between regions. Relatively higher numbers of studies were done in Amhara and Tigray regional states. However, the highest prevalence of rabies was reported from Addis Ababa. On the contrary, no study was reported from the country's eastern and southern parts, which might be due to the religious aspect that most Muslims don't keep dogs. Thus, the regional differences in data availability may have led to an over-estimation.

According to this systematic review and meta-analyses (SR&MA), rabies report has been mostly done in the northern Region of Ethiopia, particularly Amhara and Tigray national, regional state (Jemberu et al., 2013; Teklu et al., 2017; Yibrah & Damtie, 2015; Yizengaw et al., 2018). However, most reporting articles were implemented in human cases using retrospective data (Beyene et al., 2017; OIE, 2017; Reta, T., Teshale, S., Deresa, A., Ali, A., Mengistu, F., Sifer, D. and Freuling, 2014; Yibrah & Damtie, 2015). This review is a timely reminder of the need for more studies on animal reservoirs. Rabies has a devastating impact on poor third-world countries, with almost a hundred percent case fatalities in animals and humans (Coetzer et al., 2016; Jibat et al., 2016; WHO, 2013). Unlike Malaria, HIV/AIDS and TB, prioritization of rabies prevention is insufficient in Ethiopia; lack of focus on mass dog vaccination, uncontrolled animal movement and abounding free-roaming dogs makes the disease impact severe (Ali, 2012; Beyene et al., 2018; Coetzer et al., 2016; Deribe et al., 2012; Pieracci et al., 2016).

There are some limitations to this study. First, data showed a large degree of heterogeneity among studies, which remained even after subgroup analysis. Therefore, the findings may not necessarily reflect the real situation of the entire country. The publication bias test is significant, indicating a consequence of incomplete or inaccurate information provided in the publications. Despite a comprehensive search, some studies have not been found because they are not published in journals indexed by PubMed. Most of the studies reported were questionnaire-based surveys and case studies that did not report the infection prevalence rate. Therefore, we did not include these studies in our systemic review and Meta-analysis. This means that some of the potential useful studies were excluded and their data were not utilized. Subsequently, there were limited data from some Ethiopia regions such as Afar, Somalia, Harar, South-west Ethiopia because of the limited availability of laboratory-based data and unusual trend of keeping dogs in such community as mentioned earlier.

Conclusions

To our knowledge, this is the first Systemic review and Meta-analysis attempt made on rabies in humans and animals. Our review revealed a high pooled prevalence of rabies and the disease had shown a significant variation among study regions. Relatively higher numbers of studies were done in Amhara, Tigray regional states and Addis Ababa administrative city. Therefore, more scientific researches need to be executed. Critical attention is needed from the country's responsible bodies focusing on mass dog vaccination campaigns and public awareness to control rabies' risk.

Abbreviations

WHO, World Health Organization

PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses

EPHI, Ethiopian public health institute

MeSH, Medical Subject Heading

Declarations

Ethics approval and consent to participate

Not Applicable

Acknowledgments

Not Applicable

Author Contributions

The idea was conceived, designed and data collected by SB and MM.

Formal analysis: SB, AA, HD,

Writing original draft: SB

Writing review & editing: SB, MM, HD, AA

Competing interests

The authors have declared that no interests exist.

Trial registration

NA

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Consent for publication

Not Applicable

Availability of data and materials

All data presented on the main paper and raw datasets used and/or analyzed during the current study are available from the first author and corresponding author on reasonable request.

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Figures

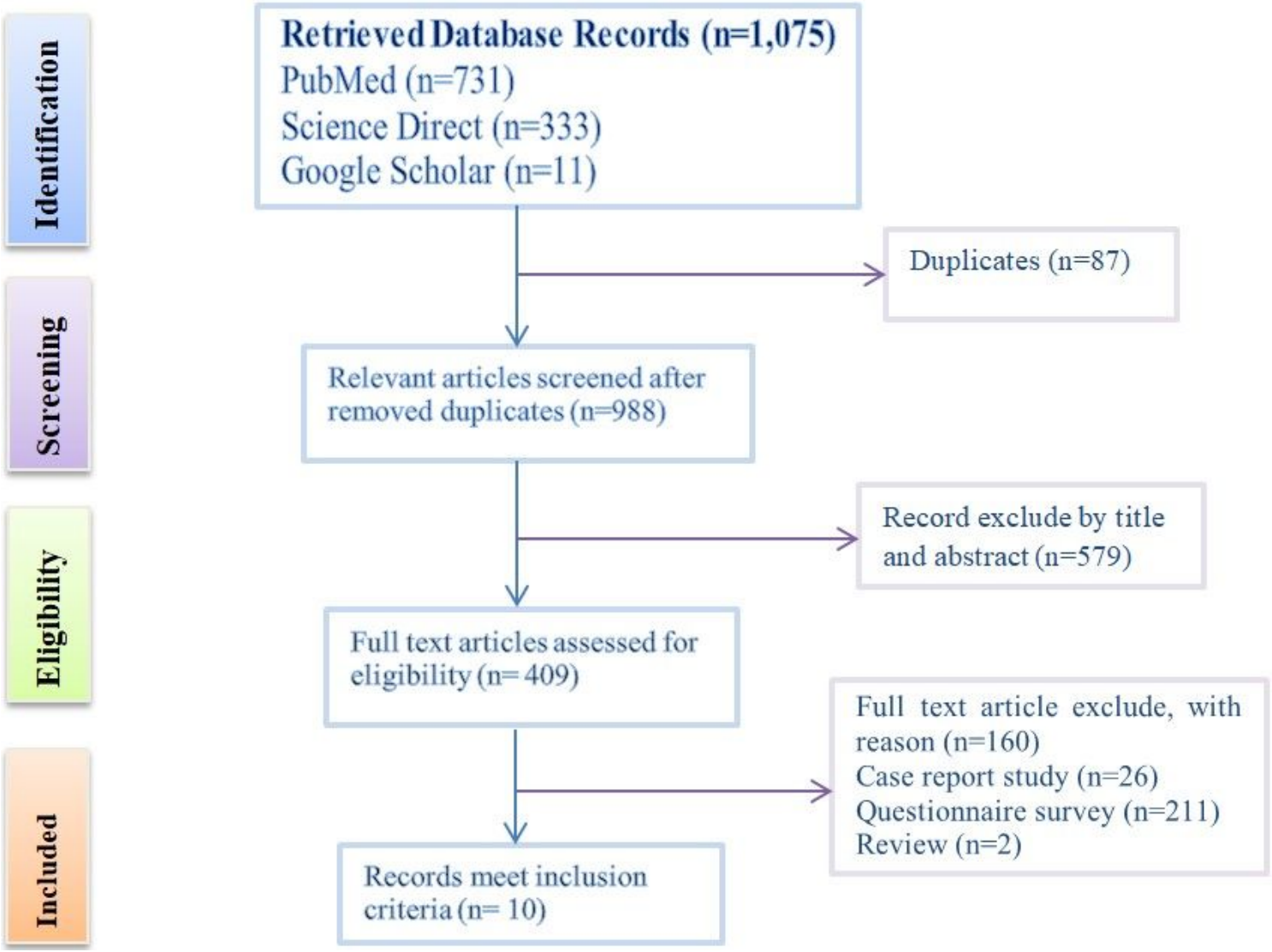

Figure 1

Flow diagram of the selection of eligible studies

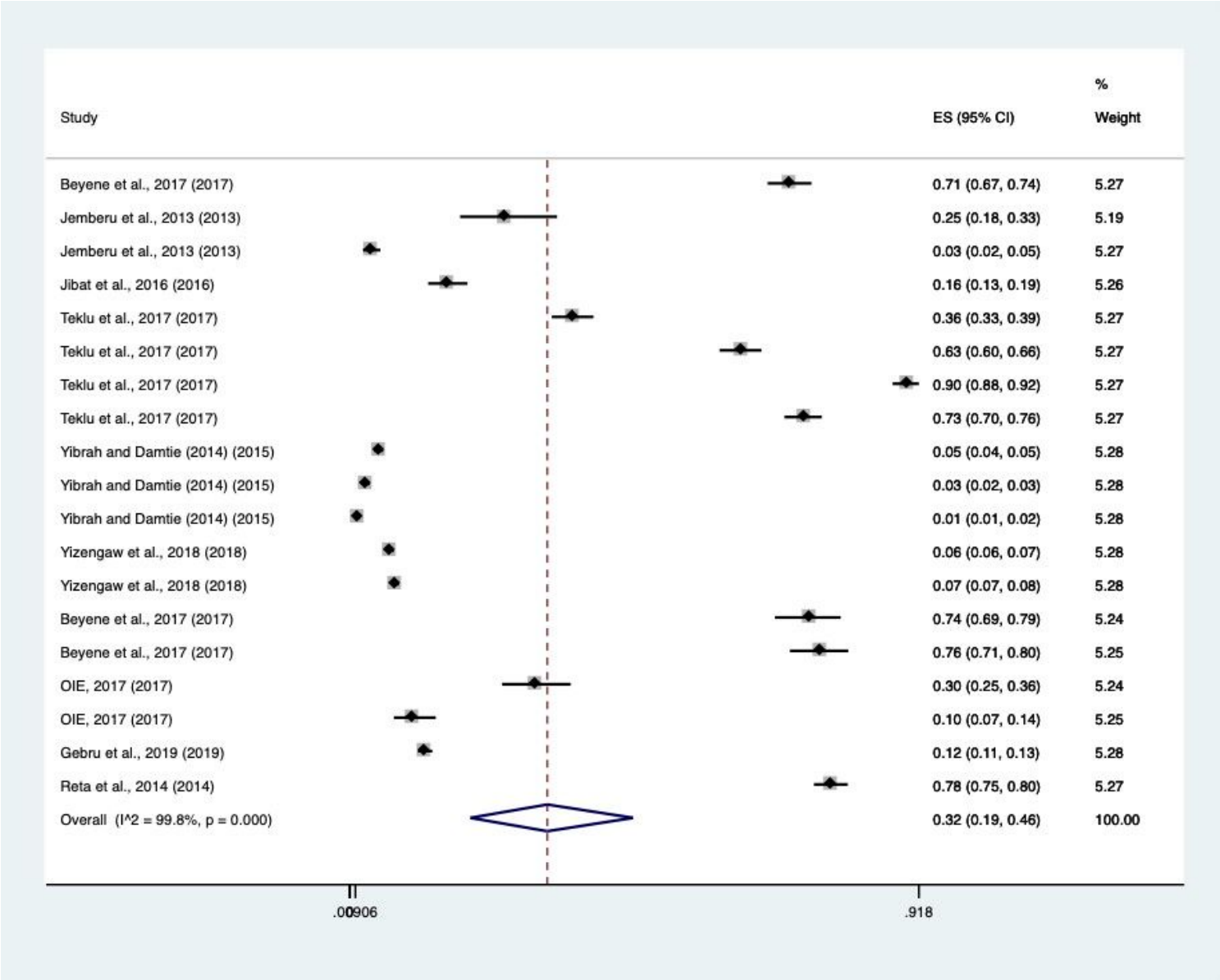

Figure 2

Forest plot for the pooled prevalence of rabies

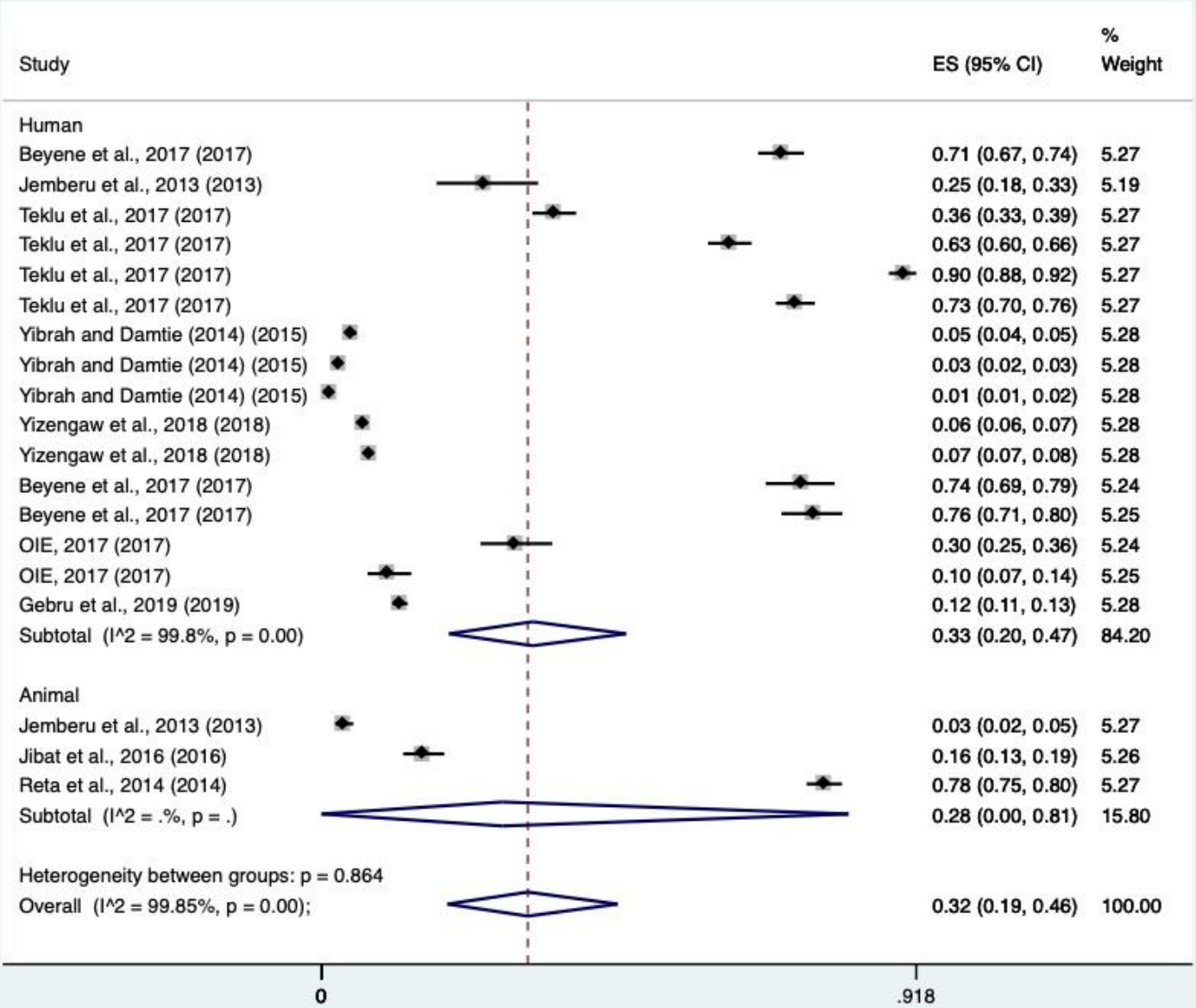

Figure 3

Subgroup analysis by host affected

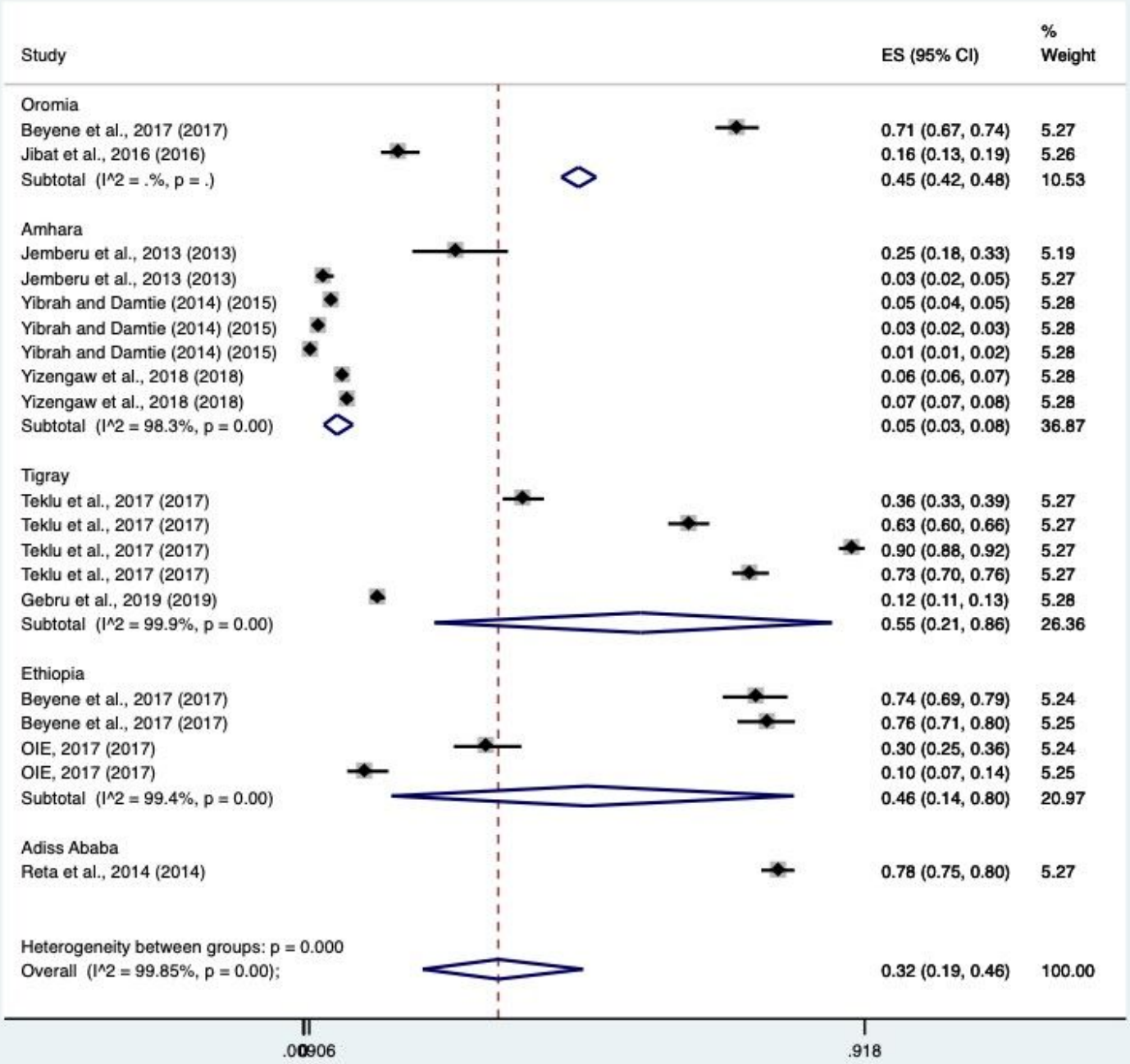

Figure 4

Subgroup analysis by Region

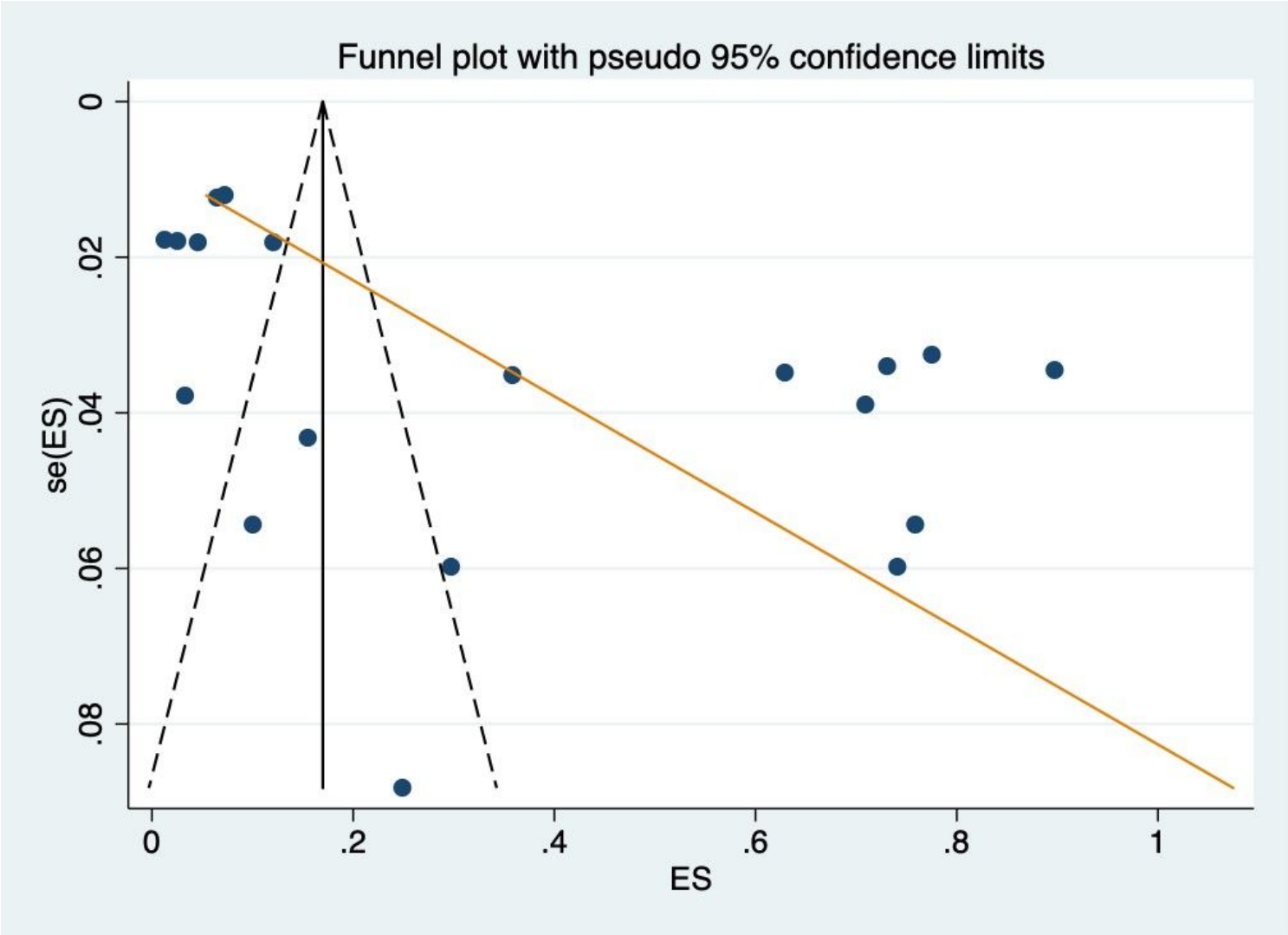

Figure 5

Funnel plot

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Additionalfile1PRISMAchecklist.docx