

Adherence to Highly Active Antiretroviral Therapy and Its Association with Serostatus Disclosure among People Living with HIV in Ethiopia: A Systematic Review and Meta-Analysis.

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Abstract

Background: Adherence to highly active antiretroviral therapy (HAART) is a public health challenge worldwide. Non-adherence to HAART leads to treatment, immunologic, and virological failure. Despite different interventions made, adherence to HAART among adult people living with HIV (PLWHIV) is still inconsistent across studies, and the effect of serostatus disclosure on adherence to HAART was not studied in Ethiopia. Therefore, the study is aimed to determine the pooled prevalence of adherence to HAART and its relationship with serostatus disclosure among adult PLWHIV in Ethiopia.

Methods: We searched 3247 original articles, both published and unpublished on Ethiopia dated from January 2016 to November 2019 by using different search engines. Data were extracted using Microsoft excel. New Castle Ottawa Scale quality assessment tool was used. STATA software version 11 was used for analysis. A random-effects model for meta-analysis was computed. Cochran Q statistics and I^2 were used to estimate heterogeneity. Egger's and Begg's test was used to assess the publication bias.

Results: A total of fifteen articles for systematic review and four articles for meta-analysis were used. The pooled prevalence of adherence to HAART is found to be 81.19% (80.1, 82.3). In the subgroup analysis, the pooled prevalence of adherence to HAART was 79.82% (73.19, 86.45) in the Oromia region, 82.51 % (73.14, 91.87) in the Amhara region, and 72.7% (63.78, 81.61) in the Southern Nations Nationalities and Peoples' Region (SNNPR). The serostatus disclosure improves adherence to HAART by nearly three times compared to non-serostatus disclosed PLWHIV ($AOR=2.99$, 95 %CI: 1.88, 4.77).

Conclusions: The pooled prevalence of adherence to HAART among adult PLWHIV in Ethiopia was found to be low compared to WHO antiretroviral treatment recommendations. Having serostatus disclosure improved adherence to HAART.

Background

The human immunodeficiency virus(HIV) affects many segments of the world's population in different ways⁽¹⁾. Africa, Asia, and Latin America are the major continents affected by HIV⁽²⁾. In this regard in 2016, there were about 36.7 million people living with HIV⁽³⁾.

Globally and in Sub-Saharan Africa there were 160,000 and 110,000 children infected with HIV in different ways respectively⁽²⁻⁴⁾. According to the WHO report in 2016, an estimated 2.1 million adolescents were living with HIV, and of this 84% were living in Sub-Saharan Africa(SSA)⁽⁵⁾. The SSA is home for 76% of the global morbidity and 75% of mortality caused by HIV/AIDS⁽⁶⁾. In Ethiopia in 2018, around 690,000 people living with HIV, 23,000 were newly infected, and 11,000 people died from an AIDS-related illness. Ethiopia launched its ART initiatives in 2003 based on a subsidized fee-based approach, and it became available free of charge in 2005. As a result, the number of ART users has increased from 47,422 in 2005 to 703,516 in 2017⁽⁷⁾. The United Nations set goals on the HIV/AIDS epidemic prevention named the 90-90-90 target indicating 90% of people who are HIV infected will be diagnosed, 90% of people who are diagnosed with HIV will be on antiretroviral treatment, and 90% of those who received antiretroviral

treatment will be virally suppressed(8, 9). Adherence to highly active antiretroviral therapy (HAART) can prolong the life of HIV patients(10). On the contrary, non-adherence to antiretroviral therapy(ART) could lead to different complications such as treatment, immunological, and virological failure(11, 12). HIV infection does not only affect the patient but also the families, communities, and the country at large (2, 6). Antiretroviral therapy has a clinical effect in decreasing viral replication and viral load which in turn increases the CD4 level and decreases the progress of HIV/AIDS(13). The clinical outcome of PLWHIV depends on adherence to antiretroviral therapy (ART). Studies showed that adherence to HAART accurately predicted the prognosis of AIDS and death(12, 14). Level of awareness about HIV, counseling about adherence, a substance used, side effects of the ART, and depression hinder the adherence to HAART (15-18). Serostatus disclosure may also attribute to adherence to HAART. Sharing one's own HIV positive diagnostic test result to a partner, family members, and friends provide the patient to take their ART medication freely(19). As far as known, there is no published systematic review and meta-analysis study on adherence to HAART among adult PLWHIV in Ethiopia. The finding of this study will strengthen adherence to HAART services and national HIV/AIDS control programs. Therefore, the study is aimed to determine the pooled prevalence of adherence to HAART and the effect of serostatus disclosure on adherence to HAART among adult PLWHIV in Ethiopia.

Methods

Study design and searching strategy

The study employed two systematic reviews/meta-analyses: one to analyze the prevalence of adherence to HAART and another to review for the role of serostatus disclosure on ART adherence. These systematic review/meta-analysis studies were carried out on published and unpublished literatures to determine the pooled prevalence of adherence to HAART among adult PLWHIV in Ethiopia. Studies were found through electronic and manual searches using databases; PSYCH INFO, EMBASE, MEDLINE/Pubmed, Google Scholar, and Google for gray literature.

Articles were searched using the following searching terms; "adherence", "nonadherence", "compliance", "noncompliance", "missing dose", "highly active antiretroviral therapy", "HAART", "antiretroviral therapy", "ART", "adult people living with HIV", "adult PLWHIV", "adult HIV positive patients", "HIV disclosure", "serostatus disclosure", and "Ethiopia", the articles were restricted to the publication date from January 2016 to November 2019 studied in Ethiopia.

Inclusion and Exclusion Criteria

Those published/unpublished articles in Ethiopia on adult PLWHIV from January 2016 to November 2019 in the English language were searched. Articles that report the prevalence of adherence/non-adherence to HAART/ART and/or articles that show the association of serostatus disclosure to adherence to HAART/ART were included in the study. Conference papers, articles without full texts, and qualitative studies were excluded from the study.

Data extraction

Two reviewers (AWA & ZBT) screened the titles and abstracts of identified studies and assessed the full text of potentially eligible studies. Any controversy was resolved by consensus. An effort was made to communicate with the authors' whenever further information was needed. Data were extracted independently by these reviewers. Data on the author(s), study year/year of publication, the region of study, study design, adherence status, sample size, and HIV serostatus disclosure such as odds ratio and standard error were extracted using Microsoft excel. The adherence status to HAART and the association of serostatus disclosure on adherence to HAART among adult PLWHIV in Ethiopia was extracted from each included study by CKM, KGY, and AJF. The whole manuscript was critically reviewed by all authors.

Quality Appraisal

Articles were assessed for quality score using the New Castle Ottawa Scale adapted for cross-sectional studies quality assessment tool with a score of ≥ 5 out of 10, considered as high-quality score(20). Two authors (AWA & ZBT) assessed the quality of each paper. The reviewers compared the quality of appraisal scores and resolved inconsistencies prior to calculating the final appraisal score. All included studies had a high quality of scores. The preferred reporting items of systematic review and meta-analysis (PRISMA) guideline(21) was used to report the result of this study.

Data analysis

Data were analyzed using STATA version 11. The summary effect estimates of the prevalence were calculated by using a meta-analysis in a random effect model. Cochrane Q statistics and I^2 were used to estimate the presence of heterogeneity. I^2 test statistic results of 25%, 50%, and 75% were declared as low, moderate, and high heterogeneity respectively(22). Subgroup analyses by region were done to estimate the regional variations in the adherence status to HAART. Sensitivity analysis was used to see the discrepancy among studies. Egger's and Begg's test was used to estimate the publication bias. Trim and fill analysis was used to treat the potential publication bias.

Results

Selection and Identification of studies

A total of 3247 studies conducted in Ethiopia were retrieved, and of which 3082 studies were rejected just by reading their titles. Of the remaining 165 studies, 147 were excluded after reviewing the abstracts. Full-text articles of 18 studies that met or potentially met the inclusion criteria were assessed. After further screening, 15 articles were retained for inclusion for the systematic review. Of 15 studies included in the systematic review, 11 studies were excluded and 4 (23-26) articles were used for meta-analysis (**Fig 1**).

Characteristics of the articles

Of the fifteen full studies; eight of them were conducted in the Oromia region, three in the Amhara region, two in the SNNPR, one in Harar, and one in Addis Ababa. Relevant features of each study such as author, year of publication, the region of study, study design, study population, sample size, adherence status to HAART, and the association of serostatus disclosure to HAART were extracted. The majority of the articles' adherent status to HAART was measured using self-report and taking $\geq 95\%$ of the prescribed doses of medication is considered as good adherence to HAART (**Table 1**).

Table 1: General characteristics of included studies that report the adherence status to HAART and/its association with HIV disclosure status.

Author/ Year	Region	Adherence to measurement	Adherence definition	Sample size(n)	Adherence to HAART (%)
Dibaba et al./2016(27)	Oromia	self-report	100%	306	65
Hassen et al./2019(28)	Oromia	self-report	≥95% of the prescribed doses	352	73.6
Molla et al./2018(23)	Amhara	pill count	≥95% of the prescribed doses	440	88.2
Negasa et al./2017(29)	Harar	self-report	100%	314	65
Nuredin et al./2017(30)	SNNPR	self-report and pharmacy refill	≥95% of the prescribed doses	428	77.1
Efrem et al./2016(31)	Oromia	self-report	100%	383	89.3
Naod et al./2017(32)	Addis Ababa	self-report	≥95% of the prescribed doses	273	80.1
Kassahun et al./2017(33)	Oromia	self-report	≥95% of the prescribed doses	321	72.3
Hailu et al./2018(34)	SNNPR	pill count	≥95% of the prescribed doses	320	68
Wendwesen et al./2017(25)	Oromia	self-report and record review	>95% of prescribed doses	190	92.6
Shewaye et al./2016(24)	Oromia	self-report	100%	420	86
Tesfaye et al./2019(35)	Amhara	self-report	≥95% of the prescribed doses	418	71.8
Jima et al./2018(36)	Oromia	self-report	as per Robinson et al(37)adherence measurement	160	85.6
Abadiga /2019(26)	Oromia	pill count	≥95% of the prescribed doses	305	73.1
Mengstie /2018(38)	Amhara	self-report	≥95% of the prescribed doses	352	87.2

Notes; Study design; Cross-sectional, **Study population;** Adult People Living with HIV; **HAART;** Highly active antiretroviral therapy, **SNNPR;** Southern Nations Nationalities and peoples' region

Adherence to HAART

Among 15 cross-sectional studies, the prevalence of adherence to HAART ranged from 65% (27, 29) to 92.6%(25). The overall pooled prevalence of adherence to HAART is found to be 81.2% (80.1- 82.3)(Table 2). Based on subgroup analysis by region, the pooled prevalence of adherence to HAART was 79.82% (73.19, 86.45) in the Oromia region, 82.51 % (73.14, 91.87) in the Amhara region, and 72.7% (63.78, 81.61) in the SNNPR (Fig 2).

Table 2: The pooled prevalence of adherence to HAART among adult people living with HIV in Ethiopia.

Author/Year	ES	[95% CI]	% Weight
Dibaba et al. (2016)	65.	59.7 70.3	3.9
Hassen et al. (2019)	73.6	69 78.2	5.3
Molla et al. (2018)	88.2	85.2 91.2	12.3
Negasa et al. (2017)	65	59.7 70.3	4.0
Nuredin et al. (2017)	77.1	73.1 81.1	7.1
Efrem et al. (2016)	89.3	86.204 92.4	11.7
Naod et al. (2017)	80.1	75.364 84.8	5.0
Kassahun et al. (2017)	72.3	67.404 77.2	4.7
Hailu et al (2018)	68	62.889 73.1	4.3
Wendwesen et al.(2017)	92.6	88.878 96.3	8.1
Shewaye et al. (2016)	86	82.682 89.3	10.2
Aychew et al (2019)	71.8	67.486 76.1	6.0
Jima et al. (2018)	85.6	80.160 91.	3.8
Abadiga (2019)	73.1	68.123 78.1	4.5
Mengstie (2018)	87.2	83.710 90.7	9.
I-V pooled	ES	81.2 80.1 82.3	100
Heterogeneity chi-squared = 257.96 (d.f. = 14) p = 0.000			
I-squared (variation in ES attributable to heterogeneity) = 94.6%			
Test of ES=0 : z= 150.39 p = 0.000			

Notes: CI; Confidence Interval, DF; Degree of Freedom, ES; Effect Size

Heterogeneity test

As shown in the table, the heterogeneity test (I^2) is 94.6%. This indicates there is a considerable variation across studies but the sensitivity analysis indicates there is no study apart from lower and upper confidence intervals. All the studies concentrated around the point of the estimation. The funnel plot test is asymmetrical (**Fig 3**).

Publication bias

Publication bias was detected based on the graphic asymmetry of funnel plots, egger's test ($p < 0.05$), and Begg's test. In the Egger test, the p-value is 0.001 which shows that there is a publication bias. Therefore, the authors used a random effect model to treat bias. Furthermore, the trim and fill analysis was also computed.

The effects of Serostatus Disclosure on Adherence to HAART

To determine the effects of serostatus disclosure on adherence to HAART among PLWHIV in Ethiopia, a total of four cross-sectional studies (23-26) were used. This study revealed that clients who disclosed their serostatus to someone else are nearly three times more likely to adhere to their HAART compared to clients who did not disclose their serostatus(AOR= 2.99, 95%CI: 1.88, 4.77)(**Fig 4**).

Heterogeneity

The heterogeneity test (I^2) is 51.8% which indicates there is a considerable variation across studies. The funnel plot test is symmetrical. The sensitivity test indicates there is no study apart from lower and upper confidence intervals. All the studies concentrated around the point of the estimation.

Publication bias

Publication bias was detected based on the graphic asymmetry of the funnel plot and egger's test ($p < 0.05$). The test indicates the graphic funnel plot is symmetrical and the egger's plot test result is 0.063.

Discussion

Adherence to the prescribed HAART is considered as a parameter for successful long-term management of HIV infection. Fifteen-cross sectional studies conducted in Ethiopia were used for this review study and from which four articles were used for meta-analysis. The prevalence of adherence to HAART ranged from 65% to 96.2%. In this systematic review, the pooled prevalence of adherence to HAART was found to be 81.2% (80.1- 82.3). In the subgroup analysis, the pooled prevalence of adherence to HAART was 79.82 %(73.19, 86.45) in the Oromia region, 82.51%(73.14, 91.87) in the Amhara region, and 72.7%(63.78, 81.61) in the SNNPR. Our study finding is higher in a study conducted in >26 countries reviewed study with an adherence rate to HAART was 63%(39), India 70% (40), 62.3% a study reviewed on 53 countries (41). The discrepancy is due to variation in adherence measurement tool, the use of multiple interventions, and use of clinical trials. The finding of this review study is lower than a study conducted in Tanzania and Botswana, 98% and 93% (42, 43) respectively. The discrepancy is due to the fact that the

former studies are small sampled studies compared to this reviewed study. Furthermore, the finding of this study is lower than the national ART treatment guideline $\geq 95\%$ (44) and other reviewed studies conducted on 20 countries 90% (45), but the population were homosexual men.

The finding of this study revealed that serostatus disclosure improved adherence to HAART nearly by three times compared to those who did not serostatus disclosed ART users ($AOR= 2.99$, $95\%CI: 1.88, 4.77$). The serostatus disclosure is an adherence enhancing intervention (46). The study is supported by a global evidence study using a treatment supporter that enhances adherence to HAART (47). Using adherence to HAART supporter is a tool/an intervention for viral load suppression (48). A study was done on developed and developing nations' fear of serostatus disclosure and suspicion on treatment which resulted in decrease adherence to HAART (49). The serostatus disclosure to others results in a higher rate of adherence to HAART (19). HIV serostatus disclosing relieves stress and anxiety, providing a trusting relationship between the patient and supporter, and sharing positive messages(44). The authors used articles solely studied in Ethiopia. Further research is recommended by incorporating other African studies and numbers of factors.

Conclusion

The pooled prevalence of adherence to HAART among adult PLWHIV in Ethiopia was found to be low compared to WHO antiretroviral treatment recommendations. Having serostatus disclosure improved adherence to HAART. Adherence to HAART and serostatus disclosure have a role in the treatment outcome of HIV patients. Successful treatment of HIV/AIDS with HAART improves a patient's CD4 count and decreases viral load.

Abbreviations

AIDS; Acquired Immune Deficiency Syndrome, AOR; Adjusted Odds Ratio, ART; Antiretroviral Therapy, HAART; Highly Active Antiretroviral Therapy, HIV; Human immune deficiency Virus, PLWHIV; People Living With Human Immune-deficiency Virus

Declarations

Ethical Approval and consent to participate

Not applicable because no primary data collected

Consent for publication

Not applicable

Availability of data and Material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interest

The authors declare that there is no competing of interest

Funding

The authors' did not receive any funding

Authors' contribution

AWA conceived the idea and design this research work. CKM, AJF, KGY, and ZBT participated in the data extraction, analysis, and interpretation. All the authors approved the final draft of the manuscript.

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Figures

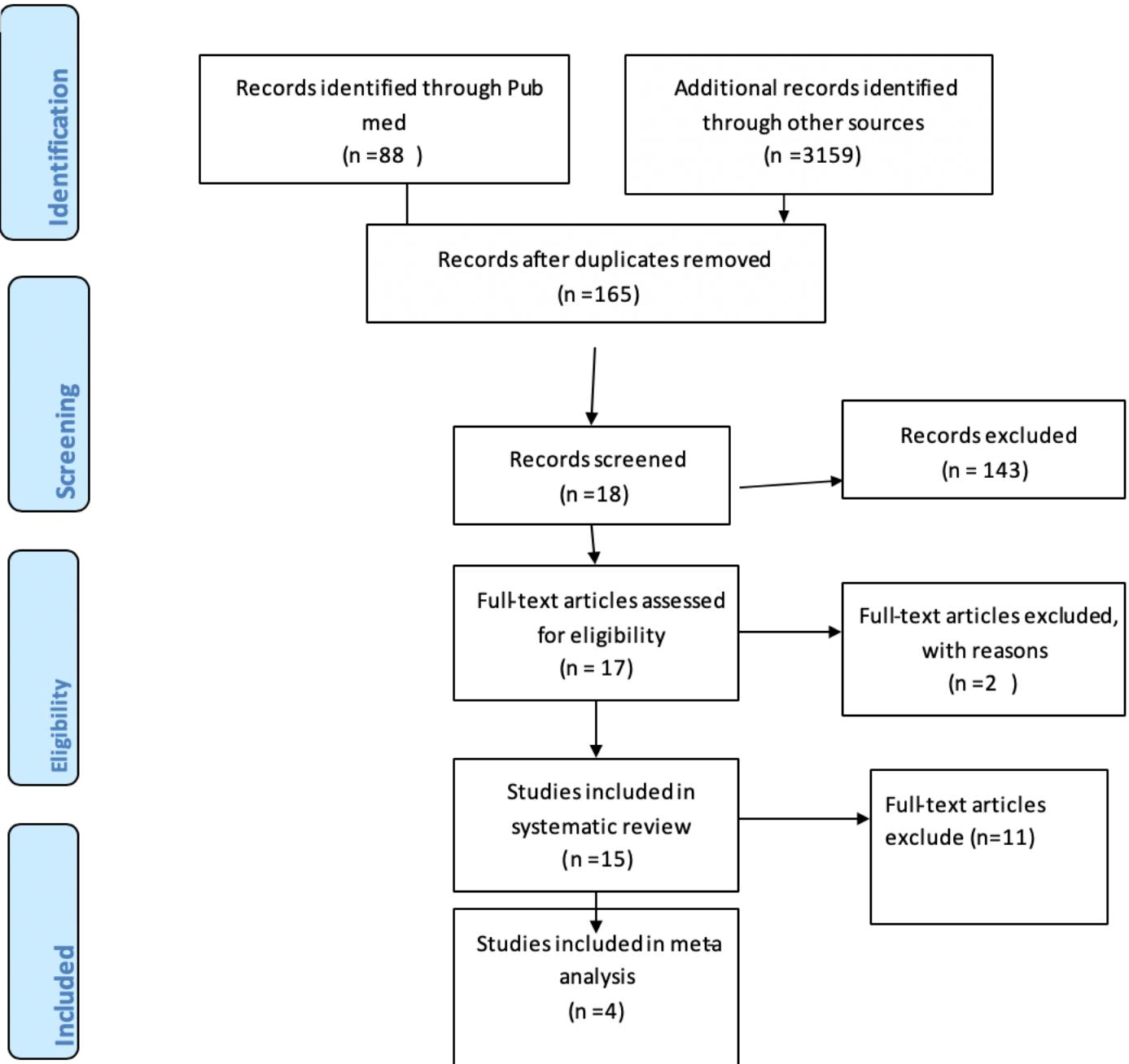


Figure 1

Flow diagram for study selection

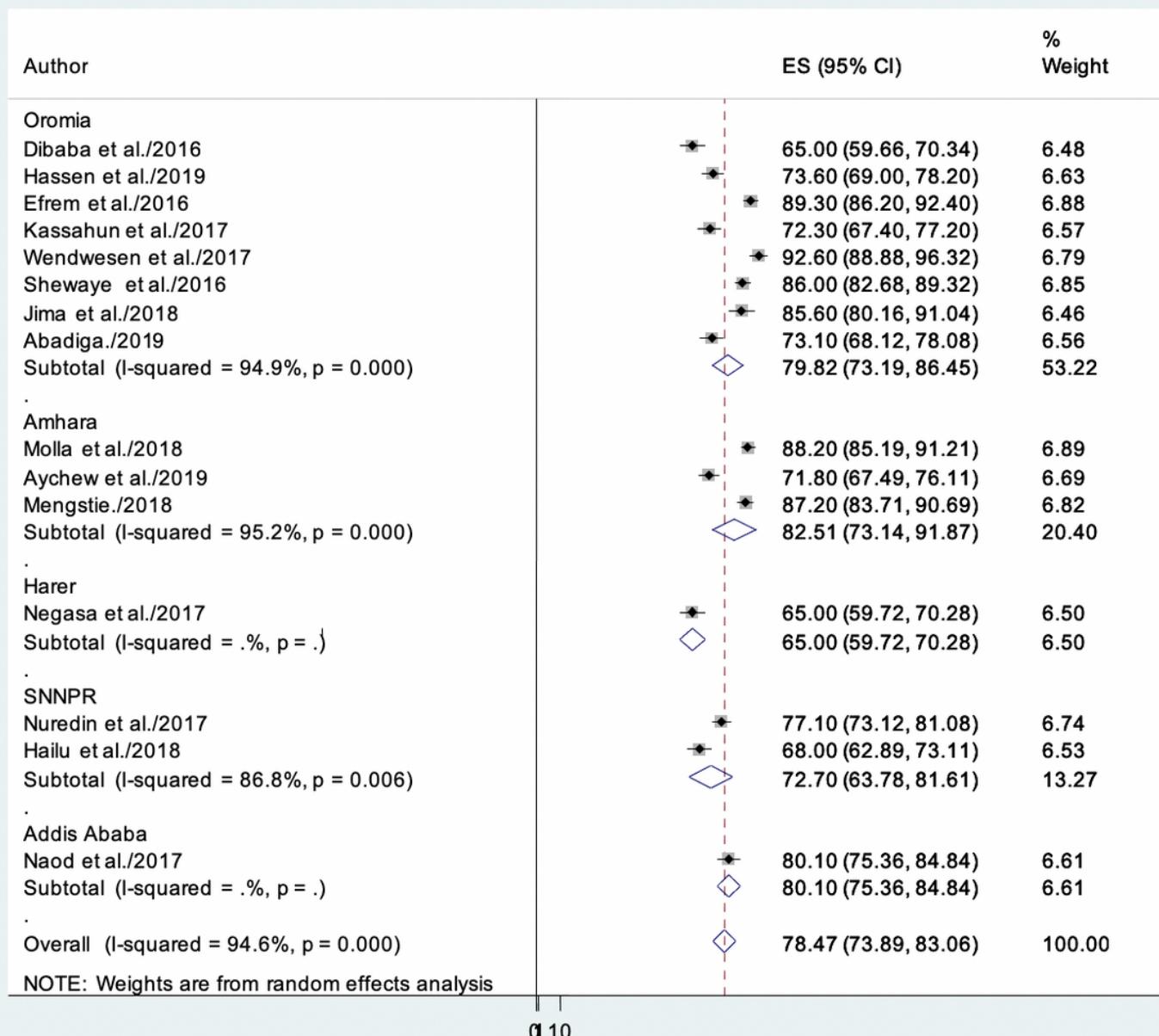


Figure 2

Subgroup analysis shows the pooled prevalence of adherence to highly active antiretroviral therapy

Funnel plot with pseudo 95% confidence limits

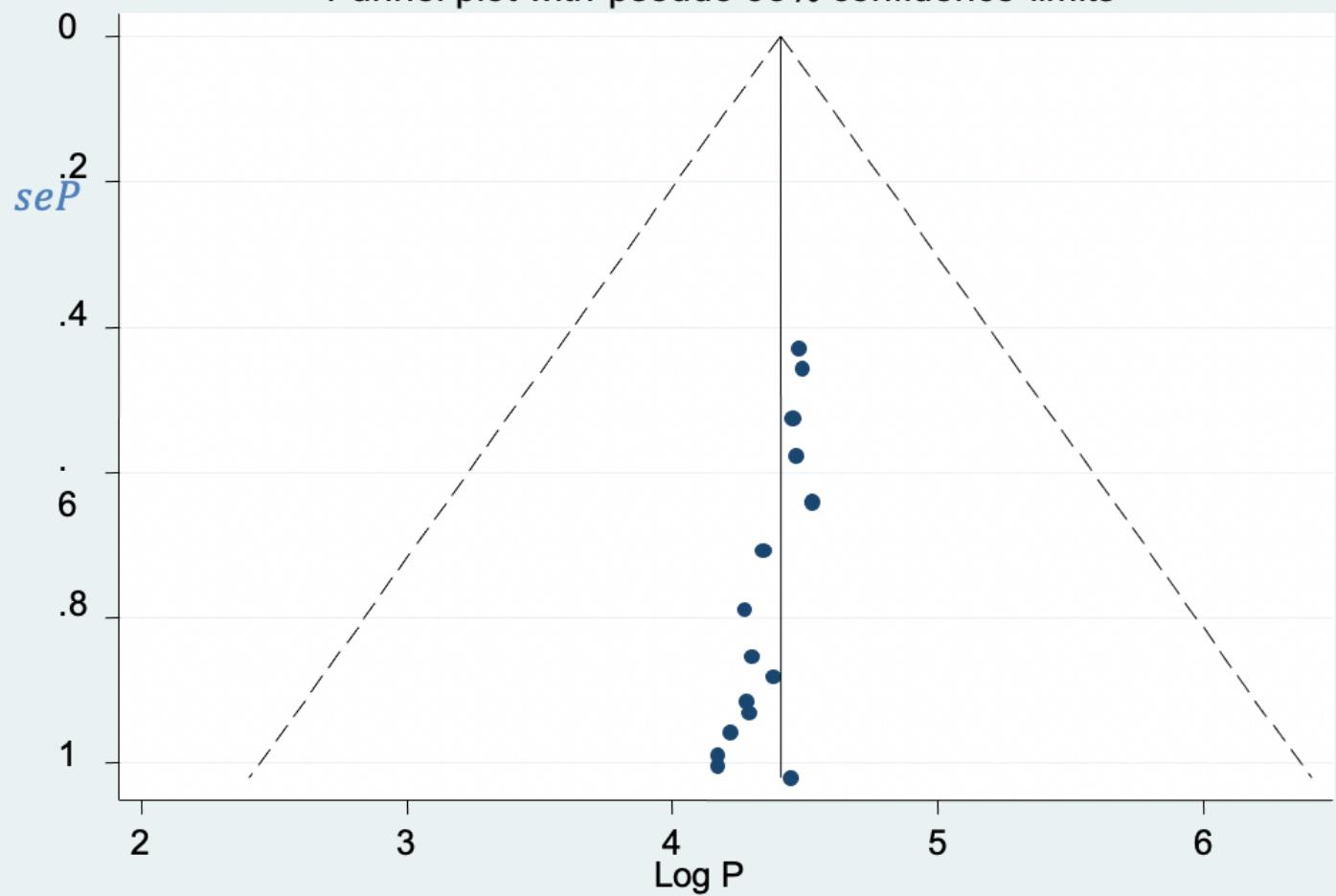


Figure 3

Funnel plot for adherence to highly active antiretroviral therapy

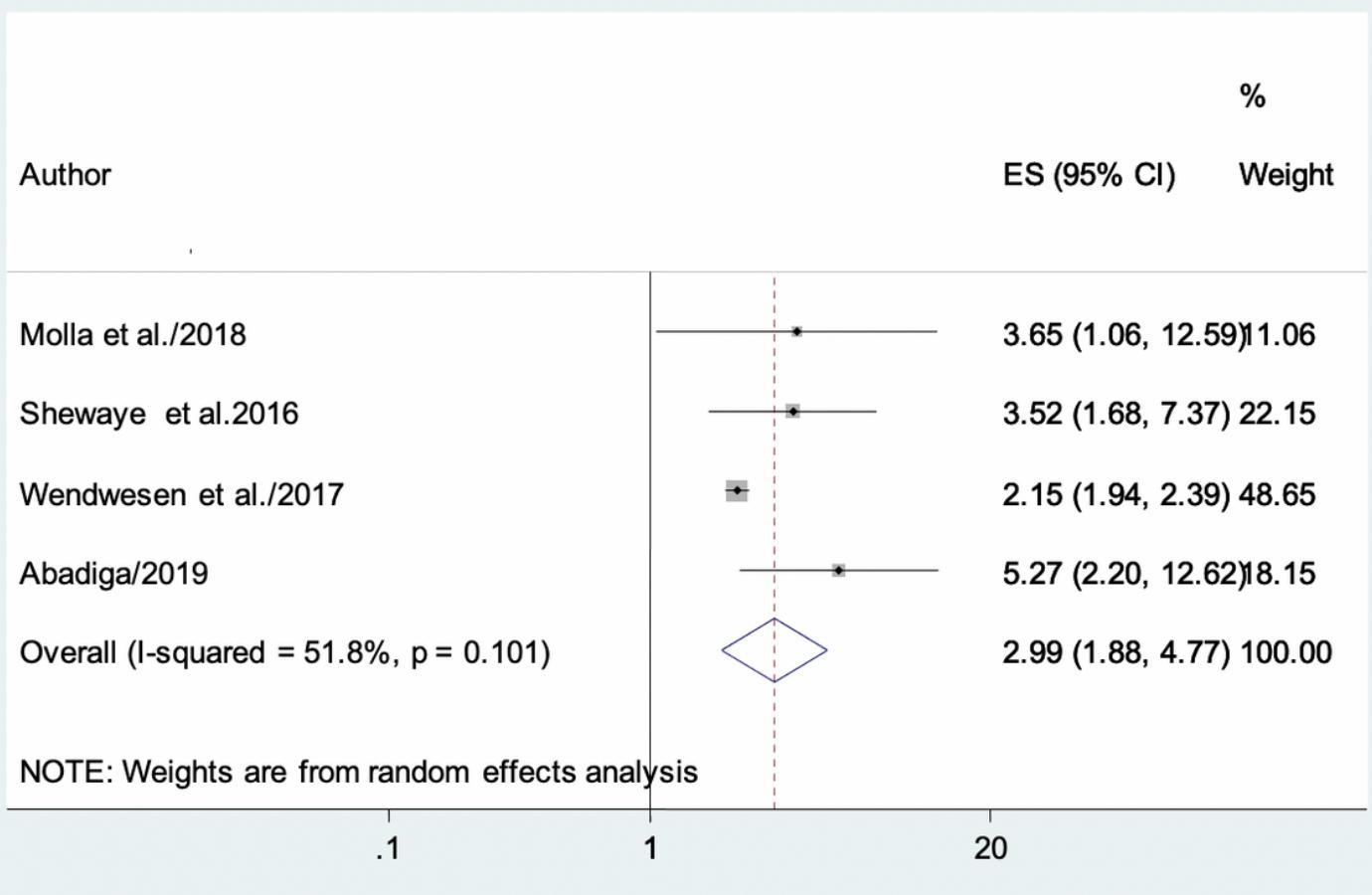


Figure 4

The effect of serostatus disclosure on adherence to highly active antiretroviral therapy

Supplementary Files

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

- PRISMA2009checklist.doc