

# Adherence to Highly Active Antiretroviral Therapy and Its Association with HIV Disclosure status among People Living with HIV/AIDS in Ethiopia: A systematic review and Meta-Analysis.

Abere Woretaw Azagew (✉ [wabere@ymail.com](mailto:wabere@ymail.com))

University of Gondar <https://orcid.org/0000-0002-6270-5992>

Chilot Kassa Mekonnen

University of Gondar

Abebaw Jember Ferede

University of Gondar

Kassahun Gebeyehu Yazew

University of Gondar

Zewdu Baye Tezera

University of Gondar

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## Research article

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# Abstract

## Background:

Adherence to Highly Active Antiretroviral Therapy (HAART) medication is the pressing public health problem worldwide. Non-adherence to HAART leads to treatment failure, immunologic failure, and virological failure. Despite different interventions made; still, HAART medication adherence among adult people living with HIV/AIDS (PLWHA) is inconsistent across studies and the effect of HIV disclosure status was not well studied. Therefore this study determines the pooled prevalence of HAART adherence and its relationship with HIV disclosure status among Adult PLWHA.

## Methods

We searched 3247 both published and unpublished original articles from January 2016 to November 2019 in Ethiopia using different search engines.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 meta-analysis was performed. Cochran Q statistics and  $I^2$  were used to estimate heterogeneity. Eggers and Begg's test was used to assess the publication bias.

## Results

A total of 15 studies for systematic review and four studies for Meta-analysis were used. The pooled prevalence of HAART medication adherence is found to be 81.19% (80.132, 82.248). In the subgroup analysis, the pooled prevalence of HAART adherence 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. HIV disclosure improves HAART adherence by nearly three times compared to non-HIV disclosed HAART users (AOR=2.99, 95%CI: 1.88, 4.77).

## Conclusions

The pooled prevalence of HAART adherence among adult PLWHA was found to be low. Having HIV disclosure improved HAART medication adherence.

# Background

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

Globally and in sub-Saharan Africa there were 160,000 and 110,000 children had got HIV infection in different ways respectively (2–4). According to the WHO report in 2016, an estimated 2.1 million

adolescents were living with HIV of this 84% were living in sub-Saharan Africa(5). Sub-Saharan Africa(SSA) is the home for 76% of the global morbidity and 75% mortality of HIV/AIDS(6). According to the WHO global burden disease report at the end of 2016 in Ethiopia, there had been 39,140 new HIV infections,768,040 people living with the virus, and 28,650 HIV/AIDS deaths(6). Having good adherence to antiretroviral therapy (ART) known to prolong the life of HIV patients(7). On the contrary; non-adherence to antiretroviral therapy(ART) could lead to different complications such as treatment, immunological, and virological failure(8, 9). The human immune deficiency virus infection does not only affect the patient but also the families, communities, and the development of the country at large (2, 6). Furthermore, the country could also suffer from other infectious diseases, and end up with economic instability(10).

Antiretroviral therapy has a crucial clinical effect in decreasing viral replication and viral load which in turn increases the CD4 level and decreases the progress of HIV/AIDS(11). Though, the clinical outcome of ART depends mainly on the adherence of the patients to antiretroviral therapy (ART). Studies showed that ART adherence is second to CD4 count for accurately predicting the prognosis of AIDS and death(9, 12). There are different factors which have been contributing for ART adherence as stated by studies such as level of awareness about HIV, counseling about adherence, absence of co-morbidity, social support, a substance used, a side effect of the drug, depression, and disclosure(13–16).

As far as known, there is no published systematic review and meta-analysis on this topic. Besides, the lack of high quality data on the level of adherence and its associated factors was a great challenge to the national HIV/AIDS control programs for providing accurate data to run intervention strategies. This study aimed to determine the pooled adherence of ART and its factors among adults PLHIV in Ethiopia.

## **Methods**

### **Study design and searching strategy**

This systematic review study was carried out from published and unpublished literature to determine the pooled prevalence of adherence to antiretroviral therapy among adult people living with HIV/AIDS patients in Ethiopia. Studies were found through electronic and manual searches using databases; PSYCH INFO, EMBASE, MIDLINE/Pub med, Google scholar and Google for gray literatures. Using search terms; ((adherence or “non-adherence” or compliance or “non-compliance” or “missing dose” and “Highly Active Anti Retroviral Therapy” or HAART or “Anti Retroviral Therapy” or ART) and (“Adult People Living with HIV/AIDS” or “Adult PLWHA” or Adult HIV positive patients) and Ethiopia)) restricted to the publication date from January 2016 to November 2019.

### **Inclusion Criteria**

All observational studies reported on the adherence or non-adherence or non-compliance or a missed dose of Highly Active Anti Retroviral Therapy among Adult people Living with HIV/AIDS were included in

the study. Peer-reviewed studies with cross-sectional design and primary outcome of interest were included in the study.

### **Exclusion criteria**

Those studies which showed an unclear prevalence of adherence to HAART and their HIV disclosure status among adult PLWHIV were excluded in the study.

### **Data extraction**

Two reviewers (AW & ZB) screened the titles and abstracts of identified studies and assessed the full text of potentially eligible studies. Any controversy was resolved by consensus. We made some efforts to communicate the authors whenever further information was needed. Data from included studies were extracted independently by these reviewers. Data on the author(s), study year, a region of study, study design, the prevalence of adherence, sample size, and HIV disclosure status were extracted using Microsoft excel. The prevalence of adherence to HAART among adult PLWHA was extracted from each included study CKM, KGY, and AJF critically reviewed the whole manuscript.

### **Quality Appraisal**

Articles were assessed for quality score using the New Castle Ottawa Scale adapted for cross-sectional studies quality assessment tool, a score of  $\geq 5$  out of 10 considered as high quality score. Two authors (AW & ZB) assessed the quality of each paper. The reviewers compared the quality of appraisal scores and resolved any inconviency before calculating the final appraisal score. All included studies had a high quality of the score.

### **Data analysis**

A systematic review of pooled prevalence adherence to HAART was carried out using a random effect model, generating a pooled prevalence with 95% CIs using STATA software version 11. Cochrane Q statistics and  $I^2$  were used to estimate the presence of heterogeneity. Subgroup analyses by region were carried out because of significant heterogeneity between studies. 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 were used to treat the potential publication bias.

## **Results**

### **Selection and Identification of studies**

After removing duplicates, a total of 3247 studies were retrieved of which 3082 studies were rejected just by reading the titles. Of the remaining 165 studies, 143 were excluded after reviewing the abstracts. Full-text copies of 18 studies that met or potentially met the inclusion criteria were assessed. After further screening 15 papers were retained for inclusion for the systematic review. Of 15 studies included in

systematic review; 11 studies were excluded and 4 (10, 17-19) articles were used for meta-analysis (Figure 1).

## Characteristics of the articles

Of the 15 full studies, 8 of them were from the Oromia region, 3 in the Amhara region, 2 in the South nations and nationalities of republic (SNNPR), 1 in Harer, and 1 in Addis Ababa. Relevant features of each study including author, year, a region of study, study design, study population sample size, and prevalence of ART adherence were summarized below (Table 1).

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

Author/ Year	Region	Study design	Study population	Sample size(n)	Prevalence (%)
Abay et al./2016(20)	Oromia	Cross sectional	Adult people living with HIV	306	65
Abay et al./2019(21)	Oromia	Cross sectional	Adult people living with HIV	352	73.6
Abay et al./2018(10)	Amhara	Cross sectional	Adult people living with HIV	440	88.2
Abay et al./2017(22)	Harer	Cross sectional	Adult people living with HIV	314	65
Abay et al./2017(23)	SNNPR	Cross sectional	Adult people living with HIV	428	77.1
Abay et al./2016(24)	Oromia	Cross sectional	Adult people living with HIV	383	89.3
Abay et al./2017(25)	Addis Ababa	Cross sectional	Adult people living with HIV	273	80.1
Abay et al./2017(26)	Oromia	Cross sectional	Adult people living with HIV	321	72.3
Abay et al./2018(27)	SNNPR	Cross sectional	Adult people living with HIV	320	68
Abay et al./2017(18)	Oromia	Cross sectional	Adult people living with HIV	190	92.6
Abay et al./2016(17)	Oromia	Cross sectional	Adult people living with HIV	420	86
Abay et al./2019(28)	Amhara	Cross sectional	Adult people living with HIV	418	71.8
Abay et al./2018(29)	Oromia	Cross sectional	Adult people living with HIV	160	85.6
Abay et al./2019(19)	Oromia	Cross sectional	Adult people living with HIV	305	73.1
Abay et al./2018(30)	Amhara	Cross sectional	Adult people living with HIV	352	87.2

## Adherence to HAART

Among 15 cross-sectional studies, the prevalence of ART adherence ranges from 65% (20) to 92.6%(18). The overall pooled prevalence is found to be 81.19% (80.132- 82.248) (Table 2). Based on subgroup analysis by region, the pooled prevalence of ART adherence 79.82% (73.19, 86.45) in Oromia region, 82.51%(73.14, 91.87) in Amhara region, and 72.7% (63.78, 81.61) in SNNPR (Figure 2).

**Table 2: The pooled prevalence of HAART adherence among Adult people living with HIV/AIDS in Ethiopia.**

Author/Year	ES	[95% Conf. Interval]		% Weight	
Dibaba et al. (2016)	65.000	59.656	70.344	3.92	
Hassen et al. (2019)	73.600	68.995	78.205	5.28	
Molla et al. (2018)	88.200	85.186	91.214	12.32	
Negasa et al. (2017)	65.000	59.724	70.276	4.02	
Nuredin et al. (2017)	77.100	73.119	81.081	7.07	
Efrem et al. (2016)	89.300	86.204	92.396	11.68	
Naod et al. (2017)	80.100	75.364	84.836	4.99	
Kassahun et al. (2017)	72.300	67.404	77.196	4.67	
Hailu et al (2018)	68.000	62.889	73.111	4.29	
Wendwesen et al.(2017)	92.600	88.878	96.322	8.08	
Shewaye et al. (2016)	86.000	82.682	89.318	10.17	
Aychew et al (2019)	71.800	67.486	76.114	6.02	
Jima et al. (2018)	85.600	80.160	91.040	3.78	
Abadiga (2019)	73.100	68.123	78.077	4.52	
Mengstie (2018)	87.200	83.710	90.690	9.19	
I-V pooled	ES	81.190	80.132	82.248	100.00
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					

## Heterogeneity test

As shown from 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 away from a lower and upper confidence intervals. All the studies concentrated around the point of the estimations. The funnel plot test is asymmetrical (**Figure 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 author used a random effect model to treat bias. Furthermore, the trim and fill analysis was performed.

## The effect of disclosure status on ART Adherence

To determine the effect of HIV disclosure on ART adherence among PLWHIV, a total of four cross-sectional studies (10, 17-19) were used. The study showed that HIV disclosure improves ART adherence nearly by three times compared to non-disclosed HIV positive ART users (AOR= 2.99, 95%CI: 1.88, 4.77) (Figure 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 away from a lower and upper confidence intervals. All the studies concentrated around the point of the estimations.

## 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 was 0.063.

## Discussion

A high level of adherence to prescribed antiretroviral therapy is considered as a key parameter for successful long-term management of HIV infection. Fifteen-cross sectional studies were used for this review study, and the ART adherence ranges from 65–96.2%. In this systematic review, the pooled prevalence of HAART adherence was found to be 81.19% (80.132–82.248). In the subgroup analysis, the pooled prevalence of HAART adherence 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 Southern nations nationalities and people. Our study finding is higher in a study conducted in > 26 countries with an adherence rate of 63% (31), India 70% (32), 62.3% in 53 countries (33). The discrepancy is due to variation in using the optimal level of ART adherence, the cut point used, use of multiple interventions, and use of clinical trials. The finding of this review study is lower than a study conducted in Tanzania 84% (34, 35), Botswana, Tanzania and Uganda; on which the ART adherence was 98% for two-day recall, 92% for one-month self recall and 93% for one-month pharmacy pill count (34), and in a reviewed articles 90% (36), national ART guidelines in which adherence is > 95% (37).

The finding of this study revealed that HIV disclosure improved ART adherence nearly by three times compared to non-HIV disclosed ART users (AOR = 2.99, 95%CI: 1.88, 4.77). HIV disclosure is an adherence

enhancing intervention (38). The study is supported by a global evidence study using a treatment supporter that enhances ART adherence (39). Using ART adherence supporter is a tool/an intervention for viral load suppression (40). A study was done on developed and developing nations' fear of disclosure and suspicious on treatment decrease ART adherence (41). Sero-status disclosure to others results in a higher rate of ART adherence (42). Early and fully disclosure improved ART adherence. Disclosure is an essential tool in improving adherence and reduce mortality (43). HIV disclosure is a predictor of ART adherence HIV patients who disclosed their sero-status have strong support at the household level, but the stigma is the obstacle for disclosure (44). Stigma, lack of care/social support, and non-disclosure of HIV status are barriers to ART adherence (34, 45). HIV disclosing relieves stress and anxiety, providing a trusting relationship between the patient and supporter, and sharing positive messages(37). The authors used ART adherence measured by different adherence measurement scales which may over/underestimate the ART adherence status.

## **Conclusion**

The pooled prevalence of HAART adherence among adult PLWHA was found to be low. Having HIV disclosure improved HAART medication adherence. HAART adherence and HIV disclosure have a crucial role in the treatment outcome of HIV patients. Successful treatment of HIV/AIDS with HAART improves the 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 analysed during the current study are available from the corresponding author on reasonable request.

### **Competing interest**

The author 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

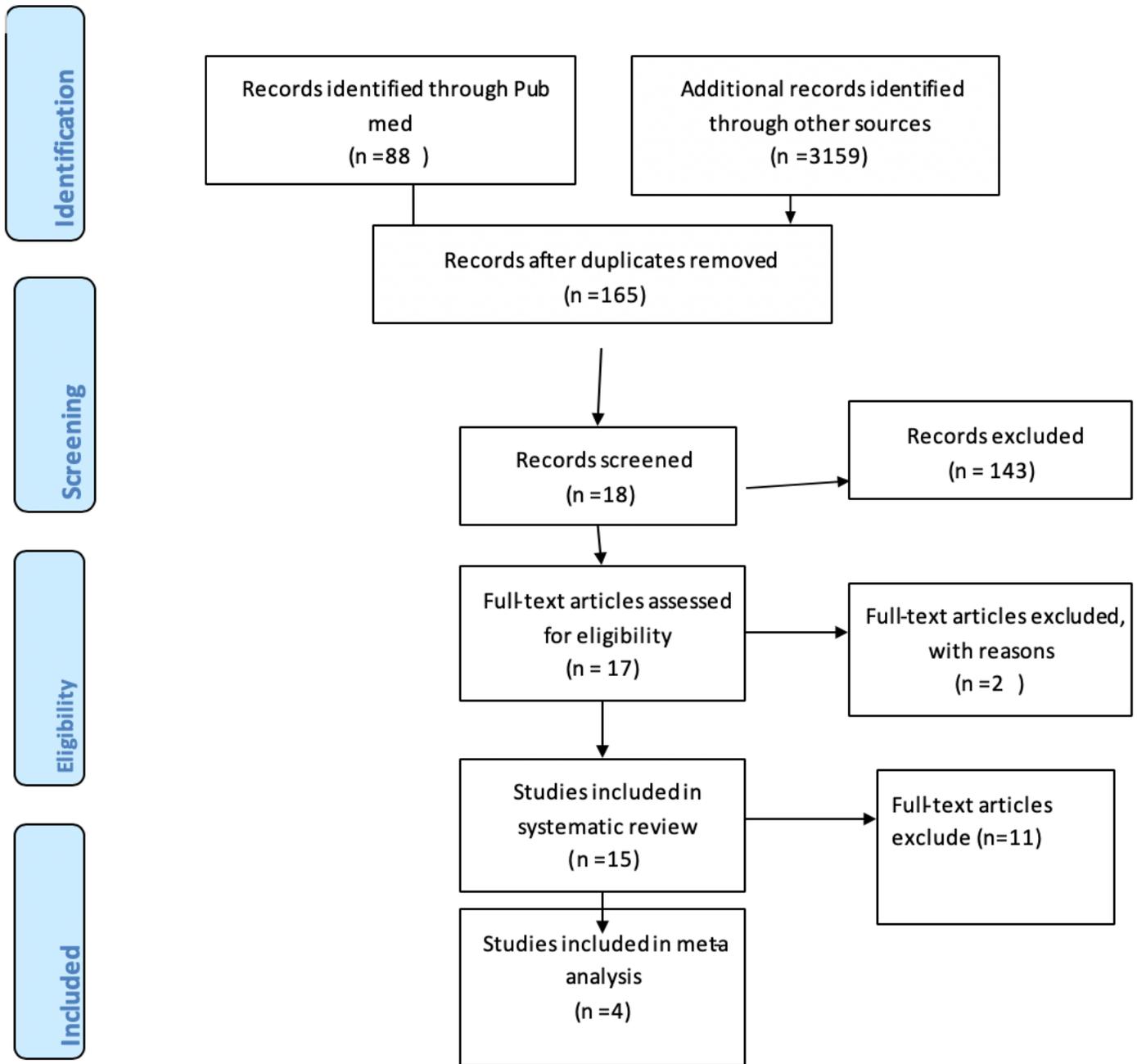
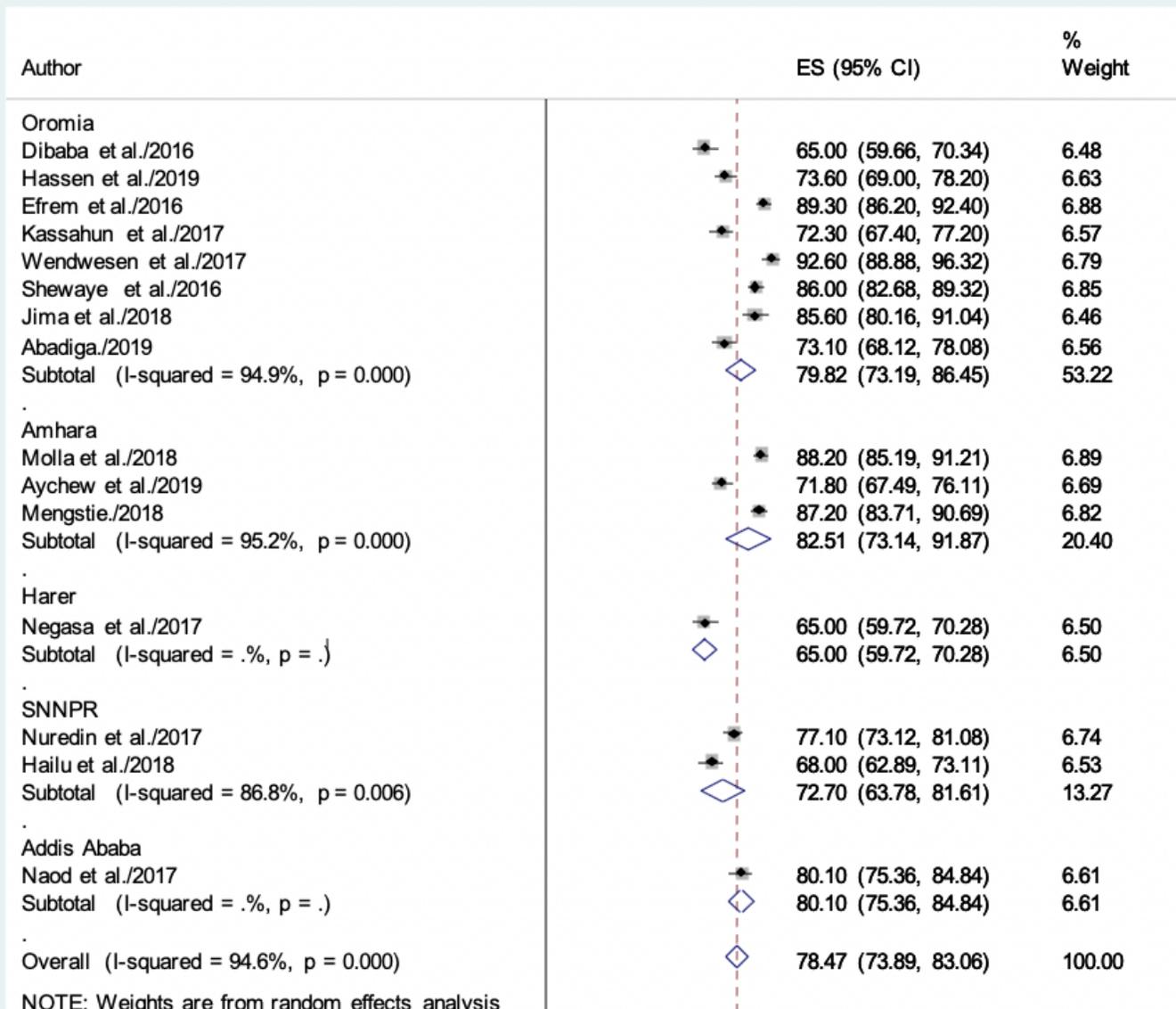


Figure 1

Flow diagram of Study selection



10

Figure 2

Subgroup analysis shows the pooled prevalence of HAART adherence

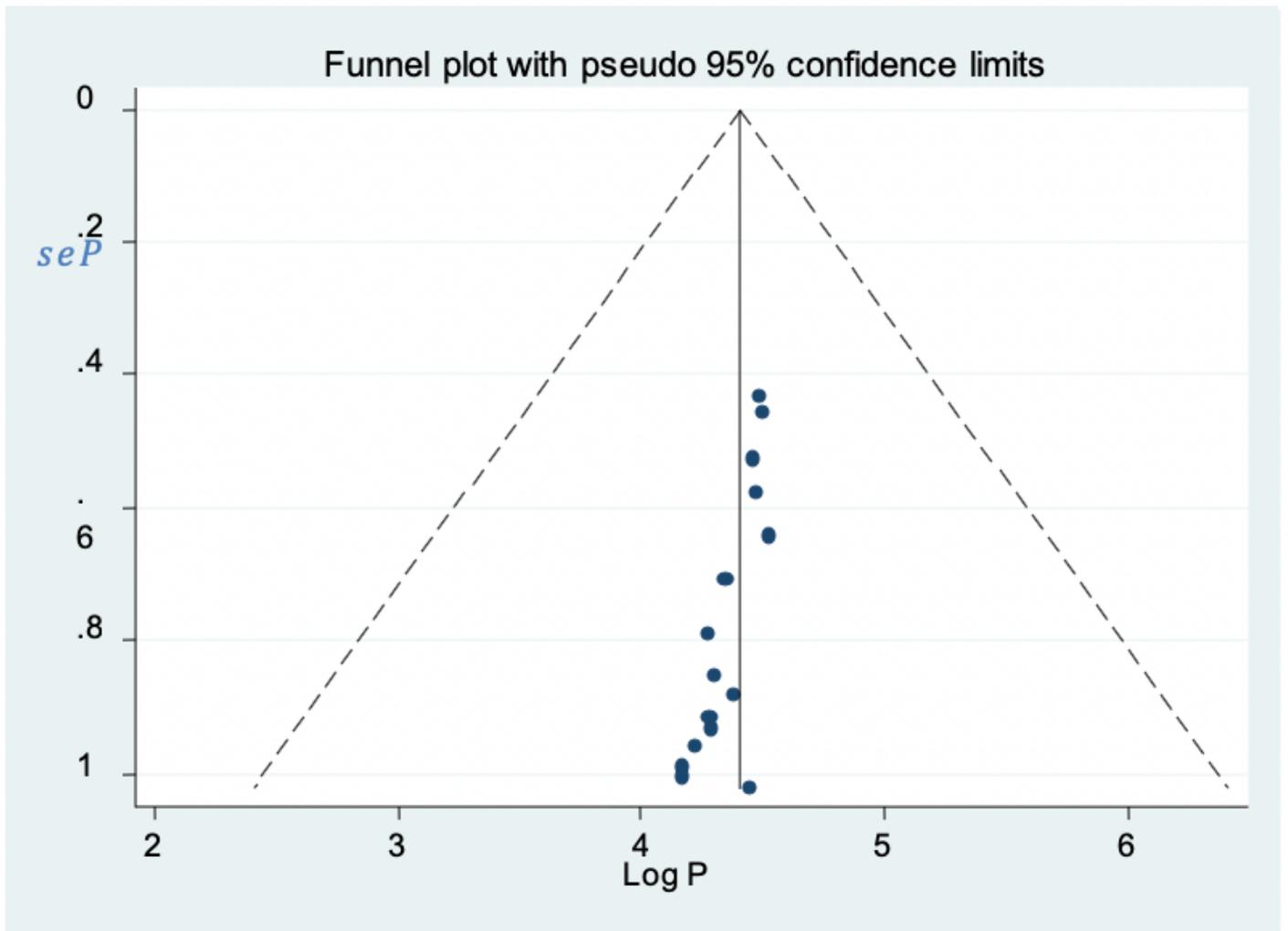
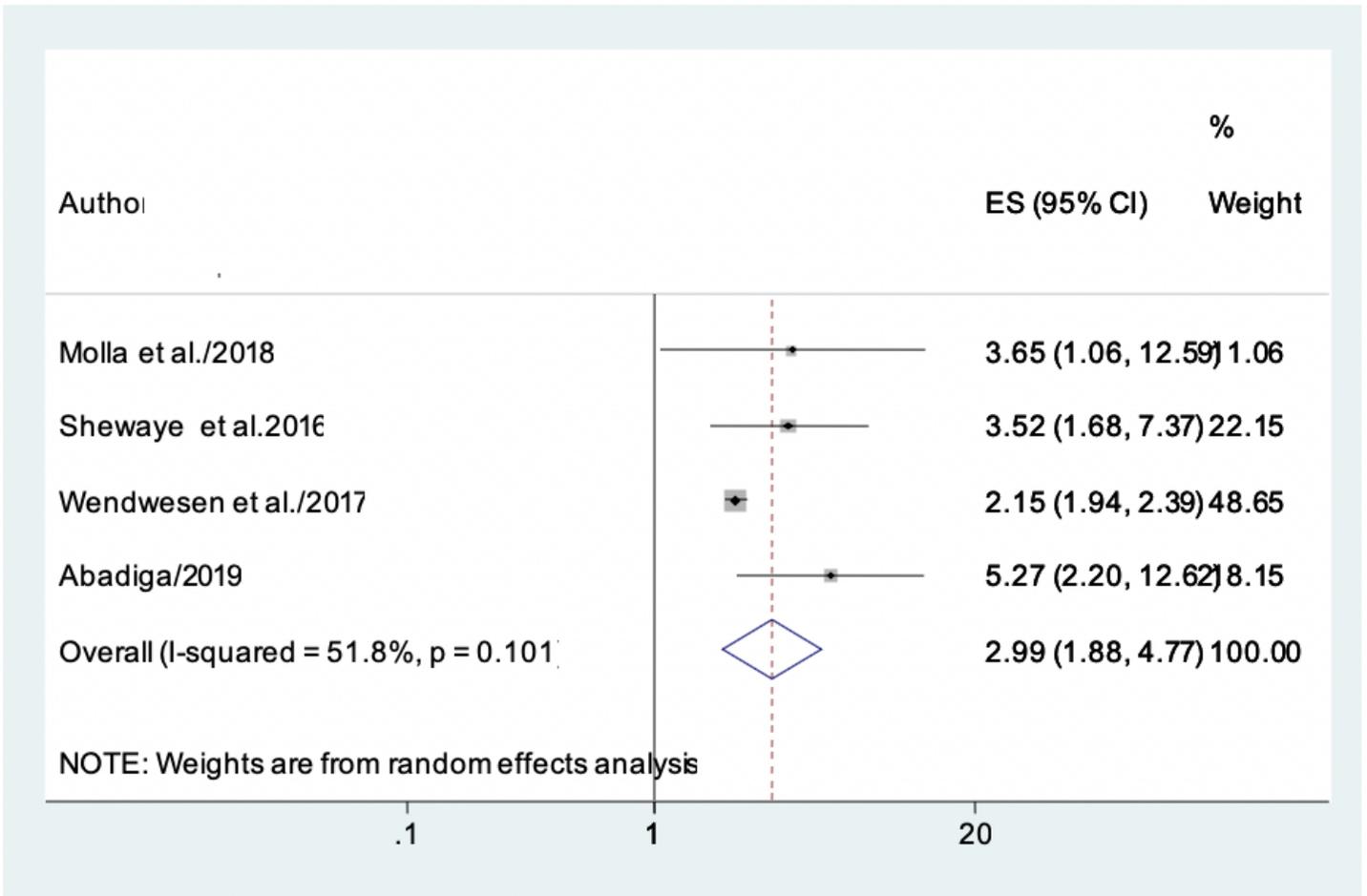


Figure 3

Funnel plot for the ART adherence



**Figure 4**

The effect of HIV disclosure on HAART adherence

## Supplementary Files

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