SUBSTANTIVE REVIEW

Associations Between Anxiety and Adherence to Antiretroviral Medications in Low- and Middle-Income Countries: A Systematic Review and Meta-analysis

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Abstract

Untreated mental health disorders among people living with HIV (PLHIV) may prevent low- and middle-income countries (LMICs) from achieving the UNAIDS 90-90-90 targets. Anxiety disorders may be associated with decreased adherence to antiretroviral therapy (ART). We sought to review and meta-analyze studies estimating associations between anxiety and ART adherence in LMICs. We searched PubMed, PsychINFO, CINAHL and EMBASE for relevant studies published before July 18, 2018. We defined anxiety as reported anxiety scores from screening questionnaires or having a clinical diagnosis of an anxiety disorder, and poor ART adherence as missed doses, poor visit attendance, or scores from structured adherence questionnaires. We used a random effects model to conduct a meta-analysis for calculating a pooled odds ratio, and conducted sensitivity analyses by time on ART, anxiety evaluation method, and study region. From 472 screened manuscripts, thirteen studies met our inclusion criteria. Eleven studies were included in the meta-analysis. PLHIV who reported anxiety had 59% higher odds of poor ART adherence compared with those who did not report anxiety disorder (pooled odds ratio [pOR]: 1.59, 95% confidence interval [CI] 1.29–1.96, p < 0.001). When excluding PLHIV who initiated ART within 6 months, reported anxiety remained strongly associated with poor ART adherence (pOR: 1.61, 95% CI 1.18–2.20, p = 0.003). Among PLHIV in LMICs, reported anxiety was associated with poor ART adherence. This association persisted after the ART initiation period. Increased resources for mental health may be important for achieving virologic suppression in LMICs.

Keywords HIV · Antiretroviral therapy · Anxiety · Adherence · Low-income countries

Introduction

While many high-income countries have achieved significant progress towards the UNAIDS 90-90-90 goals [1, 2], four years after their inception, many low- and middle-income countries (LMICs) are not on target to reach these goals [2]. Closing this gap will require interventions tailored to vulnerable populations, including people living with co-morbid HIV and mental health disorders [2]. Health systems in most LMICs do not provide adequate mental health services; an estimated 74% of people living with mental illness in LMICs still receive no treatment [3]. In 2014, the World Health Organization (WHO) set a goal for 80% of countries to have at least two national programs to better address mental health by 2020. Currently, however, only 32% of countries meet this criteria [4].

The majority of existing literature on mental health and HIV in LMICs focuses on depression. Depression is associated with poor ART adherence [5], risky sexual behavior [6], lower CD4 counts [7], and treatment failure [8, 9]. While not as well studied, anxiety disorders may also interrupt the cascade of HIV care by making individuals less likely to present for HIV testing, remain engaged in HIV care, and adhere to antiretroviral therapy (ART) [10–15]. Anxiety has also been associated with risky sexual behavior, increasing the risk for

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further transmission [10, 16, 17]. Although estimates suggest there is a substantial burden of anxiety among people living with HIV (PLHIV) in LMICs, research and interventions targeting anxiety in these settings have been limited [4, 18]. Thus, little is known about the effects of untreated anxiety on HIV viral load suppression and mortality.

Previous reviews have focused on the epidemiology of all mental health conditions and their prevalence among PLHIV, but have not assessed associations between mental health and HIV-related clinical outcomes [19]. Moreover, previous reviews on anxiety and HIV predate the change to the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) removing post-traumatic stress disorder (PTSD) from the "anxiety disorder" category [18–21]. We sought to describe associations between anxiety and poor ART adherence among PLHIV in LMICs, with the aim of addressing these gaps in the literature and motivating further research.

Methods

Search Strategy

Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22], we searched PubMed, CINAHL, PsycINFO, and Embase for articles published from database inception until July 16th, 2018. Our search included keywords relating to HIV, antiretroviral therapy, adherence, mental health, anxiety disorders, screening for anxiety disorders, and a list of LMICs (Appendix 1). We also manually searched the reference lists of all studies included in the final sample for eligible studies not captured by our database search.

Study Selection and Extraction

Results from each database search were uploaded to Covidence.org [23]. Duplicate articles were removed, and two authors (JW and CK) independently reviewed titles and abstracts and discussed any disagreement prior to making a final decision. The same two authors then performed full-text review on the included articles, alternating primary and secondary extraction with a standardized form. When data clarifications were needed, we contacted corresponding authors to request or clarify additional data.

Eligibility Criteria

Study Design and Population

We included cross-sectional studies, case–control studies, retrospective and prospective cohort studies, and randomized controlled trials. We excluded qualitative studies, systematic reviews, and non-peer reviewed abstracts. When multiple time points were reported from randomized controlled trials and cohort studies, we used the initial enrollment data to better correspond with the data reported in the other cross-sectional studies. Using World Bank Classifications [24], we included any paper reporting data from a low-income, lower middle-income, or upper middle-income country. We did not exclude articles based on the duration of ART use. We excluded studies recruiting participants under age 15, or participants not on ART, unless eligible subgroup analyses were available.

Exposure

Our primary exposure of interest was reported anxiety. We included papers that included either the diagnosis of an anxiety disorder or self-reported anxiety symptoms as an exposure variable. We defined anxiety by positive responses on a structured screening questionnaire, or a clinical diagnosis made during a diagnostic interview. When anxiety scores were reported in multiple groups (e.g., "mild," "moderate," and "severe" anxiety) we categorized the data into "no anxiety" and "some anxiety" for the analysis. We excluded papers that focused exclusively on PTSD. In addition, we extracted data on the prevalence of anxiety and methods used to measure anxiety.

Outcomes

Our primary outcome of interest was poor ART adherence. When multiple measures were used to evaluate adherence in the same population, we used whichever measure was more consistent with a "gold standard" method (previously used in a similar population and validated in prior research). However, when it was not possible to ascertain a "gold standard" measure, or the results were equivocal, we utilized the measure that evaluated adherence over a longer course of time. We attempted to include HIV-1 RNA levels (viral load) and CD4 count as secondary outcomes. However, as none of the included studies reported data related to these outcomes, we were unable to complete this analysis.

Data Analysis

We conducted a random effects meta-analysis to assess the pooled association between any reported anxiety and poor ART adherence. Our model included odds ratios as the common measure of association across eleven studies; we excluded data from studies reporting hazard ratio, risk differences, or correlation coefficient estimates which were not comparable to odds ratios. Of the included studies, six reported adjusted odds ratios that accounted for the influence

of potential confounding variables in their study populations, and five reported unadjusted odds ratios or proportions only.

We used a random effects model to adjust for within-study and between-study variance, given the different study locations and data collection measures [25]. We assessed between-study heterogeneity using the Cochrane Q statistic, I^2 proportion, and τ^2 statistic. We conducted analyses examining the influence of publication bias on our pooled odds ratio. All analyses were conducted using the *metan* package in Stata version 14 (StataCorp, College Station, TX).

We conducted four sensitivity analyses. The first focused only on studies where all participants had been on ART for at least six months to determine whether an association between reported anxiety and ART adherence might persist after an ART initiation phase. The second analysis included studies that used the Hospital Anxiety and Depression Scale to evaluate for reported anxiety, as this was the most commonly used measure to assess anxiety among the included studies. The final two sensitivity analyses were regional, with the first including studies located in Asia, and the second including studies located in Africa.

Results

Our search returned 664 titles for review. After removing 192 duplicate studies, 472 titles were included for abstract review (Fig. 1). 302 abstracts were excluded at the title/abstract level, leaving 170 articles for full-text review. Full-text review initially yielded 16 articles for inclusion. Three studies appeared to collect data that would have been compatible with our analysis, however, they did not report poor adherence outcomes in the manuscript. The authors were contacted and asked to provide this data, but none of these authors responded to multiple queries [26–28]. Consequently, these three articles were excluded, leaving 13
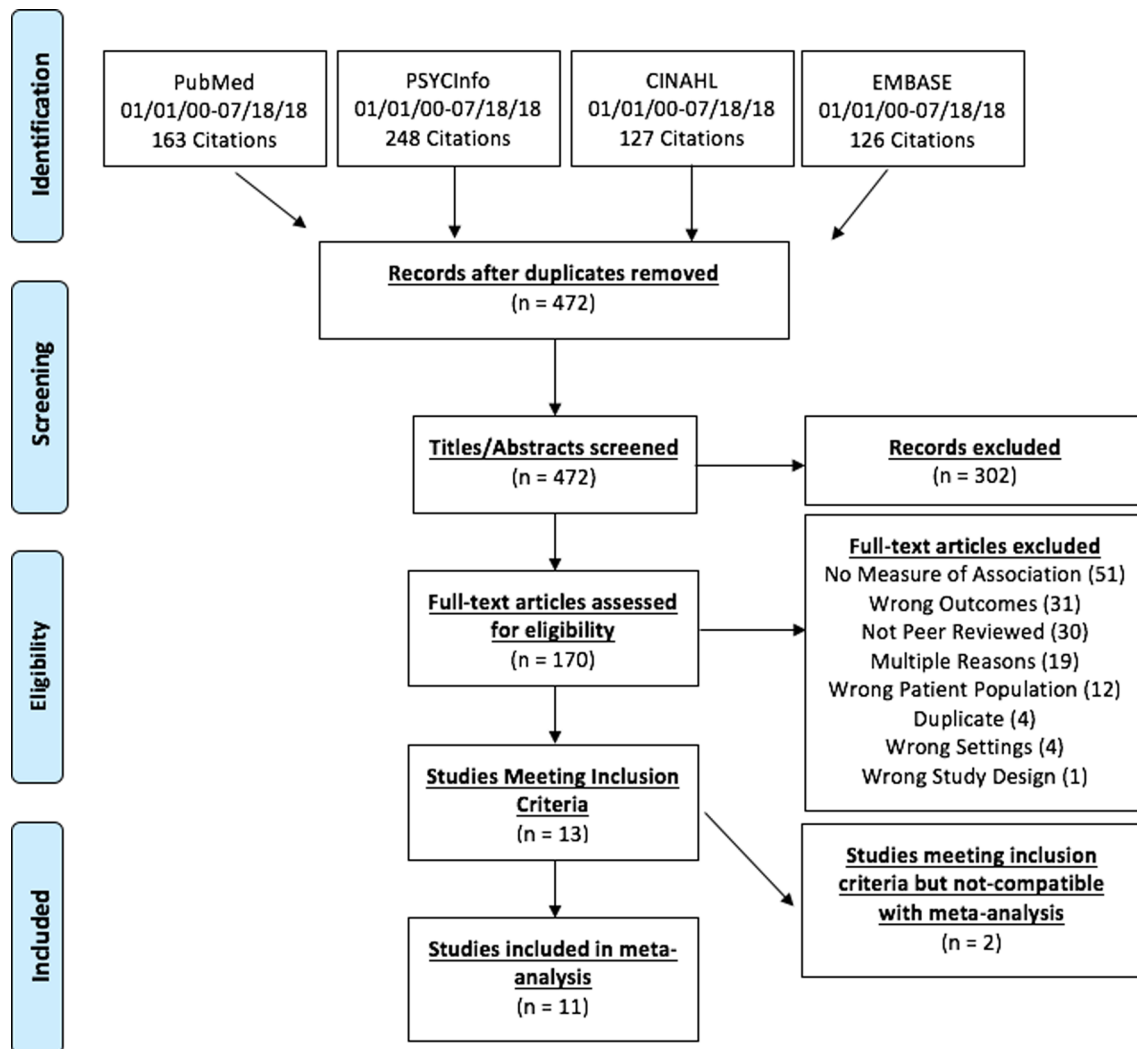

Fig. 1 PRISMA flow diagram of study identification, screening, and inclusion

articles for inclusion. Two titles met criteria for inclusion in the review but did not report data that could not be summarized for the planned meta-analysis [29, 30]. Of these two studies, one reported the association between anxiety and poor adherence as a hazard ratio [29], and the other reported it as a Pearson's correlation coefficient [30].

Characteristics of Included Sample

In total, the 13 studies included in the review (Table 1) ranged in sample size from 101 to 2924 participants [29–39]. One study included only male participants [39]. Among the other twelve studies, proportion of female to male participants varied from 11% [40] to 82% female [33]. Not all included studies reported participants' ages, however, among those that did the mean age ranged from 34.2 [27] to 42.1 years [26]. These papers were from eight unique countries, distributed across Africa, Asia, and South America. In ten studies, all participants had been taking ART for greater than six months, while two studies focused only on newly initiating patients, and one study did not distinguish between newly initiating and previously established patients. One paper focused exclusively on men who have sex with men (MSM) [39], while the remaining papers did not specify if any portion of the study population identified as MSM. None reported data relating to CD4 count and HIV viral load.

Measurement of Anxiety and Adherence

Six different tools were used to assess anxiety (Table 2). Six studies used the Hospital Anxiety and Depression Scale (HADS) [29, 31, 34, 35, 37, 39], two studies used the Generalized Anxiety Disorder 7-item scale (GAD-7) [38, 40] and two studies used the Comprehensive International Diagnostic Instrument [36, 41]. The remaining three studies used unique methods: Beck's Anxiety Inventory [33], the EQ-5D-5L [42], and the Zung Self-Rating Anxiety Scale [30]. Eleven of thirteen studies used questionnaires developed as screening tools for anxiety, while two [36, 41] used a structured interview and questionnaire. The total prevalence of reported anxiety ranged from 2.5% to 69.8%. Three studies used the same tool to assess adherence, [30, 34, 41], the AACTG questionnaire. The other ten studies each used a unique method. Of these, two [33, 40] used standardized, validated questionnaire tools, while the other used non-standardized self-report measures.

Outcomes

Among the eleven studies included in the final meta-analysis, reported anxiety was positively and strongly associated with poor ART adherence (pooled odds ratio [pOR]: 1.59, 95% confidence interval [CI] 1.29–1.96, p < 0.001) (Fig. 2).

Separate subgroup analysis excluding patients newly initiating ART also showed that anxiety was positively associated with poor ART adherence in participants previously established on ART (pOR: 1.61, 95% CI 1.18–2.20, p = 0.003) (Fig. 3a). Reported anxiety was also positively associated with poor ART adherence in a pooled analysis of the five studies that used the Hospital Anxiety and Depression Scale to assess anxiety (pOR: 1.78, 95% CI 1.18–2.68, p = 0.006) (Fig. 3b).

In the six studies located in Asia, anxiety was positively associated with poor adherence (pOR: 1.70, 95% CI 1.30–2.23, p < 0.001) (Fig. 3c). This included studies located in China, Nepal, Vietnam, Thailand, and India [31, 34, 39–42]. Among the four studies located in Africa, anxiety was not statistically significantly associated with poor ART adherence, (pOR: 1.15, 95% CI 0.79–1.67, p = 0.455) (Fig. 3d). These four studies were located in Cameroon, Nigeria, and South Africa [33, 36–38]. We did not pursue subgroup analysis for Latin American countries due to our search only returning one study, located in Brazil, that was compatible with our analysis [35].

Assessments of Heterogeneity and Publication Bias

For the eleven included studies, the Cochrane Q statistic was 18.15 (p = 0.052) and the I^2 proportion was 44.9%, representing moderate heterogeneity. The estimate of between-study variance (τ^2) was 0.045. Egger's test failed to demonstrate a statistically significant difference in effect size between smaller and larger studies (p = 0.898). A funnel plot of the eleven studies was asymmetric, however, subsequent trim and fill analysis which included three new hypothetical studies only slightly moved the random effects estimate closer to the null value (pOR: 1.39, 95% CI 1.00–1.78), and the pooled estimate remained statistically significant when these two hypothetical studies were included (p = 0.01).

Discussion

In this meta-analysis of 11 studies, reported anxiety was strongly associated with poor ART adherence among PLHIV in LMICs. This strong association persisted among those PLHIV received ART for at least six months. There was a wide range in reported anxiety prevalence. Anxiety was also associated with poor adherence among the five studies that used the Hospital Anxiety and Depression Scale (HADS) to assess adherence. Regional subgroup analysis demonstrated that reported anxiety was positively associated with poor ART adherence in Asia but failed to demonstrate a statistically significant association in among studies in Africa.

While the reported prevalence of anxiety varied among included studies, the reported prevalence of anxiety in

Table 1 Characteristics of included studies (n = 13)

Study	Location	Cohort description	Anxiety evaluation method	Study type	Anxiety prevalence	Adherence evaluation method	Poor adherence prevalence
Nguyen et al. 2016 [32]	Vietnam	1050 HIV + adults, on ART > 6 months	EQ-5D-5L	Cross-sectional	43.8%	30 day VAS scale	30.9%
Joshi et al. 2014 [34]	India	2924 HIV + adults, mix of newly initiating ART and on ART for > 6 months	Hospital anxiety and depression scale (HADS)	Cross-sectional	69.8%	AACTG questionnaire	24.0%
Guimares et al. 2008 [35]	Brazil	350 HIV + adults initiating ART	Hospital anxiety and depression scale (HADS)	Prospective cohort	36.0%	Patient interview	51.4%
Nel et al. 2013 [33]	South Africa	101 HIV + adults, on ART > 6 months	Beck's anxiety inventory	Cross-sectional	28.7%	Six item self-reporting questionnaire	45.5%
Adejumo et al. 2016 [36]	Nigeria	453 HIV + adults, on ART > 6 months	Composite international diagnostic instrument (CIDI)	Cross-sectional	2.5%	1 week and 1 month self-reported missed doses	9.7%
Yunusa et al. 2014 [37]	Nigeria	159 HIV + adults, on ART > 6 months	Hospital anxiety and depression scale	Cross-sectional	17.1%	Self-reported pattern of adherence	5.7%
Pefura-Yone et al. 2013 [38]	Cameroon	889 HIV + adults, on ART > 6 months	GAD-7, self-administered	Cross-sectional	11.1%	Antiretroviral medication self-report 7-day recall	22.5%
Tao et al. 2017 [39]	China	228 HIV + MSM on ART > 6 months	Hospital anxiety and depression scale	Prospective cohort	49.0%	Self-reported missed doses over last 3 months	8.0%
Prasithsirikul et al. 2017 [31]	Thailand	2023 HIV + adults, on ART > 6 months	Hospital anxiety and depression scale	Cross-sectional	4.5%	> 90% self-reported dose adherence	14.0%
Yu et al. 2018 [40]	China	207 newly diagnosed HIV + adults initiating ART	GAD-7	Cross-sectional	29.5%	CPCRA antiretroviral medications self-report questionnaire	14.5%
Pokhrel et al. 2018 [41]	Nepal	655 HIV + adults, on ART > 1 year	Comprehensive international diagnostic interview-Short Form (CIDI-SF)	Randomized controlled trial	11.6%	AACTG questionnaire	19.0%
Campos et al. 2008 [29][a]	Brazil	293 H HIV + adults, on ART > 6 months	Hospital anxiety and depression scale	Prospective cohort	12.6%	> 95% self-reported 3 day dose adherence	37.2%
Qiao et al. 2015 [30][a]	China	1254 HIV + adults, on ART > 6 months	Zung self-rating anxiety scale	Cross-sectional	Not reported	AACTG questionnaire	Not reported

[a]Not included in the final meta-analysis

Table 2 Tools for assessing anxiety

Measure of anxiety	Number of studies using this method	Number of studies using this method included in analysis	Description	Validated in study population?
Beck's anxiety inventory	1	1	21 item survey of anxiety signs/symptoms scored using a 3 point Likert scale [44]	Yes, in same country [58]
Composite international diagnostic instrument	2[a]	2	Structured comprehensive interview with standard questions assessing for mood, anxiety, and substance use disorders including 59 questions relating to anxiety signs/symptoms [59]	Yes, in same country [60–62]
EQ-5D-5L	1	1	5 questions regarding daily functioning and depression/anxiety; participants' anxiety is measured specifically by asking to answer the single question "I am ___anxious or depressed (not, slightly, moderately, severely, extremely) [48]	Yes, in same country [63]
GAD-7	2	2	7 item survey of anxiety signs/symptoms scored using a 4 point Likert scale [45]	Yes[b]
Hospital anxiety and depression scale	6	5	7 item survey of anxiety signs/symptoms scored using a 7 point Likert scale [46]	Yes [64–70] in all countries
Zung Self-rating anxiety scale	1	0	20 item survey of anxiety signs/symptoms using a 4 point Likert scale [47]	Yes [14], in the same country

[a]One of these studies used the "Short Form," which is a truncated version of the CIDI

[b]Validation not done in Cameroon, but in other sub-Saharan countries [50, 51]

studies using the HADS alone ranged from 4.5% to 69.8%, suggesting that the variation in overall prevalence found in our study is unlikely to be explained solely by the use of different diagnostic anxiety scales. In the study that reported the highest anxiety prevalence [43], conducted in India, the authors used the median HADS score to derive a categorical cut-off for anxiety, rather than a predetermined value. In comparison, the study with the lowest reported anxiety among those using the HADS [31], conducted in Thailand, used a pre-determined cutoff of anxiety scores greater than or equal to eleven out of fifteen possible points to diagnose anxiety. Despite using the same screening tool, this difference in diagnostic criteria may account for the large difference in anxiety prevalence across the included studies. Notably, the two studies with the lowest reported anxiety prevalence also reported two of the strongest associations between anxiety and poor adherence, and two of the lowest rates of poor ART adherence. [31, 36]. However, the

reported prevalence of anxiety and poor adherence also falls below prior estimates for people living with HIV in LMICs, and so it is likely that these discrepancies are related to challenges in accurately measuring anxiety and adherence in low-resource settings.

Many of the anxiety scales used in the included studies were meant primarily for screening rather than diagnosis, which could also have contributed to the variation in reported prevalence [44–48]. Screening tools are often used for diagnosis due to the lack of availability of trained clinicians, however the data presented here demonstrate the potential lack of reliability when they are used. While the WHO advocates for and outlines a general framework for screening for anxiety and other mental health conditions, they do not recommend the use of one screening tool over another [49]. A universal screening tool that has been validated for use in resource-limited settings, such as the GAD-7 [50, 51], would allow for uniformity across study data and
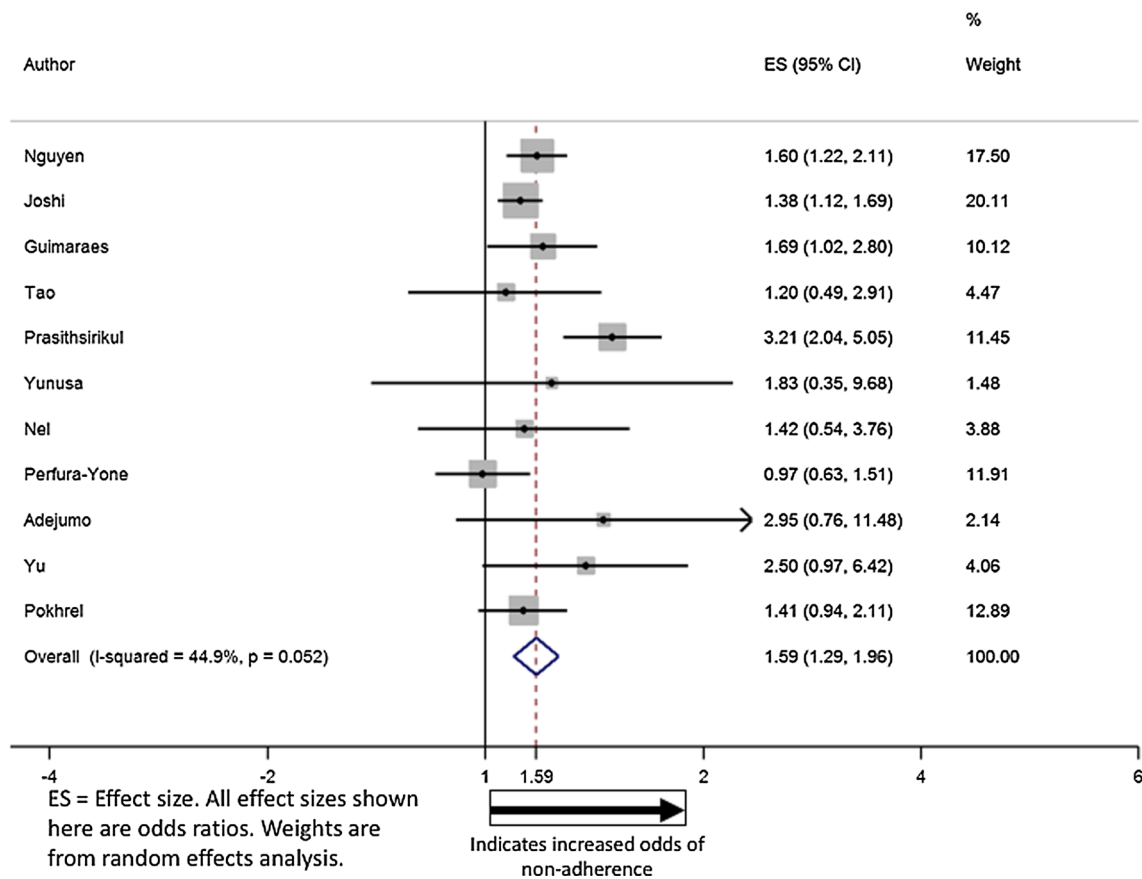
Fig. 2 Forest plot of odds ratios between anxiety and poor adherence

make training and scaling up of mental health programs easier. Regardless of the screening tool used, each instrument should be validated in the local language and culture, and adapted as needed, before widespread implementation [52, 53].

Given the limited mental health resources available in many LMICs, identifying patients that will most likely benefit from mental health-related interventions will be vital in moving towards the UNAIDS 90-90-90 treatment goals. The subgroup analysis of studies from Asia, coupled with the ongoing gap in viral suppression among people living with HIV in Asian countries [2] illustrates a clear need to scale up mental health resources in Asian countries. Though the analysis of studies located in Africa failed to demonstrate a statistically significant association, it was limited by a small sample size. For 90% of HIV-infected adults on treatment to be virally suppressed, health systems need to be able to identify those most at risk for poor adherence [54]. Though resources may be limited in many of the countries included in this review, effective, affordable mental health interventions have been validated in these settings; moving forward it is possible to increase access to these resources in a cost-effective manner [18].

This paper focuses on poor ART adherence as an outcome of anxiety disorders, however, virologic failure may be a better measure of HIV-related outcomes. While adherence can be used as a surrogate for viral suppression, it remains an imperfect marker, in part because many of the tools traditionally used to assess adherence are not completely sensitive or specific [55]. Accurately validating these tools is challenging, in part due to the lack of an inexpensive gold-standard against which to measure accuracy. As quantitative point-of-care viral load testing was recently approved by the WHO for use in resource-limited settings [56], viral load could be an effective surrogate for assessing adherence [57].

While a prior review assessed the association between symptoms of depression, alcohol use disorders, and ART adherence in sub-Saharan Africa [5], to our knowledge this is the first review specific to LMICs focused on anxiety and ART adherence. Our review is limited by the heterogeneity of the studies included, and a relatively small number of studies included in the meta-analysis. Additionally, because most of the included studies did not include outcomes stratified by age and gender, we were unable to perform further subgroup analysis. Two papers met inclusion criteria for our analysis but reported outcomes
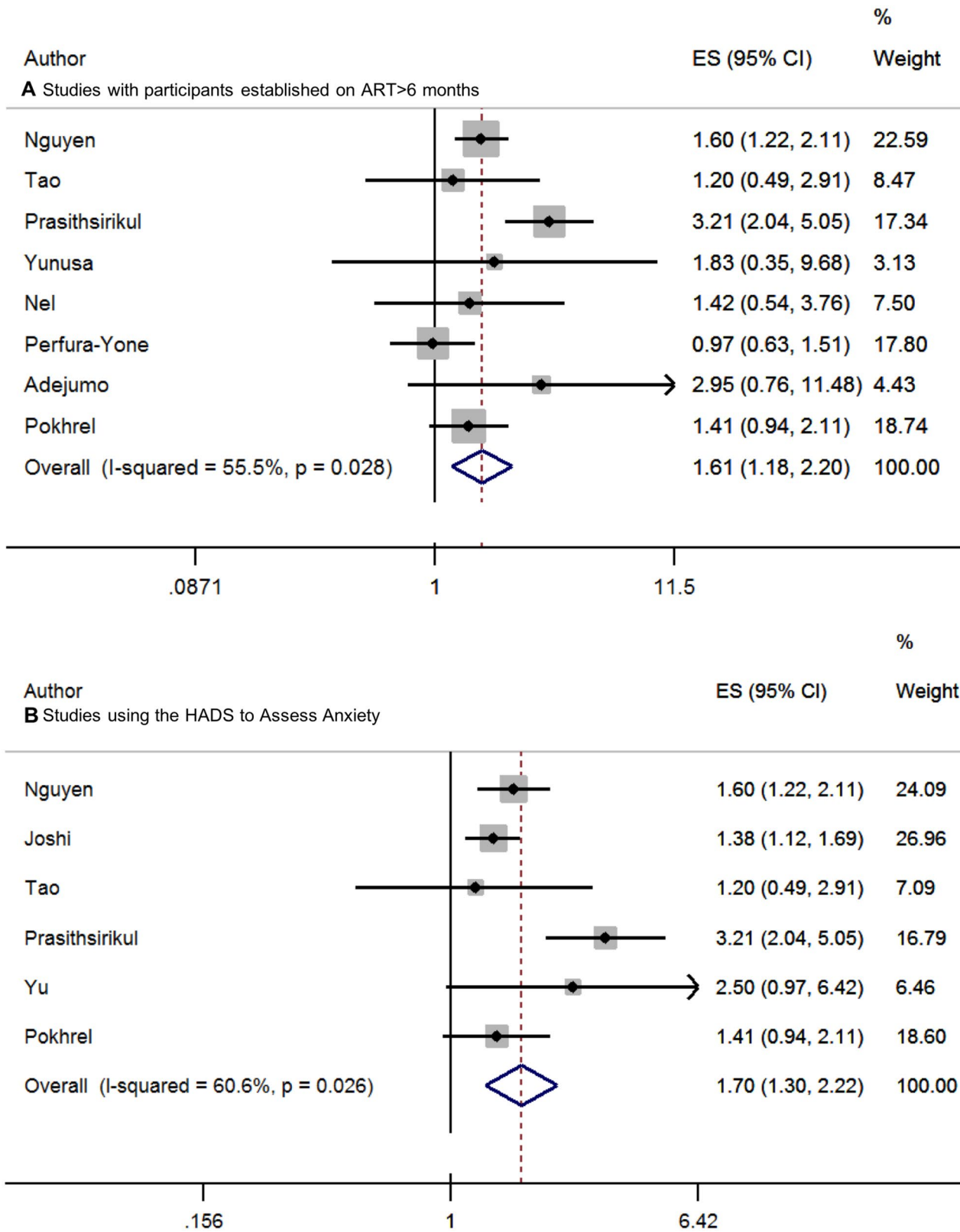
Fig. 3 a–d Forest plots of odds ratios between anxiety and poor adherence in four sensitivity analyses
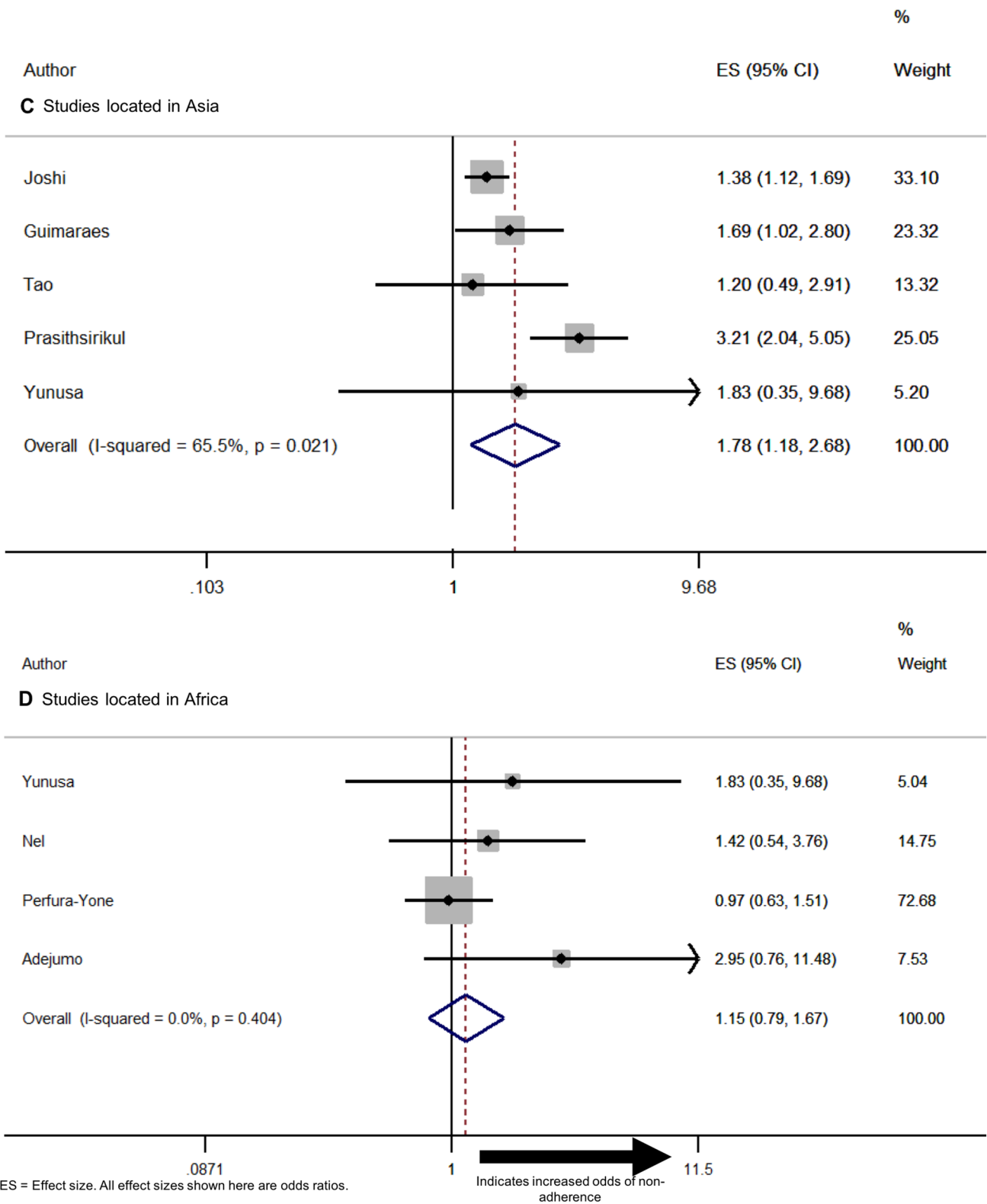
Fig. 3 (continued)

in a way that were not compatible with the meta-analysis [29, 39]. Both studies also demonstrated a positive association between anxiety and poor adherence. While our analysis demonstrated an association between anxiety and poor adherence, this does not prove a causal relationship. Additionally, due to the overall paucity of data on this topic, our analysis is limited by the inclusion of multiple study types. The majority of studies were cross-sectional, however, we also included three retrospective cohort studies, and one randomized controlled trial. Previous studies suggested that the association between anxiety disorder and ART adherence may be non-linear, with more severe anxiety disorder associated with increased ART adherence relative to no anxiety disorder. We were unable to confirm or dispute this characterization given the limited data available from LMICs.

Our analysis adds to the existing body of research regarding mental health and HIV in LMICs. Depression, alcohol use, and now anxiety have all been demonstrated to be associated with poor ART adherence. We recommend that future research on this topic focus on the role of an integrated, transdiagnostic mental health approach to screening and treatment of these related, but distinct conditions. Furthermore, we recommend further research to better characterize the association between anxiety severity and poor adherence, as this may help to better identify high-risk patients.

In conclusion, reported anxiety appears to be strongly associated with poor ART adherence among PLHIV in LMICs. The use of standardized, validated, and culturally adapted tools to measure anxiety and adherence would allow for more accurate analysis. Effective, evidence-based services for the treatment of anxiety disorder and other common mental disorders are warranted across LMICs. Once such services are available, PLHIV should be routinely screened for mental health issues, including anxiety.

Compliance with Ethical Standards

Appendix 1: Anxiety and ART Adherence in Sub-Saharan Africa: Systematic Review

Search Protocol

Specific Aims

1. Meta-analyze associations between anxiety and ART adherence in Sub-Saharan Africa

    a. Sub-aim: anxiety and viral load, anxiety and CD4 count

Methods

Search Terms

PsycINFO, PubMed, CINAHL

(antiretroviral therapy, highly active OR ART OR anti-hiv agents OR hiv infections/drug therapy OR HAART OR antiretroviral* OR HIV treatment* OR hiv therap* OR HIV)
    AND
(adherence OR nonadherence OR compliance OR non-compliance OR non-adherence OR non-compliance OR viral load OR CD4 OR viral suppress*)
    AND
(anxiety OR anxious OR "GAD" OR "Generalized anxiety disorder" OR "BAI" OR "Beck Anxiety Inventory" OR "HADS-A" OR "HOSPITAL ANXIETY AND DEPRESSION SCALE-ANXIETY" OR "STAI" OR "STATE-TRAIT ANXIETY INVENTORY")
    AND
(Afghanistan OR Albania OR Algeria OR Samoa OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Botswana OR Brazil OR Bulgaria OR Burkina Faso OR Burundi OR Cambodia OR Cameroon OR Cabo Verde OR Central African Republic OR Chad OR Chile OR China OR Colombia OR Comoros OR Congo OR Costa Rica OR Côte d'Ivoire OR Cote d'Ivoire OR Ivory OR Cuba OR Djibouti OR Dominica OR Dominican OR Ecuador OR

Egypt OR Salvador OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guinea-Bissau OR Guyana OR Haiti OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Lao OR Laos OR Latvia OR Lebanon OR Lesotho OR Liberia OR Libya OR Lithuania OR Macedonia OR Madagascar OR Malawi OR Malaysia OR Maldives OR Mali OR Marshall OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Panama OR Papua New Guinea OR Paraguay OR Peru OR Philippines OR Romania OR Russia OR Russian OR Rwanda OR Samoa OR Sao Tome OR Senegal OR Serbia OR Seychelles OR Sierra Leone OR Solomon Islands OR Somalia OR South Africa OR Sri Lanka OR St. Lucia OR St. Vincent OR Grenadines OR Sudan OR Suriname OR Swaziland OR Syrian OR Syria OR Tajikistan OR Tanzania OR Thailand OR Timor-Leste OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uruguay OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR "West Bank" OR Gaza OR Yemen OR Zambia OR Zimbabwe OR Africa OR sub-saharan OR developing countries[mh] OR "developing countries" OR "resource-limited" OR "resource-constrained" OR "low-and middle-income" OR LMIC OR "third world" OR "low income countries")

EMBASE

('highly active antiretroviral therapy' OR ART OR 'anti-hiv agents' OR 'hiv infections/drug therapy' OR HAART OR antiretroviral* OR 'HIV treatment*' OR 'hiv therap*' OR HIV)

AND

(adherence OR nonadherence OR compliance OR non-compliance OR non-adherence OR non-compliance OR 'viral load' OR CD4 OR 'viral suppress*')

AND

(anxiety OR anxious OR 'GAD' OR 'Generalized anxiety disorder' OR 'BAI' OR 'Beck Anxiety Inventory' OR 'HADS-A' OR 'HOSPITAL ANXIETY AND DEPRESSION SCALE-ANXIETY' OR 'STAI' OR 'STATE-TRAIT ANXIETY INVENTORY')

AND

(Afghanistan OR Albania OR Algeria OR Samoa OR Angola OR Antigua OR Barbuda OR Argentina OR Armenia OR Azerbaijan OR Bangladesh OR Belarus OR Belize OR Benin OR Bhutan OR Bolivia OR Bosnia OR Herzegovina OR Botswana OR Brazil OR Bulgaria OR 'Burkina Faso' OR Burundi OR Cambodia OR Cameroon OR 'Cabo Verde' OR

'Central African Republic' OR Chad OR Chile OR China OR Colombia OR Comoros OR Congo OR 'Costa Rica' OR Ivoire OR Ivory OR Cuba OR Djibouti OR Dominica OR Dominican OR Ecuador OR Egypt OR Salvador OR Eritrea OR Ethiopia OR Fiji OR Gabon OR Gambia OR Georgia OR Ghana OR Grenada OR Guatemala OR Guinea OR Guinea-Bissau OR Guyana OR Haiti OR Honduras OR India OR Indonesia OR Iran OR Iraq OR Jamaica OR Jordan OR Kazakhstan OR Kenya OR Kiribati OR Korea OR Kosovo OR Kyrgyz OR Lao OR Laos OR Latvia OR Lebanon OR Lesotho OR Liberia OR Libya OR Lithuania OR Macedonia OR Madagascar OR Malawi OR Malaysia OR Maldives OR Mali OR Marshall OR Mauritania OR Mauritius OR Mexico OR Micronesia OR Moldova OR Mongolia OR Montenegro OR Morocco OR Mozambique OR Myanmar OR Namibia OR Nepal OR Nicaragua OR Niger OR Nigeria OR Pakistan OR Palau OR Panama OR 'Papua New Guinea' OR Paraguay OR Peru OR Philippines OR Romania OR Russia OR Russian OR Rwanda OR Samoa OR 'Sao Tome' OR Senegal OR Serbia OR Seychelles OR 'Sierra Leone' OR 'Solomon Islands' OR Somalia OR 'South Africa' OR 'Sri Lanka' OR 'St. Lucia' OR 'St. Vincent' OR Grenadines OR Sudan OR Suriname OR Swaziland OR Syrian OR Syria OR Tajikistan OR Tanzania OR Thailand OR Timor-Leste OR Togo OR Tonga OR Tunisia OR Turkey OR Turkmenistan OR Tuvalu OR Uganda OR Ukraine OR Uruguay OR Uzbekistan OR Vanuatu OR Venezuela OR Vietnam OR 'West Bank' OR Gaza OR Yemen OR Zambia OR Zimbabwe OR Africa OR sub-saharan OR 'developing countries' OR 'developing country' OR resource-limited OR resource-constrained OR 'low- and middle-income' OR LMIC OR 'third world' OR 'low income countries')

Search Results (Date): 07/16/2018

Database	Number of results
PubMed	163
PsycINFO	248
CINAHL	127
EMBASE	126

Other Sources

– Reference lists of included articles
– "Cited by" lists of included articles

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