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A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

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TITLE PAGE

Title: A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

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A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

ABSTRACT

Objectives Although HIV-infected patients have been disproportionately affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among people living with HIV (PLWH) is unknown. This study aimed to systematically review the prevalence of PTSD among PLWH worldwide and explore variation in prevalence across sociodemographic and methodological factors.

Design A meta-analysis using a random-effect model was conducted to pool the prevalence estimated from individual studies, and subgroup analyses were used to analyze heterogeneities.

Setting, participants and measures Observational studies providing PTSD prevalence in an adult HIV population were included. Measurements were not restricted except that the definition of PTSD should be in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.

Results A total of 34 articles were included among 2396 records identified initially. The estimated global rate of PTSD in PLWH was 27% (95% CI 23-31%). Significant heterogeneity was detected in the proportion of PLWH who reported PTSD across studies, which was partially explained by geographic area, population group,

measurement and sampling method (p<0.05).

Conclusion PTSD among PLWH is common worldwide. We strongly suggest that PTSD should be routinely screened for and that more effective prevention strategies and treatment packages targeting PTSD are needed in PLWH.

Strengths and limitations of this study

- This is the first meta-analysis providing comprehensive assessment on the prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
- Several subgroup analyses were conducted to examine the influence of diverse sociodemographic backgrounds as well as methodological heterogeneity.
- This review was conducted with specified definition of PTSD in inclusion criteria to help in acquiring high level of evidence, which also limited the number of eligible studies.
- A lack of studies carried out on the topic in low-income and middle-income countries could underestimate the burden of HIV-PTSD prevalence of the world.

INTRODUCTION

Globally, there were more than 36 million people living with HIV (PLWH) by the end of 2017.[1] Although increasingly expanded access to antiretroviral therapy (ART) has lead to a prolonged life span, a large portion of PLWH still suffer a significant burden due to psychiatric disorders.[2 3] A growing body of literature recognizes HIV infection as a traumatic event,[4 5] and HIV-infected people have a heightened risk for posttraumatic stress disorder (PTSD). PTSD is a mental health condition following exposure to a life-threatening event, or extreme or repeated exposure to traumatic events.[6] Infection with HIV not only causes a progressive destruction of the immune system, which increases the susceptibility to malignancies that threaten a person's life greatly, but being labeled and associated with HIV stigma, taking multiple daily medications and experiencing repeated unpleasant side effects also constitute traumatic events.[7] PLWH are more likely to report a history of traumatic and stressful life experiences than found in the general population, including childhood sexual/physical abuse and intimate partner violence.[8–10] These high rates of previous trauma exposure among PLWH increase the likelihood of developing PTSD.

Generally, the concept of PTSD has been broadly applied to military veterans, survivors of disasters and accidents, and victims of violent assaults. PTSD as a serious and costly health problem in the general population also is well recognized, which not only impairs a person's physical health, but also greatly influences social functioning.[11] The co-occurrence of PTSD and HIV-infection creates even more challenges regarding

both the treatment of PTSD and the management of HIV. PTSD can negatively impact medication adherence and impair immune functioning,[12–15] all of which are especially critical for PLWH. HIV-infected patients with PTSD have been found to be at increased risk of somatization and physical disorders.[16] The illness experience of PTSD, such as persistent avoidance and re-experiencing the traumatic event, may also compromise quality of life and cause significant distress in PLWH.[7 17] Subsequently, prolonged and untreated PTSD may lead to exacerbation of both PTSD and HIV progression.[18] There is also evidence suggesting that reductions in PTSD symptom severity are related to improved HIV-risk related outcomes.[19] Given that PTSD elevates HIV-risk behaviors[20 21] and the possibility of HIV transmission also increases along with disease progression, PLWH suffering from PTSD are an important group to understand and with whom to intervene.

Valid data on PTSD prevalence rates among PLWH is essential. Evidence on the extent of PTSD among PLWH is needed to raise awareness and recommend clinical management. Although a number of studies have investigated the prevalence of PTSD in PLWH, findings have been inconsistent.[22] While studies have reported varied incidence, few efforts have been made to aggregate existing research using meta-analysis techniques. There was one published meta-analysis estimating the pooled prevalence of PTSD among women living with HIV in 2012.[23] But the lack of studies with other groups lowered the generalizability and global relevance of their findings. Moreover, the meta-analysis was conducted in 2012, and an increase of publications

about PTSD among PLWH since then[24–26] suggests that a timely update is urgently needed. Indeed, several reviews provide a useful overview of the possible prevalence of PTSD among PLWH;[22 27] however, a number of gaps remain. First, to date, there has been no attempt to achieve a better understanding of the epidemiology of PTSD in PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second, economically and politically, while precise estimates of prevalence can support efficient allocation of resources, factors that might influence PTSD prevalence rates, such as population characteristics and socio-cultural context have been neglected.

Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in PLWH differs based upon population group, country income groups and study characteristics. This information can then be used to inform further practice and research for this highly co-morbid group.

METHODS

Search strategy

Systematic searches were conducted through 5 electronic English databases (Medline, Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence among PLWH up to May 2018. The search terms were: posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV, acquired immunodeficiency syndrome, AIDS, OR PLWH$; AND epidemiology, occurrence, incidence, OR

prevalence. The reference lists of review articles and retrieved full-text articles were also examined for additional papers that were eligible for this review.

Eligibility criteria

Studies were included for this meta-analysis if they met the following predetermined selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2) observational study where prevalence figures for PTSD were stated or can be calculated in an adult HIV population; and (3) underlined that PTSD cases were identified in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.[28 29] Studies were excluded if (1) they only recruited those who had mental distress; (2) they specifically targeted only youth under 18 or children affected by HIV; or (3) participants had been exposed to war, genocide or natural disasters. No restriction was applied regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed closely, and if repeated data were observed, only the earlier publication with one set of complete data was included.

Data extraction and analysis

Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.) following PRISMA recommendations. C.T and X.X. searched the English papers and J.M. screened the Chinese language papers. After duplicates were deleted, each investigator read titles and abstracts closely to capture all potential studies. Full-text articles were obtained and reviewed for all criteria. Any discrepancies were resolved by

discussion with the research team. The PRISMA flow chart shows the results of the systematic search (figure 1)

Data extraction

Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data independently from included papers: first author, year of publication, country of study, sampling method, sample size, number of patients with PTSD, measurements and outcome data. The third investigator (H.W.) helped to verify all extracted data and resolve any uncertainties. To facilitate detection of sample/methodological heterogeneity, countries were categorized according to their income level, and measurements were classified into diagnostic questionnaire and clinical interview based on the approach to diagnosing PTSD. Selection bias was also examined. Gender and sexual orientation were considered because of underlying differences in the epidemics of HIV and trauma.[30–32] Specifically, populations were grouped as women and men, and samples of HIV-infected men were further classified into men who have sex with men (MSM) and non-MSM males.

Assessment of methodological quality

We used the quality assessment forms for cross-sectional/prevalence studies recommended by the Agency for Healthcare Research and Quality (AHRQ) [33] to assess the reliability of the eligible studies. The checklist included 11 items. Each item was coded with a "Yes/No/Unclear": "No" or "Unclear" was scored "0", and "Yes" was scored "1". Consistent with previous meta-analyses studies using AHRQ, a total score

of 8-11, 4-7, and 0-3 indicated high, moderate and low quality, respectively.

Meta-analysis

In this study, all statistical analyses were performed using Stata 12.0 software (STATA Corporation, College Station, TX). Heterogeneity was tested and quantified by the chi-square Q statistic and the I^2 statistic. The rates of PTSD among PLWH were combined and reported as proportions with corresponding 95% Confidential Intervals (CI). The pooled prevalence was estimated using a random-effects model when heterogeneity was statistically significant (I^2 >50%, $p \leqslant 0.10$). Otherwise, a fix-effects model was conducted. [34]As sources of heterogeneity may arise from socio-demographic and methodological factors, subgroup analyses were performed to assess the effects of (1) economic levels of the study country, (2) gender/sexual orientation, (3) sampling method and (4) measure type on the prevalence of PTSD among PLWH. Chi-square tests were further used to investigate whether there were significant differences between groups. We only performed these subgroup analyses when data were extractable and sufficient. Separate sensitivity analyses were used for studies with low quality to examine the stability of the pooled prevalence. Publication bias was assessed using the Egger's and the Begg's tests. Significant level of p values < 0.05 were employed for all analyses.

Patient and public involvement

Patients and the public were not involved in this study.

RESULTS

Search results

A total of 2396 records were identified by the electronic bibliographic database searches. Eight additional manuscripts were identified through other sources (e.g., reference lists of review papers). From an initial screen of 2299 records after duplicates were removed, 2185 records were excluded on basis of title or abstract because those studies were not relevant to this review (n=2107) or were reviews/commentary (n= 78). The remaining 114 full articles were selected for the eligibility assessment. Of those, 5 were excluded for repeated data, 9 were excluded for targeting PLWH who received psychological intervention or suffered from genocide/natural disaster, and 66 were excluded for not reporting the PTSD prevalence among PLWH. Finally, a total of 34 studies [14 24 25 35-65] met inclusion criteria and were included in this meta-analysis. Search results are elaborated in Figure 1.

Study characteristics

Most of the papers (82.4%) scored 4 or more according to the AHRQ scale indicating a generally moderate to high level of data quality. Table 1 shows the characteristics of the included studies. These studies were published between 2002[65] and 2018. [35–37] Geographically, over half (n=20, 58.8%) of the 34 included studies were conducted in the USA, followed by South Africa (n=6, 17.6%), the United Kingdom (n=2, 5.9%), China (n=2, 5.9%), and low-income countries including Gambia (n=1, 2.9%), Nigeria (n=1, 2.9%), Uganda (n=1, 2.9%), and Zimbabwe (n=1, 2.9%). Twenty-one studies (61.8%) measured PTSD using diagnostic self-report questionnaires, while the other 13

studies (38.2%) conducted clinical interviews to diagnose PTSD. Though 6 studies (17.6%) did not report their sampling methods, convenience sampling methods were adopted in most studies (n=18, 52.9%), followed by consecutive sampling (n=7, 20.6%), and probability sampling (n=3, 8.8%). In all, 10161 PLWH were involved (sample size varied from 41 to 1489), of which 2088 were identified with PTSD.

Table 1 Characteristics of the included studies

First author	Year of publication	Location of study	Sampling methods	Sample size*	No. of patients with PTSD	Measurements	Data Collection	Quality
Spies[35]	2018	South Africa	convenient sampling	68	10	DTS	self-report questionnaire	moderate
Verhey[36]	2018	Zimbabwe	random sampling	91	22	CAPS	clinical interview	moderate
Gao[37]	2018	China	convenient sampling	520	89	PCL-C	self-report questionnaire	moderate
McLean[38]	2017	USA	convenient sampling	42	12	PSS	clinical interview	moderate
Kemppainen[25]	2017	USA	convenient sampling	60	26	PCL-C	self-report questionnaire	low
Gonzalez[24]	2016	USA	convenient sampling	137	47	PDS	self-report questionnaire	moderate
Rubin[39]	2016	USA	convenient sampling	1004	174	PCL-C	self-report questionnaire	moderate
John[40]	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
Julnes[14]	2016	USA	convenient sampling	114	39	CDQ	self-report questionnaire	moderate

Zhang[41]	2016	China	convenient sampling	243	106	PCL-C	self-report questionnaire	low
Battaglia[42]	2015	USA	convenient sampling	200	72	PTSD checklist	self-report questionnaire	moderate
Hansrod[43]	2015	South Africa	convenient sampling	114	29	MINI	clinical interview	moderate
Brownley[44]	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
Malee[45]	2014	USA	convenient sampling	1223	281	CDQ	self-report questionnaire	high
Glémaud[46]	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
Gore-Felton[47]	2013	USA	convenient sampling	94	28	PCL-C	self-report questionnaire	low
Glover[48]	2013	USA	convenient sampling	99	24	PDS	self-report questionnaire	high
Peterson[49]	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
Kinyanda[50]	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
Bogart[51]	2011	USA	convenient sampling	181	72	PDS	self-report questionnaire	moderate

Martin[52]	2011	UK	convenient sampling	85	46	CIDI	clinical interview	moderate
Reisner[53]	2011	USA	convenient sampling	63	16	AUDADIS-IV	clinical interview	moderate
Theuninck[54]	2010	UK	convenient sampling	100	33	PCL-C	self-report questionnaire	low
Joska[55]	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
Adewuya[56]	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
Spies[57]	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
Fincham[58]	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate
Zanjani[59]	2007	USA	random sampling	109	13	MINI	clinical interview	moderate
Israelski[60]	2007	USA	unclear	210	71	PCL-C	self-report questionnaire	low
Boarts[61]	2006	USA	convenient sampling	57	24	PDS	self-report questionnaire	moderate
Leserman[62]	2005	USA	consecutive sampling	611	98	PTSD checklist	self-report questionnaire	high

Olley[63]	2003	South Africa	consecutive sampling	149	42	MINI	clinical interview	moderate
Vitiello[64]	2003	USA	probability sample	1489	155	CIDI	clinical interview	moderate
Martinez[65]	2002	USA	consecutive sampling	41	17	PCL-C	self-report questionnaire	moderate

* Total number of adults living with HIV

PCL-C Posttraumatic Stress Disorder Checklist-Civilian Version; *DTS* Davidson Trauma Scale; *CAPS* Clinician Administered Post-traumatic Stress Scale; *CDQ* Client Diagnostic Questionnaire; *PDS* Posttraumatic Stress Diagnostic Scale – Self-report version; *PSS* Posttraumatic Stress Symptom Scale; *PRIME MD PHQ* Primary Care Evaluation of Mental Disorders Patient Health Questionnaire; *AUDADIS-IV* The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; *MINI* Mini-International Neuropsychiatric Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV

Prevalence of PTSD in PLWH

The reported prevalence of PTSD in PLWH ranged from 1.6% [50] to 54.1% [52]. The overall pooled prevalence was 27% (95%CI: 23% to 31%), estimated by a random effects model, as significant heterogeneity ($p \leqslant 0.001$, $I^2=97.5\%$) was observed among the included studies. Meta-analyses are shown as forest plots (Fig. 2).

Publication bias and sensitivity analysis

Possible publication bias was indicated according to the results of Egger's linear test (t= 8.07, p<0.05) and Begg's rank test (z=0.39, p=0.70). However, low sensitivity was suggested with the pooled prevalence of PTSD changed slightly from 27% (95%CI: 23% to 31%) to 25% (95%CI: 20% to 29%) after excluding low-quality articles.

Subgroup Analyses

The results of subgroup analyses are shown in Table 2. The prevalence of PTSD in PLWH differed significantly by geographic area, population group, sampling and measurement method. Specifically, the proportion of PLWH with PTSD in high-income countries tended to be higher (pooled rate= 29%, 95%CI 25% to 34%) than middle-income countries (pooled rate= 23%, 95%CI 14% to 32%) and low-income countries (pooled rate= 21%, 95%CI 3% to 39%). Studies using clinical interviews reported lower rates of PTSD (pooled rate= 22%, 95%CI 16% to 27%) compared with those using self-report questionnaires (pooled rate= 29%, 95%CI 25% to 33%). The pooled PTSD prevalence among HIV-positive MSM, HIV-positive women and non-MSM men were 33% (95%CI: 29% to 38%), 24% (95%CI: 22% to 25%) and 20%

(95%CI: 17% to 23%), respectively. Also, studies conducted with convenience sampling were more likely to achieve higher PTSD prevalence (pooled rate= 31%, 95%CI 26% to 36%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to 24%).

Table 2 Subgroup analyses of the prevalence of PTSD in PLWH

Subgroup		Number of studies	Positive PTSD screening (Diagnosis)	Sample size (Tested)	Pooled prevalence of PTSD (95%CI)	Heterogeneity (I^2)	Between group difference	
							χ^2	P value
Geographic area	High-income countries	22	1403	6594	0.29(0.25-0.34)	94.60%	48.93	<0.001
	Middle-income countries	8	555	2515	0.23(0.14-0.32)	97.40%		
	Low-income countries	4	130	1052	0.21(0.03-0.39)	97.90%		
Population group	MSM	3	129	380	0.33(0.29-0.38)	73.70%	19.80	<0.001
	Female	12	805	3212	0.24(0.22-0.25)	90.70%		
	non-MSM male	4	165	754	0.20(0.17-0.23)	89.10%		
Sampling	Consecutive sampling	7	280	2387	0.17(0.10-0.24)	97.30%	181.54	<0.001
	Convenient sampling	18	1128	4404	0.31(0.26-0.36)	91.00%		

Data collection	Self-report questionnaire	21	1543	6230	0.29(0.25-0.33)	92.50%	175.49	<0.001
	Clinical interview	13	545	3931	0.22(0.16-0.27)	97.20%		

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to provide the pooled estimated rate of PTSD among PLWH. A comprehensive search of the literature assessing the rate of comorbidity between PTSD and HIV-infection was performed, and 34 studies met the predefined criteria and were included in the meta-analysis. A total of 10161 participants were involved, of which 2088 were identified with PTSD. The estimated pooled prevalence rate was 27% (95% CI: 23% to 31%), which suggests a considerable burden of PTSD in the HIV-infected population. High heterogeneity across studies was detected, and factors such as differences in region, population characteristic, sampling, and measurement were associated with prevalence rates.

As indicated, the PTSD prevalence rate among PLWH found in this study (27%) not only far exceeded that among the general population (3.9%), [66] but was also much higher than the prevalence of PTSD among other vulnerable groups in some previous studies. For example, the prevalence rate for cancer-related PTSD was 5.1%-15.3%;[67] in persons with chronic pain, the estimated mean prevalence of PTSD was 9.7%. [68] The pooled prevalence of PTSD among PLWH found in this study heightened the high rate of co-morbidity between HIV infection and PTSD, which is consistent with previous demonstrations. [9 69] For PLWH, although depressive symptoms have been the focus of many studies, and 36% of PLWH were likely to have depression according to nationally representative data in the U.S., [70] this pooled estimated rate of PTSD among PLWH showed that PTSD is also a common mental disorder among individuals living with

HIV/AIDS. Therefore, the results of our study significantly underscore the importance of early assessment and trauma-directed psychological interventions for PLWH.

Undoubtedly, heterogeneity between studies is expected in such a relatively large topic of review. In this review, the estimated PTSD prevalence rates in PLWH varied widely (1.6%-54.1%) across studies and countries, which is also a common problem in the epidemiology of psychological and mental health disorders. [71] [72] Consistent with the findings of previous research, [52] the majority of studies which have determined the incidence of HIV-related PTSD have been conducted in developed countries (n=22). Compared with lower-income countries, higher-income countries reported relatively higher rates of PTSD. This tendency and the varied prevalence of PTSD among PLWH may be explained by the cross-cultural differences in attitudes towards HIV infection. Turan et al.[73] found that the level of perceived HIV-related stigma in the community experienced by PLWH may cause adverse health and psychosocial outcomes. Social isolation and stigma might exacerbate symptoms of PTSD. [74] In high-income countries, PLWH may experience "compound" or "layered" stigma, where stigmatizing beliefs not only associated with HIV infection but also related to sexual orientation, commercial sexual behaviors, etc. [75] Although, HIV-related stigma is highly burdensome in some mid-income countries, such as China, [76] [77] the reported prevalence of PLWH with PTSD was lower compared to higher-income countries. The differences between collectivism and individualism rooted in eastern and western culture may be an explanation. [78] It is worth noting that social context may not only influence the susceptibility of mental

health disorders, but it also constitutes an important factor in perceived stigma among individuals with mental illness. Compared to high-income countries, stigmatization-beliefs about the causes and presence of mental illness are still widespread in low- and middle-income countries, [79 80] which may lead to less disease reporting. Caution must be applied, since there is a lack of studies investigating HIV-related PTSD in lower- (n=4) and middle-income (n=8) countries. In particular, detection of prevalence is associated with the representativeness and size of sample. In the context of low- and middle-income countries, it could be argued that lower HIV testing rate may underestimate the PTSD prevalence and impact generalizability. Thus, more epidemiological studies are warranted to better understanding and clarify the difference in PTSD prevalence among PLWH globally.

Subgroup analyses indicated that the prevalence of PTSD differed significantly when gender and sexual orientation were taken into consideration. Specifically, MSM infected with HIV exhibited a higher rate of PTSD (33%) in comparison with both female (24%) and non-MSM male (20%) groups. As suggested by the aforementioned findings, one possible explanation is that HIV-infected MSM may experience higher levels of stigma and trauma related to their sexual orientation. [30 81] Compared with heterosexual counterparts, MSM reported higher risk for suicidal ideation, [82] which also indicates greater psychological stress and mental health problems (i.e. PTSD and depression). In addition, estimated PTSD prevalence in HIV-infected females was higher than that among non-MSM males. This matches the pattern of prevalence in

PTSD, in which being female is a risk factor associated with PTSD development. [16] The findings that MSM and female HIV-infected individuals are at higher risk of developing PTSD may indicate that related health promotion campaigns should be directed to these groups. Clinicians should also take into consideration the PTSD susceptibility in different groups of HIV-infected populations during diagnoses as well. Notably, most eligible studies did not provide separate prevalence rates regarding the gender of participants, and only 3 studies identified PTSD prevalence among MSM living with HIV. Given that these data are from a small number of studies and/or participants, this finding should be interpreted with caution. Nonetheless, given the high prevalence of PTSD in this group, future efforts should be made to obtain more prevalence data on PTSD among MSM.

In our study, we assessed methodological differences that may result in heterogeneity. Factors including sampling strategies (convenience vs consecutive) and measurement (self-report vs clinical interview) were evaluated by subgroup analyses. Among 34 studies providing estimated prevalence of PTSD, 7 reported participants were consecutively enrolled via self-referral from flyers describing the study or advertisements from HIV health care providers, and generated a lower pooled prevalence rate (17%) compared with the other 18 studies using convenience sampling (31%), though both sampling methods were non-probabilistic. An increase in reporting rate due to convenience sampling has also been found in another meta-analysis synthesizing the HCV seroconversion rates in HIV-positive MSM. [83] Convenience

samples may allow researchers to select participants who are more likely to have PTSD symptoms and lead to over-estimation, but given that only 4 studies were rated as high quality and limited description of study methods was detected in some studies, the reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness of calculating pooled prevalence estimates could be questioned, and the pooled prevalence estimate regarding varied recruitment approaches of the studies should be interpreted with caution.

In this review, a total of 14 different tools were used to assess PTSD symptoms among PLWH across studies. Overall, the rate of PTSD screened by self-report instruments (29%) was higher than that assessed by clinical interview (22%). Though both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD), clinical interviews most likely do a much better job of assessing symptoms carefully – for example, not counting symptoms that do not meet clinically meaningful thresholds, and self-report measures may inflate the prevalence estimates; [84] alternatively, subjects may be more comfortable reporting symptoms using self-report questionnaires (presumably paper or online surveys rather than face-to-face interviews). Screening or diagnosing with survey instruments is a common and practical method, especially in resource-limited regions. We found that, though a number of PTSD measures have been used to assess PTSD among PLWH, there is no tool designed for this population specifically. As the sensitivity and specificity of the measures may impact accurate PTSD detection, further research is required to identify a standardized measure

accordingly to improve validity.

Certain limitations should be acknowledged in this meta-analysis. First, though minimal potential for publication bias was presumed as all data drawn for this review were from studies reporting estimated point prevalence without intervention, publication bias cannot be ruled out for there are a number of studies published in languages other than English and Chinese. Second, the heterogeneity was high in the whole sample and most subgroups. Considering the eligible studies included in this meta-analysis were from diverse sociodemographic backgrounds, we have analysed the influences of region, population group, recruitment venue, and measurement method, which explained parts of the heterogeneity. Third, though some studies have indicated that several sociodemographic factors such as age may be associated with PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified by age due to the lack of detailed information reported in the published studies. As the quality of reporting could increase the susceptibility to bias, it is imperative for the researchers to report their findings of observational studies in accordance with the appropriate guidelines, such as the STROBE checklist.

CONCLUSIONS

This review contributes to evidence on the quantitatively pooled prevalence of PTSD among PLWH. Stratified subgroups including geographic area, population group, sampling and measurement method were found to be significant factors accounting for the varied prevalence of PTSD among PLWH. More effective intervention strategies

targeting PTSD among PLWH are urgently needed. Future efforts should be made to obtain countries' own PTSD prevalence data among PLWH as well as specific vulnerable minorities, which will provide a basis for public health policy, health-care planning, and resource allocation for PTSD intervention initiatives. Our study also suggests that more research using robust and comprehensive methodology is needed to provide rigorous evidence for designing the targeted psychological interventions.

Figure 1 Flow chart of study inclusion

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

Contributors: Conception of the work: HW and CT. Systematic review and article evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT, LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the authors. All the authors fulfill the ICMJE criteria for authorship.

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REFERENCES

1. UNAIDS. UNAIDS Data 2018. http://www.unaids.org/en/resources/documents/2018/unaids-data-2018 (Accessed 18 March 2019).
2. Niu L, Luo D, Liu Y, *et al.* The mental health of people living with HIV in China, 1998–2014: a systematic review. *PLoS One*. 2016;11:e0153489.
3. Adams C, Zacharia S, Masters L, *et al*. Mental health problems in people living with HIV: changes in the last two decades: the London experience 1990–2014. *AIDS care*. 2016;28:56–9.
4. Young C. Understanding HIV-related posttraumatic stress disorder in South Africa: a review and conceptual framework. *African Journal of AIDS Research*. 2011;10:139–48.
5. Sherr L, Nagra N, Kulubya G, *et al.* HIV infection associated post-traumatic stress disorder and post-traumatic growth–a systematic review. *Psychology, health & medicine*. 2011;16:612–29.
6. Friedman MJ, Resick PA, Bryant RA, *et al.* Considering PTSD for DSM-5. *Depression and anxiety.* 2011;28:750–69.
7. Luo S, Lin C, Ji G, *et al.* Post-traumatic Stress Disorder Symptoms Among People Living with HIV/AIDS in Rural China. *AIDS Behav*. 2017;21:3202–8.
8. Cavanaugh CE, Hansen NB, Sullivan TP. HIV sexual risk behavior among low-income women experiencing intimate partner violence: The role of

posttraumatic stress disorder. *AIDS Behav.* 2010;14:318–27.

9. Neigh GN, Rhodes ST, Valdez A, *et al.* PTSD co-morbid with HIV: Separate but equal, or two parts of a whole? *Neurobiology of disease*. 2016;92:116–23.
10. Borwein A, Salters KA, Palmer AK, *et al.* High rates of lifetime and recent violence observed among harder-to-reach women living with HIV. *AIDS care*. 2014;26:587–94.
11. Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *The Journal of clinical psychiatry*. 2000;61(Suppl 5):4-14.
12. Pence BW. The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS. *Journal of Antimicrobial Chemotherapy.* 2009;63:636–40.
13. Ebrahimzadeh Z, Goodarzi MA, Joulaei H. Predicting the Antiretroviral Medication Adherence and CD4 Measure in Patients with HIV/AIDS Based on the Post Traumatic Stress Disorder and Depression. *Iranian Journal of Public Health*. 2019;48:139–46.
14. Julnes PS, Auh S, Krakora R, *et al.* The association between post-traumatic stress disorder and markers of inflammation and immune activation in HIV-infected individuals with controlled viremia. *Psychosomatics.* 2016;57:423–30.
15. Lynn C, Chenneville T, Bradley-Klug K, *et al.* Depression, anxiety, and posttraumatic stress as predictors of immune functioning: differences between youth with behaviorally and perinatally acquired HIV. *AIDS care*. 2019 Mar 4:1–10.

16. Brief DJ, Bollinger AR, Vielhauer MJ, *et al.* Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*. 2004;16:97–120.

17. Nightingale VR, Sher TG, Mattson M, *et al.* The effects of traumatic stressors and HIV-related trauma symptoms on health and health related quality of life. *AIDS Behav*. 2011;15:1870–8.

18. Koegler E, Kennedy CE. A scoping review of the associations between mental health and factors related to HIV acquisition and disease progression in conflict-affected populations. *Confl Health*. 2018;12:20.

19. Pearson CR, Kaysen D, Huh D, *et al.* Randomized Control Trial of Culturally Adapted Cognitive Processing Therapy for PTSD Substance Misuse and HIV Sexual Risk Behavior for Native American Women. *AIDS Behav*. 2019;23:695–706.

20. Tull MT, Weiss NH, McDermott MJ. Post-traumatic stress disorder and impulsive and risky behavior: Overview and discussion of potential mechanisms. *Comprehensive guide to post-traumatic stress disorders*. 2016;803–16.

21. Weiss NH, Tull MT, Borne MER, *et al.* Posttraumatic stress disorder symptom severity and HIV-risk behaviors among substance-dependent inpatients. *AIDS care*. 2013;25:1219–26.

22. Applebaum AJ, Bedoya CA, Hendriksen ES, *et al.* Future directions for interventions targeting PTSD in HIV-infected adults. *Journal of the Association of Nurses in AIDS Care*. 2015;26:127–38.

23. Machtinger E, Wilson T, Haberer JE, *et al.* Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS Behav*. 2012;16:2091–100.

24. Gonzalez A, Locicero B, Mahaffey B, *et al.* Internalized HIV stigma and mindfulness: associations with PTSD symptom severity in trauma-exposed adults with HIV/AIDS. *Behavior modification*. 2016;40:144–63.

25. Kemppainen JK, MacKain S, Alexander M, *et al.* Posttraumatic stress disorder and stressful life events among rural women with HIV disease. *Journal of the Association of Nurses in AIDS Care*. 2017;28:216–25.

26. Rubin LH, Cook JA, Springer G, *et al.* Perceived and post-traumatic stress are associated with decreased learning, memory, and fluency in HIV-infected women. *AIDS (London, England)*. 2017;31:2393–1401.

27. Seedat S. Interventions to improve psychological functioning and health outcomes of HIV-infected individuals with a history of trauma or PTSD. *Current HIV/AIDS Reports*. 2012;9:344–50.

28. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.

29. Association AP. Diagnostic and statistical manual of mental disorders. 5th Edition. Washington, DC: American Psychiatric Pub; 2013.

30. Sales JM, Swartzendruber A, Phillips AL. Trauma-Informed HIV Prevention and Treatment. *Curr HIV/AIDS Rep*. 2016;13:374–82.

31. Burnham KE, Cruess DG, Kalichman MO, *et al.* Trauma symptoms, internalized stigma, social support, and sexual risk behavior among HIV-positive gay and bisexual MSM who have sought sex partners online. *AIDS care*. 2016;28:347–53.

32. Rzeszutek M, Oniszczenko W, Firląg-Burkacka E. Gender differences in posttraumatic stress symptoms and social support in a sample of HIV-positive individuals. *Women & health*. 2017;57:792–803.

33. Rostom A, Dubé C, Cranney A, *et al.* Appendix D. Quality Assessment Forms. Agency for Healthcare Research and Quality (US); 2004 https://www.ncbi.nlm.nih.gov/books/NBK35156/ (Accessed 21 October 2018).

34. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine. 2002;21(11):1539-58.

35. Spies G, Konkiewitz EC, Seedat S. Incidence and persistence of depression among women living with and without HIV in South Africa: A longitudinal study. *AIDS Behav*. 2018;22(10):3155–65.

36. Verhey R, Chibanda D, Gibson L, *et al.* Validation of the posttraumatic stress disorder checklist - 5 (PCL-5) in a primary care population with high HIV prevalence in Zimbabwe. *BMC Psychiatry.* 2018;18:109.

37. Gao M, Xiao C, Zhang X, *et al.* Social capital and PTSD among PLWHA in China: the mediating role of resilience and internalized stigma. *Psychology, health & medicine*. 2018;23:698–706.

38. McLean CP, Gay NG, Metzger DA, *et al.* Psychiatric Symptoms and Barriers to

Care in HIV-Infected Individuals Who Are Lost to Care. *J Int Assoc Provid AIDS Care.* 2017;16:423–9.

39. Rubin LH, Pyra M, Cook JA, *et al.* Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women. *Journal of neurovirology.* 2016;22:159–69.
40. John M, Greene M, Hessol NA, *et al.* Geriatric assessments and association with VACS index among HIV-infected older adults in San Francisco. *Journal of acquired immune deficiency syndromes (1999).* 2016;72:534.
41. Zhang X, Wang T, Liu M, *et al.* Post-traumatic stress disorder among people living with HIV/AIDS and its influence factors. *Chongqing Medicine.* 2016;232–5.
42. Battaglia TA, Gunn CM, McCoy ME, *et al.* Beliefs About Anal Cancer among HIV-Infected Women: Barriers and Motivators to Participation in Research. *Womens Health Issues*. 2015;25:720–6.
43. Hansrod F, Spies G, Seedat S. Type and severity of intimate partner violence and its relationship with PTSD in HIV-infected women. *Psychology, health & medicine.* 2015;20:697–709.
44. Brownley JR, Fallot RD, Berley RW, *et al.* Trauma history in African-American women living with HIV: effects on psychiatric symptom severity and religious coping. *AIDS care.* 2015;27:964–71.
45. Malee K, Mellins CA, Huo Y, *et al.* Prevalence, incidence and persistence of psychiatric and substance use disorders among mothers living with HIV. *Journal of*

acquired immune deficiency syndromes (1999). 2014;65:526.

46. Glémaud M, Illa L, Echenique M, *et al.* Abuse and mental health concerns among HIV-infected Haitian women living in the United States. Journal of the Association of Nurses in *AIDS Care*. 2014;25:S62–9.
47. Gore-Felton C, Ginzburg K, Chartier M, *et al.* Attachment style and coping in relation to posttraumatic stress disorder symptoms among adults living with HIV/AIDS. *Journal of behavioral medicine*. 2013;36:51–60.
48. Glover DA, Williams JK, Kisler KA. Using novel methods to examine stress among HIV-positive African American men who have sex with men and women. *J Behav Med*. 2013;36:283–94.
49. Peterson K, Togun T, Klis S, *et al.* Depression and posttraumatic stress disorder among HIV-infected Gambians on antiretroviral therapy. *AIDS patient care and STDs*. 2012;26:589–96.
50. Kinyanda E, Hoskins S, Nakku J, *et al.* Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. *BMC psychiatry*. 2011;11:205.
51. Bogart LM, Wagner GJ, Galvan FH, *et al.* Perceived discrimination and mental health symptoms among Black men with HIV. *Cultural Diversity and Ethnic Minority Psychology*. 2011;17:295.
52. Martin L, Kagee A. Lifetime and HIV-related PTSD among persons recently diagnosed with HIV. *AIDS Behav*. 2011;15:125–31.

53. Reisner SL, Falb KL, Mimiaga MJ. Early life traumatic stressors and the mediating role of PTSD in incident HIV infection among US men, comparisons by sexual orientation and race/ethnicity: results from the NESARC, 2004–2005. *Journal of Acquired Immune Deficiency Syndromes.* 2011;57:340–50.

54. Theuninck AC, Lake N, Gibson S. HIV-related posttraumatic stress disorder: Investigating the traumatic events. *AIDS Patient care and STDS*. 2010;24:485–91.

55. Joska JA, Fincham DS, Stein DJ, *et al.* Clinical correlates of HIV-associated neurocognitive disorders in South Africa. *AIDS Behav*. 2010;14:371–8.

56. Adewuya AO, Afolabi MO, Ola BA, *et al.* Post-traumatic stress disorder (PTSD) after stigma related events in HIV infected individuals in Nigeria. *Social Psychiatry and Psychiatric Epidemiology*. 2009;44:761.

57. Spies G, Kader K, Kidd M, *et al.* Validity of the K-10 in detecting DSM-IV-defined depression and anxiety disorders among HIV-infected individuals. *AIDS care*. 2009;21:1163–8.

58. Fincham D, Smit J, Carey P, *et al.* The relationship between behavioural inhibition, anxiety disorders, depression and CD4 counts in HIV-positive adults: a cross-sectional controlled study. *AIDS care.* 2008;20:1279–83.

59. Zanjani F, Saboe K, Oslin D. Age difference in rates of mental health/substance abuse and behavioral care in HIV-positive adults. *AIDS patient care and STDs*. 2007;21:347–55.

60. Israelski DM, Prentiss DE, Lubega S, *et al.* Psychiatric co-morbidity in vulnerable

populations receiving primary care for HIV/AIDS. *AIDS care*. 2007;19:220–5.

61. Boarts JM, Sledjeski EM, Bogart LM, *et al.* The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS Behav.* 2006;10:253–61.
62. Leserman J, Whetten K, Lowe K, *et al.* How trauma, recent stressful events, and PTSD affect functional health status and health utilization in HIV-infected patients in the south. *Psychosomatic medicine*. 2005;67:500–7.
63. Olley BO, Gxamza F, Seedat S, *et al.* Psychopathology and coping in recently diagnosed HIV/AIDS patients-the role of gender. *South African Medical Journal*. 2003;93:928–31.
64. Vitiello B, Burnam MA, Bing EG, *et al.* Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry*. 2003;160:547–54.
65. Martinez A, Israelski D, Walker C, *et al.* Posttraumatic stress disorder in women attending human immunodeficiency virus outpatient clinics. *AIDS patient care and STDs.* 2002;16:283–91.
66. Koenen KC, Ratanatharathorn A, Ng L, *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med.* 2017;47:2260–74.
67. Abbey G, Thompson SBN, Hickish T, *et al.* A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology*. 2015;24:371–81.

68. Siqveland J, Hussain A, Lindstrøm JC, *et al.* Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. *Frontiers in Psychiatry.* 2017;8:164.

69. Kelly B, Raphael B, Judd F, *et al.* Posttraumatic stress disorder in response to HIV infection. *General Hospital Psychiatry*. 1998;20:345–52.

70. Bing EG, Burnam MA, Longshore D, *et al.* Psychiatric disorders and drug use among human immunodeficiency virus–infected adults in the United States. *Archives of general psychiatry.* 2001;58:721–8.

71. Pringsheim T, Jette N, Frolkis A, *et al.* The prevalence of Parkinson's disease: A systematic review and meta-analysis. *Movement disorders.* 2014;29:1583–90.

72. Wang T, Fu H, Kaminga AC, *et al*. Prevalence of depression or depressive symptoms among people living with HIV/AIDS in China: a systematic review and meta-analysis. *BMC psychiatry.* 2018 Dec;18(1):160.

73. Turan B, Budhwani H, Fazeli PL, *et al.* How Does Stigma Affect People Living with HIV? The Mediating Roles of Internalized and Anticipated HIV Stigma in the Effects of Perceived Community Stigma on Health and Psychosocial Outcomes. *AIDS Behav*. 2017;21:283–91.

74. Kamen C, Vorasarun C, Canning T, *et al.* The impact of stigma and social support on development of post-traumatic growth among persons living with HIV. *Journal of clinical psychology in medical settings*. 2016;23:126–34.

75. Lowther K, Selman L, Harding R, *et al.* Experience of persistent psychological

symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): a systematic review. *International journal of nursing studies*. 2014;51(8):1171-89.

76. Li Z, Morano JP, Khoshnood K, *et al.* HIV-related stigma among people living with HIV/AIDS in rural Central China. *BMC Health Serv Res*. 2018;18:453.
77. Li L, Liang L-J, Lin C, *et al.* HIV prevention intervention to reduce HIV-related stigma: evidence from China. *AIDS (London, England)*. 2010;24:115.
78. Shavitt S, Cho YI, Johnson TP, *et al.* Culture Moderates the Relation Between Perceived Stress, Social Support, and Mental and Physical Health. *Journal of Cross-Cultural Psychology*. 2016;47:956–80.
79. Lauber C, Rössler W. Stigma towards people with mental illness in developing countries in Asia. *International Review of Psychiatry*. 2007;19:157–78.
80. Seeman N, Tang S, Brown AD, *et al.* World survey of mental illness stigma. *Journal of Affective Disorders*. 2016;190:115–21.
81. Reisner SL, Mimiaga MJ, Safren SA, *et al.* Stressful or traumatic life events, post-traumatic stress disorder (PTSD) symptoms, and HIV sexual risk taking among men who have sex with men. *AIDS care*. 2009;21:1481–9.
82. Luo Z, Feng T, Fu H, *et al.* Lifetime prevalence of suicidal ideation among men who have sex with men: a meta-analysis. *BMC psychiatry*. 2017;17:406.
83. Hagan H, Jordan AE, Neurer J, *et al.* Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS*.

2015;29:2335–45.

84. Ayers S, Wright DB, Ford E. Hyperarousal symptoms after traumatic and nontraumatic births. *Journal of Reproductive and Infant Psychology.* 2015;33:282–93.

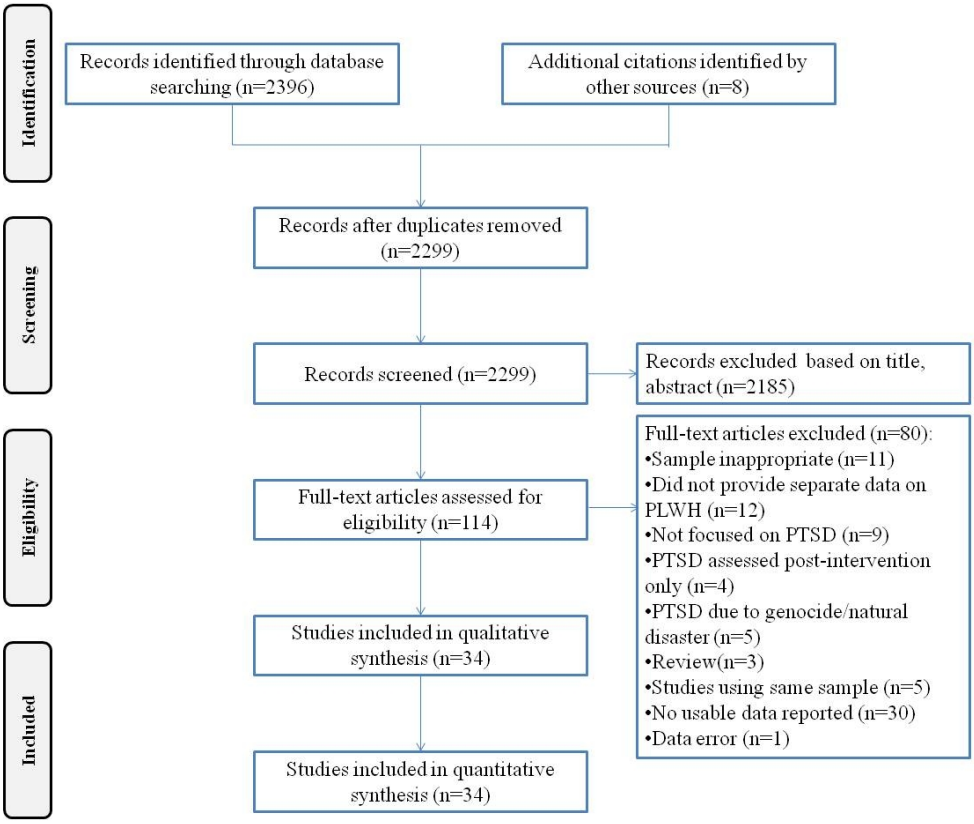

Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

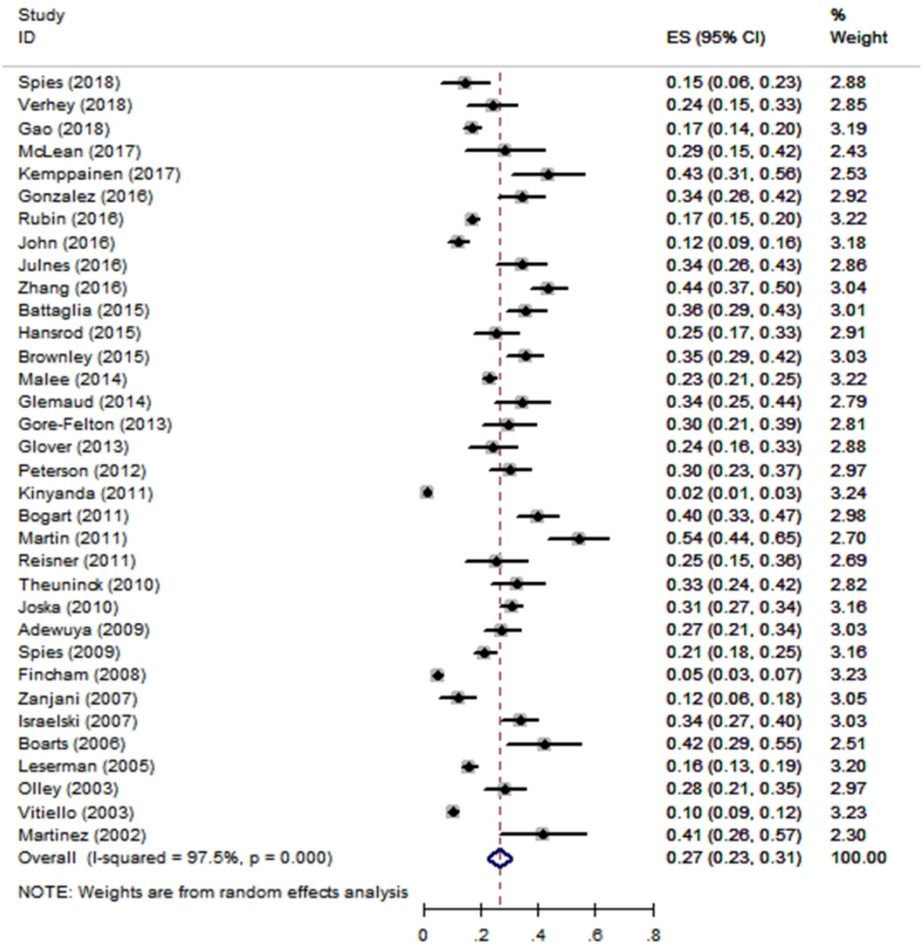

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

MOOSE Checklist

Items	Page #	Comments
TITLE Identify the study as a meta-analysis (or systematic review)	3	
ABSTRACT Use the journal's structured format	3,4	
INTRODUCTION		
· The clinical problem	5,6	
· The hypothesis	5	
· A statement of objectives that includes the study population, the condition of interest, the exposure or intervention, and the outcome(s) considered	7	
SOURCES		
· Qualifications of searchers (eg, librarians and investigators)	8	1 psychiatrist
· Search strategy, including time period included in the synthesis and keywords	7,8	
· Effort to include all available studies, including contact with authors	8	
· Databases and registries searched	7	
· Search software used, name and version, including special features used (eg, explosion)	-	
· Use of hand searching (eg, reference lists of obtained articles)	8	
· List of citations located and those excluded, including justification	figure 1	
· Method of addressing articles published in languages other than English	7	
· Method of handling abstracts and unpublished studies	-	Not applicable
· Description of any contact with authors	-	
STUDY SELECTION		
· Types of study designs considered	8	Observational
· Relevance or appropriateness of studies gathered for assessing the hypothesis to be tested	7,8	
· Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7,8	
· Documentation of how data were classified and coded (eg, multiple raters, blinding, etc)	8,9	
· Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	-	Not applicable
· Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	9,10	
· Assessment of heterogeneity	10	
· Statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	10	
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· A table giving descriptive information for each included study	Tables 1	
· Results of sensitivity testing (eg, subgroup analysis)	17,18	
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DISCUSSION		
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· Potential biases in the review process (eg, publication bias)	26	
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BMJ Open

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TITLE PAGE

Title: A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

Running head: Posttraumatic stress disorder, HIV, Prevalence, Meta-analysis

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A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

ABSTRACT

Objectives Although people living with HIV (PLWH) have been disproportionately affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among PLWH is unknown. This study aimed to systematically review the prevalence of PTSD among PLWH worldwide and explore variation in prevalence across sociodemographic and methodological factors.

Design A meta-analysis using a random-effect model was conducted to pool the prevalence estimated from individual studies, and subgroup analyses were used to analyze heterogeneities.

Setting, participants and measures Observational studies providing PTSD prevalence data in an adult HIV population were searched from January 2000 to November 2019. Measurements were not restricted, although the definition of PTSD had to align with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.

Results A total of 38 articles were included among 2406 records identified initially. The estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant heterogeneity was detected in the proportion of PLWH who reported PTSD across studies, which was partially explained by geographic area, population group,

measurement and sampling method (p<0.05).

Conclusion PTSD among PLWH is common worldwide. This review highlights that PTSD should be routinely screened for and that more effective prevention strategies and treatment packages targeting PTSD are needed in PLWH.

Strengths and limitations of this study

- This is the first meta-analysis providing comprehensive assessment on the prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
- Several subgroup analyses were conducted to examine the influence of diverse sociodemographic backgrounds as well as methodological heterogeneity.
- This review was conducted with specific definitions of PTSD as part of the inclusion criteria to help in acquiring high level of evidence, which also limited the number of eligible studies.
- A lack of studies carried out on the topic in low-income and middle-income countries could underestimate the burden of HIV-PTSD prevalence of the world.
- We did not undertake a search of grey literature, restricting our sample to articles published in peer-reviewed journals.

INTRODUCTION

Globally, there were more than 36 million people living with HIV (PLWH) by the end of 2017.[1] Although increasingly expanded access to antiretroviral therapy (ART) has led to a prolonged life span, a large portion of PLWH still suffer a significant burden due to psychiatric disorders.[2 3] Posttraumatic stress disorder (PTSD) is a mental health condition following exposure to a life-threatening event, or extreme or repeated exposure to traumatic events.[4] A growing body of literature indicates that HIV-infected people have a heightened risk for PTSD. [5-6] PLWH are more likely to report a history of traumatic and stressful life experiences than the general population, including childhood sexual/physical abuse and intimate partner violence. [7–9] PTSD may precede an HIV-positive diagnosis due to previous traumatic experiences. In addition, being diagnosed with HIV, a life-threatening illness, is a potentially traumatic event in and of itself, and PTSD may emerge as a result of this diagnosis. Infection with HIV not only causes a progressive destruction of the immune system, which increases the susceptibility to malignancies that threaten a person's life, but being labeled and associated with HIV stigma, taking multiple daily medications and experiencing repeated unpleasant side effects also constitute potentially traumatic events.[10] These high rates of potential trauma exposure during the course of the illness may also increase the likelihood of developing PTSD.

Generally, the concept of PTSD has been broadly applied to military veterans, survivors of disasters and accidents, and victims of violent assaults. PTSD as a serious

and costly health problem in the general population is well recognized, and not only impairs a person's physical health, but also greatly influences social functioning.[11] The co-occurrence of PTSD and HIV-infection creates even more challenges regarding both the treatment of PTSD and the management of HIV. PTSD can negatively impact medication adherence and impair immune functioning,[12–15] both of which are especially critical for PLWH. HIV-infected patients with PTSD have been found to be at increased risk of somatization and physical disorders.[16] The illness experience of PTSD, such as persistent avoidance and re-experiencing the traumatic event, may also compromise quality of life and cause significant distress in PLWH.[7 17] Subsequently, prolonged and untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.[18] There is also evidence suggesting that reductions in PTSD symptom severity are related to improved HIV-risk related outcomes.[19] Given that PTSD elevates HIV-risk behaviors[20 21] and the possibility of HIV transmission also increases along with disease progression, PLWH suffering from PTSD are an important group to understand and with whom to intervene.

Valid data on PTSD prevalence rates among PLWH is essential. Evidence on the extent of PTSD among PLWH is needed to raise awareness and recommend clinical management. Although a number of studies have investigated the prevalence of PTSD in PLWH, findings have been inconsistent.[22] While studies have reported varied incidence, few efforts have been made to aggregate existing research using meta-analysis techniques. There was one published meta-analysis estimating the pooled

prevalence of PTSD among women living with HIV in 2012.[23] But the lack of studies with other groups lowered the generalizability and global relevance of their findings. Moreover, the meta-analysis was conducted in 2012, and the increase of publications about PTSD among PLWH since then[24–26] suggests that a timely update is urgently needed. Indeed, several reviews provide a useful overview of the possible prevalence of PTSD among PLWH;[22 27] however, a number of gaps remain. First, to date, there has been no attempt to achieve a better understanding of the epidemiology of PTSD in PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second, economically and politically, while precise estimates of prevalence can support efficient allocation of resources, factors that might influence PTSD prevalence rates, such as population characteristics and socio-cultural context have been neglected.

Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in PLWH differs based between population groups, country income groups and study characteristics. This information can then be used to inform further practice and research for this highly co-morbid group.

METHODS

Search strategy

Systematic searches were conducted through 5 electronic English databases (Medline, Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence

among PLWH from January 2000 to November 2019. The search terms were: posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV, acquired immunodeficiency syndrome, AIDS, OR PLWH$; AND epidemiology, occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the precise search strategy). The reference lists of review articles and retrieved full-text articles were also examined for additional papers that were eligible for this review.

Eligibility criteria

Studies were included for this meta-analysis if they met the following predetermined selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2) observational study where prevalence figures for PTSD were stated or can be calculated in an adult HIV population; and (3) underlined that PTSD cases were identified in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.[28 29] Studies were excluded if (1) they only recruited those who had mental distress; (2) they specifically targeted only youth under 18 or children affected by HIV. No restriction was applied regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed closely, and if repeated data were observed, only the earlier publication with one set of complete data was included.

Data extraction and analysis

Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.) following PRISMA recommendations. C.T and X.X. searched the English papers and

J.M. screened the Chinese language papers. After duplicates were deleted, each investigator read titles and abstracts closely to capture all potential studies. Full-text articles were obtained and reviewed for all criteria. Any discrepancies were resolved by discussion with the research team. The PRISMA flow chart shows the results of the systematic search (figure 1)

Data extraction

Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data independently from included papers: first author, year of publication, country of study, sampling method, sample size, number of patients with PTSD, measurements and outcome data. The third investigator (H.W.) helped to verify all extracted data and resolve any uncertainties. To facilitate detection of sample/methodological heterogeneity, countries were categorized according to their income level, and measurements were classified into diagnostic questionnaire and clinical interview based on the approach to diagnosing PTSD. Selection bias was examined by reviewing the articles included in the meta-analysis to ensure they met eligibility criteria. Gender and sexual orientation were considered because of underlying differences in the epidemics of HIV and trauma.[30–32] Specifically, populations were grouped as women and men, and samples of HIV-infected men were further classified into men who have sex with men (MSM) and non-MSM males.

Assessment of methodological quality

We used the quality assessment forms for cross-sectional/prevalence studies

recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ) [33] to assess the reliability of the eligible studies. The checklist included 11 items. Each item was coded with a "Yes/No/Unclear": "No" or "Unclear" was scored "0", and "Yes" was scored "1". Consistent with previous meta-analyses studies using the AHRQ assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low quality, respectively.

Meta-analysis

In this study, all statistical analyses were performed using Stata 12.0 software (STATA Corporation, College Station, TX) [34]. Heterogeneity was tested and quantified by the chi-square Q statistic and the I^2 statistic. The prevalence rates of PTSD among PLWH were combined and reported as proportions with corresponding 95% Confidence Intervals (CI). The pooled prevalence was estimated using a random-effects model when heterogeneity was statistically significant (I^2 >50%, $p \leqslant 0.10$). Otherwise, a fix-effects model was conducted. [35]As sources of heterogeneity may arise from socio-demographic and methodological factors, subgroup analyses were performed by dividing subgroups based on (1) economic levels of the study country, (2) gender/sexual orientation, (3) sampling method and (4) assessment method for PTSD, when enough data was available. Chi-square (χ^2) tests were further used to investigate whether there were significant differences between groups. We only performed these subgroup analyses when data were extractable and sufficient. Separate sensitivity analyses were used for studies with low quality to examine the stability of the pooled prevalence.

Publication bias was assessed using the Egger's and the Begg's tests. [36-37] Significance level of p values < 0.05 were employed for all analyses.

Patient and public involvement

Patients and the public were not involved in this study.

Ethics approval

As this study is a systematic review based on published studies, ethical approval is not required.

RESULTS

Search results

A total of 2396 records were identified by the electronic bibliographic database searches. Ten additional manuscripts were identified through other sources (e.g., reference lists of review papers). From an initial screen of 2301 records after duplicates were removed, 2185 records were excluded on basis of title or abstract because those studies were not relevant to this review (n=2107) or were reviews/commentary (n= 78). The remaining 116 full articles were selected for the eligibility assessment. Of those, 7 were excluded for repeated data, 9 were excluded for targeting PLWH who received psychological intervention or suffered from genocide/natural disaster, and 62 were excluded for not reporting the PTSD prevalence among PLWH. Finally, a total of 38 studies [14 24 25 38-72] met inclusion criteria and were included in this meta-analysis. Search results are elaborated in Figure 1.

Study characteristics

Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a generally moderate to high level of data quality (online supplementary appendix 2). Table 1 shows the characteristics of the included studies. These studies were published between 2002[72] and 2019. [38] Geographically, over half (n=21, 55.3%) of the 38 included studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%), Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%) conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not report their sampling methods, convenience sampling methods were adopted in most studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41 to 1489), of which 2742 were identified with PTSD.

Table 1 Characteristics of the included studies

First author	Year of publication	Location of study	Sampling methods	Sample size*	No. of patients with PTSD	Measurements	Data Collection	Quality
Fabian[38]	2019	USA	convenience sampling	238	80	PCL-C	self-report questionnaire	moderate
Cheng[39]	2018	China	unclear	535	142	PCL-C	self-report questionnaire	moderate
Spies[40]	2018	South Africa	convenience sampling	68	10	DTS	self-report questionnaire	moderate
Verhey[41]	2018	Zimbabwe	random sampling	91	22	CAPS	clinical interview	moderate
Gao[42]	2018	China	convenience sampling	520	89	PCL-C	self-report questionnaire	moderate
McLean[43]	2017	USA	convenience sampling	42	12	PSS	clinical interview	moderate
Kemppainen[25]	2017	USA	convenience sampling	60	26	PCL-C	self-report questionnaire	low
Gonzalez[24]	2016	USA	convenience sampling	137	47	PDS	self-report questionnaire	moderate
Rubin[44]	2016	USA	convenience sampling	1004	174	PCL-C	self-report questionnaire	moderate

John[45]	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
Julnes[14]	2016	USA	convenience sampling	114	39	CDQ	self-report questionnaire	moderate
Zhang[46]	2016	China	convenience sampling	243	106	PCL-C	self-report questionnaire	low
Battaglia[47]	2015	USA	convenience sampling	200	72	PTSD checklist	self-report questionnaire	moderate
Hansrod[48]	2015	South Africa	convenience sampling	114	29	MINI	clinical interview	moderate
Brownley[49]	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
Malee[50]	2014	USA	convenience sampling	1223	281	CDQ	self-report questionnaire	high
Glémaud[51]	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
Gore-Felton[52]	2013	USA	convenience sampling	94	28	PCL-C	self-report questionnaire	low
Glover[53]	2013	USA	convenience sampling	99	24	PDS	self-report questionnaire	high
Dévieux[54]	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate

Gard[55]	2013	Rwanda	unclear	705	380	HTS	self-report questionnaire	moderate
Peterson[56]	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
Kinyanda[57]	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
Bogart[58]	2011	USA	convenience sampling	181	72	PDS	self-report questionnaire	moderate
Martin[59]	2011	UK	convenience sampling	85	46	CIDI	clinical interview	moderate
Reisner[60]	2011	USA	convenience sampling	63	16	AUDADIS-IV	clinical interview	moderate
Theuninck[61]	2010	UK	convenience sampling	100	33	PCL-C	self-report questionnaire	low
Joska[62]	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
Adewuya[63]	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
Spies[64]	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
Fincham[65]	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate

Zanjani[66]	2007	USA	random sampling	109	13	MINI	clinical interview	moderate
Israelski[67]	2007	USA	unclear	210	71	PCL-C	self-report questionnaire	low
Boarts[68]	2006	USA	convenience sampling	57	24	PDS	self-report questionnaire	moderate
Leserman[69]	2005	USA	consecutive sampling	611	98	PTSD checklist	self-report questionnaire	high
Olley[70]	2003	South Africa	consecutive sampling	149	42	MINI	clinical interview	moderate
Vitiello[71]	2003	USA	probability sample	1489	155	CIDI	clinical interview	moderate
Martinez[72]	2002	USA	consecutive sampling	41	17	PCL-C	self-report questionnaire	moderate

* Total number of adults living with HIV

PCL-C Posttraumatic Stress Disorder Checklist-Civilian Version; *DTS* Davidson Trauma Scale; *CAPS* Clinician Administered Post-traumatic Stress Scale; *CDQ* Client Diagnostic Questionnaire; *PDS* Posttraumatic Stress Diagnostic Scale – Self-report version; *PSS* Posttraumatic Stress Symptom Scale; *PRIME MD PHQ* Primary Care Evaluation of Mental Disorders Patient Health Questionnaire; *AUDADIS-IV* The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; *MINI* Mini-International Neuropsychiatric

Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV

Prevalence of PTSD in PLWH

The reported prevalence of PTSD in PLWH ranged from 1.6% [57] to 54.1% [59]. The overall pooled prevalence was 28% (95%CI: 24% to 33%), estimated by a random effects model, as significant heterogeneity ($p \leqslant 0.001$, $I^2=98.1\%$) was observed among the included studies. Meta-analyses are shown as forest plots (Fig. 2).

Publication bias and sensitivity analysis

Possible publication bias was indicated according to the results of Egger's linear test (t= 6.84, p<0.05) and Begg's rank test (z=0.58, p=0.56). However, low sensitivity was suggested with the pooled prevalence of PTSD changed slightly from 28% (95%CI: 24% to 33%) to 27% (95%CI: 22% to 32%) after excluding low-quality articles.

Subgroup Analyses

The results of subgroup analyses are shown in Table 2. The prevalence of PTSD in PLWH differed significantly by geographic area, population group, sampling and measurement method. Specifically, the proportion of PLWH with PTSD in high-income countries tended to be higher (pooled rate= 29%, 95%CI 25% to 34%) than middle-income countries (pooled rate= 27%, 95%CI 16% to 37%) and low-income countries (pooled rate= 26%, 95%CI 7% to 45%). Studies using clinical interviews reported lower prevalence rates of PTSD (pooled rate= 22%, 95%CI 16% to 27%) compared with those using self-report questionnaires (pooled rate= 31%, 95%CI 27% to 36%). The pooled PTSD prevalence among women living with HIV, MSM living with HIV and non-MSM men living with HIV were 35% (95%CI: 28% to 43%), 33% (95%CI: 29% to 38%) and

20% (95%CI: 17% to 23%), respectively. Also, studies conducted with convenience sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to 24%).

Table 2 Subgroup analyses of the prevalence of PTSD in PLWH

Subgroup		Number of studies	Positive PTSD screening (Diagnosis)	Sample size (Tested)	Pooled prevalence of PTSD (95%CI)	Heterogeneity (I^2)	Between group difference	
							χ^2	P value
Geographic area	High-income countries	23	1483	6832	0.29(0.25-0.34)	94.70%	107.32	<0.001
	Middle-income countries	10	1077	3755	0.27(0.16-0.37)	98.60%		
	Low-income countries	5	182	1156	0.26(0.07-0.45)	98.30%		
Population group	Women living with HIV	15	1282	4190	0.35(0.28-0.43)	96.10%	26.99	<0.001
	MSM living with HIV	3	129	380	0.33(0.29-0.38)	73.70%		
	non-MSM male living with HIV	4	165	754	0.20(0.17-0.23)	89.10%		
Sampling	Consecutive sampling	7	280	2387	0.17(0.10-0.24)	97.30%	206.01	<0.001
	Convenience sampling	20	1260	4746	0.32(0.27-0.37)	91.60%		

Data collection	Self-report questionnaire	25	2197	7812	0.31(0.27-0.36)	95.70%	297.01	<0.001
	Clinical interview	13	545	3931	0.22(0.16-0.27)	97.20%		

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to provide the pooled estimated prevalence of PTSD among PLWH. A comprehensive search of the literature assessing the rate of comorbidity between PTSD and HIV-infection was performed, and 38 studies met the predefined criteria and were included in the meta-analysis. A total of 11743 participants were involved, of which 2742 were identified with PTSD. The estimated pooled prevalence rate was 28% (95% CI: 24% to 33%), which suggests a considerable burden of PTSD in the HIV-infected population. High heterogeneity across studies was detected, and factors such as differences in region, population characteristics, sampling, and measurement were associated with prevalence rates.

As indicated, the PTSD prevalence rate among PLWH found in this study (28%) not only far exceeded that among the general population (3.9%), [73] but was also much higher than the prevalence of PTSD among other vulnerable groups in some previous studies. For example, the prevalence rate for cancer-related PTSD was 5.1%-15.3%;[74] in persons with chronic pain, the estimated mean prevalence of PTSD was 9.7%. [75] The pooled prevalence of PTSD among PLWH found in this study heightened the high rate of co-morbidity between HIV infection and PTSD, which is consistent with previous demonstrations. [8 76] For PLWH, although depressive symptoms have been the focus of many studies, and 36% of PLWH were likely to have depression according to nationally representative data in the U.S., [77] this pooled estimated prevalence of PTSD among PLWH showed that PTSD is also a common mental disorder among individuals living

with HIV/AIDS. Therefore, the results of our study significantly underscore the importance of early assessment and trauma-directed psychological interventions for PLWH.

Undoubtedly, heterogeneity between studies is expected in such a relatively large topic of review. In this review, the estimated PTSD prevalence rates in PLWH varied widely (1.6%-54.1%) across studies and countries, which is also a common problem in the epidemiology of psychological and mental health disorders. [78 79] Consistent with the findings of previous research, [59] the majority of studies which have determined the incidence of HIV-related PTSD have been conducted in developed countries (n=23). Compared with lower-income countries, higher-income countries reported relatively higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among PLWH may be explained by the cross-cultural differences in attitudes towards HIV infection. Turan et al.[80] found that the level of perceived HIV-related stigma in the community experienced by PLWH may cause adverse health and psychosocial outcomes. Social isolation and stigma might exacerbate symptoms of PTSD. [81] In high-income countries, PLWH may experience "compound" or "layered" stigma, where stigmatizing beliefs are not only associated with HIV infection but also related to sexual orientation, commercial sexual behaviors, etc. [82] Although, HIV-related stigma is highly burdensome in some mid-income countries, such as China, [83 84] the reported prevalence of PLWH with PTSD was lower compared to higher-income countries. The differences between collectivism and individualism rooted in eastern and western culture may be an

explanation. [85] It is worth noting that social context may not only influence the susceptibility of mental health disorders, but also constitutes an important factor in perceived stigma among individuals with mental illness. Compared to high-income countries, stigmatizing beliefs about the causes and presence of mental illness are still widespread in low- and middle-income countries, [86 87] which may lead to less disease reporting. Caution must be applied, since there is a lack of studies investigating HIV-related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular, detection of prevalence is associated with the representativeness and size of sample. In the context of low- and middle-income countries, it could be argued that lower HIV testing rates may underestimate the PTSD prevalence and impact generalizability. Thus, more epidemiological studies are warranted to better understand and clarify the difference in PTSD prevalence among PLWH globally.

Subgroup analyses indicated that the prevalence of PTSD differed significantly when gender and sexual orientation were taken into consideration. Specifically, women living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence in PTSD, in which being female is a risk factor associated with PTSD development. [16] As suggested by the aforementioned findings, HIV-infected MSM may experience higher levels of stigma and trauma related to their sexual orientation. [30 88] Compared with heterosexual counterparts, MSM reported higher risk for suicidal ideation, [89] which also indicates greater psychological stress and mental health problems (i.e. PTSD and

depression). The findings that MSM and female HIV-infected individuals are at higher risk of developing PTSD may indicate that related health promotion campaigns should be directed to these groups. Clinicians should also take into consideration the PTSD susceptibility in different groups of HIV-infected populations during diagnoses. Notably, most eligible studies did not provide separate prevalence rates regarding the gender of participants, and only 3 studies identified PTSD prevalence among MSM living with HIV. Given that these data are from a small number of studies and/or participants, this finding should be interpreted with caution. Nonetheless, given the high prevalence of PTSD in this group, future efforts should be made to obtain more prevalence data on PTSD among MSM living with HIV.

In our study, we assessed methodological differences that may result in heterogeneity. Factors including sampling strategies (convenience vs consecutive) and measurement (self-report vs clinical interview) were evaluated by subgroup analyses. Among 38 studies providing estimated prevalence of PTSD, 7 reported participants were consecutively enrolled via self-referral from flyers describing the study or advertisements from HIV health care providers, and generated a lower pooled prevalence rate (17%) compared with the other 20 studies using convenience sampling (32%), though both sampling methods were non-probabilistic. An increase in reporting rate due to convenience sampling has also been found in another meta-analysis synthesizing the HCV seroconversion rates in HIV-positive MSM. [90] Convenience samples may allow researchers to select participants who are more likely to have PTSD

symptoms and lead to over-estimation, but given that only 4 studies were rated as high quality and limited description of study methods was detected in some studies, the reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness of calculating pooled prevalence estimates could be questioned, and the pooled prevalence estimate regarding the varied recruitment approaches of the studies should be interpreted with caution.

In this review, a total of 14 different tools were used to assess PTSD symptoms among PLWH across studies. Overall, the prevalence rate of PTSD screened by self-report instruments (31%) was higher than that assessed by clinical interview (22%). Though both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD), clinical interviews most likely do a much better job of assessing symptoms carefully – for example, not counting symptoms that do not meet clinically meaningful thresholds, and self-report measures may inflate the prevalence estimates; [91] alternatively, subjects may be more comfortable reporting symptoms using self-report questionnaires (presumably paper or online surveys rather than face-to-face interviews). Screening or diagnosing with survey instruments is a common and practical method, especially in resource-limited regions. We found that, though a number of measures have been used to assess PTSD among PLWH, there is no tool designed for this population specifically. As the sensitivity and specificity of the measures may impact accurate PTSD detection, further research is required to identify a standardized measure accordingly to improve validity.

Certain limitations should be acknowledged in this meta-analysis. First, though minimal potential for publication bias was presumed as all data drawn for this review were from studies reporting estimated point prevalence without intervention, publication bias cannot be ruled out for there are a number of studies published in languages other than English and Chinese. Second, the heterogeneity was high in the whole sample and most subgroups. Heterogeneity importantly influences the reliability and accuracy of a meta-analysis, and only careful selection of appropriate studies is the reliable method for acquiring correct inferences. [92] Even though strict eligibility criteria were employed in addressing HIV-PTSD prevalence in this study, it should be noted that getting HIV is only one possible traumatic event. This review suggests the need to consider traumatic experiences for further studies assessing PTSD among PLWH. In addition, we have analysed the influences of region, population group, recruitment venue, and measurement method, which explained some of the heterogeneity. However, the results should be interpreted with caution. Third, though some studies have indicated that several sociodemographic factors such as age may be associated with PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified by age due to the lack of detailed information reported in the published studies. As the quality of reporting could increase the susceptibility to bias, it is imperative for researchers to report their findings of observational studies in accordance with the appropriate guidelines, such as the STROBE checklist.

CONCLUSIONS

This review contributes to evidence on the quantitatively pooled prevalence of PTSD among PLWH. Stratified subgroups including geographic area, population group, sampling and measurement method were found to be significant factors accounting for the varied prevalence of PTSD among PLWH. More effective intervention strategies targeting PTSD among PLWH are urgently needed. Future efforts should be made to obtain countries' own PTSD prevalence data among PLWH as well as specific vulnerable minorities, which will provide a basis for public health policy, health-care planning, and resource allocation for PTSD intervention initiatives. Our study also suggests that more research using robust and comprehensive methodology is needed to provide rigorous evidence for designing the targeted psychological interventions.

Figure 1 Flow chart of study inclusion

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

Contributors: Conception of the work: HW and CT. Systematic review and article evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT, LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the authors. All the authors fulfill the ICMJE criteria for authorship.

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REFERENCES

1. UNAIDS. UNAIDS Data 2018. http://www.unaids.org/en/resources/documents/2018/unaids-data-2018 (Accessed 18 March 2019).
2. Niu L, Luo D, Liu Y, *et al.* The mental health of people living with HIV in China, 1998–2014: a systematic review. *PLoS One*. 2016;11:e0153489.
3. Adams C, Zacharia S, Masters L, *et al*. Mental health problems in people living with HIV: changes in the last two decades: the London experience 1990–2014. *AIDS care*. 2016;28:56–9.
4. Friedman MJ, Resick PA, Bryant RA, *et al.* Considering PTSD for DSM-5. *Depression and anxiety.* 2011;28:750–69.
5. Young C. Understanding HIV-related posttraumatic stress disorder in South Africa: a review and conceptual framework. *African Journal of AIDS Research*. 2011;10:139–48.
6. Sherr L, Nagra N, Kulubya G, *et al.* HIV infection associated post-traumatic stress

disorder and post-traumatic growth–a systematic review. *Psychology, health & medicine*. 2011;16:612–29.

7. Cavanaugh CE, Hansen NB, Sullivan TP. HIV sexual risk behavior among low-income women experiencing intimate partner violence: The role of posttraumatic stress disorder. *AIDS Behav.* 2010;14:318–27.
8. Neigh GN, Rhodes ST, Valdez A, *et al.* PTSD co-morbid with HIV: Separate but equal, or two parts of a whole? *Neurobiology of disease*. 2016;92:116–23.
9. Borwein A, Salters KA, Palmer AK, *et al.* High rates of lifetime and recent violence observed among harder-to-reach women living with HIV. *AIDS care*. 2014;26:587–94.
10. Luo S, Lin C, Ji G, *et al.* Post-traumatic Stress Disorder Symptoms Among People Living with HIV/AIDS in Rural China. *AIDS Behav*. 2017;21:3202–8.
11. Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *The Journal of clinical psychiatry*. 2000;61(Suppl 5):4-14.
12. Pence BW. The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS. *Journal of Antimicrobial Chemotherapy.* 2009;63:636–40.
13. Ebrahimzadeh Z, Goodarzi MA, Joulaei H. Predicting the Antiretroviral Medication Adherence and CD4 Measure in Patients with HIV/AIDS Based on the Post Traumatic Stress Disorder and Depression. *Iranian Journal of Public Health*. 2019;48:139–46.

14. Julnes PS, Auh S, Krakora R, *et al.* The association between post-traumatic stress disorder and markers of inflammation and immune activation in HIV-infected individuals with controlled viremia. *Psychosomatics.* 2016;57:423–30.

15. Lynn C, Chenneville T, Bradley-Klug K, *et al.* Depression, anxiety, and posttraumatic stress as predictors of immune functioning: differences between youth with behaviorally and perinatally acquired HIV. *AIDS care*. 2019 Mar 4:1–10.

16. Brief DJ, Bollinger AR, Vielhauer MJ, *et al.* Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*. 2004;16:97–120.

17. Nightingale VR, Sher TG, Mattson M, *et al.* The effects of traumatic stressors and HIV-related trauma symptoms on health and health related quality of life. *AIDS Behav*. 2011;15:1870–8.

18. Koegler E, Kennedy CE. A scoping review of the associations between mental health and factors related to HIV acquisition and disease progression in conflict-affected populations. *Confl Health*. 2018;12:20.

19. Pearson CR, Kaysen D, Huh D, *et al.* Randomized Control Trial of Culturally Adapted Cognitive Processing Therapy for PTSD Substance Misuse and HIV Sexual Risk Behavior for Native American Women. *AIDS Behav*. 2019;23:695–706.

20. Tull MT, Weiss NH, McDermott MJ. Post-traumatic stress disorder and impulsive and risky behavior: Overview and discussion of potential mechanisms. *Comprehensive guide to post-traumatic stress disorders*. 2016;803–16.

21. Weiss NH, Tull MT, Borne MER, *et al.* Posttraumatic stress disorder symptom severity and HIV-risk behaviors among substance-dependent inpatients. *AIDS care*. 2013;25:1219–26.

22. Applebaum AJ, Bedoya CA, Hendriksen ES, *et al.* Future directions for interventions targeting PTSD in HIV-infected adults. *Journal of the Association of Nurses in AIDS Care*. 2015;26:127–38.

23. Machtinger E, Wilson T, Haberer JE, *et al.* Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS Behav*. 2012;16:2091–100.

24. Gonzalez A, Locicero B, Mahaffey B, *et al.* Internalized HIV stigma and mindfulness: associations with PTSD symptom severity in trauma-exposed adults with HIV/AIDS. *Behavior modification*. 2016;40:144–63.

25. Kemppainen JK, MacKain S, Alexander M, *et al.* Posttraumatic stress disorder and stressful life events among rural women with HIV disease. *Journal of the Association of Nurses in AIDS Care*. 2017;28:216–25.

26. Rubin LH, Cook JA, Springer G, *et al.* Perceived and post-traumatic stress are associated with decreased learning, memory, and fluency in HIV-infected women. *AIDS (London, England)*. 2017;31:2393–1401.

27. Seedat S. Interventions to improve psychological functioning and health outcomes of HIV-infected individuals with a history of trauma or PTSD. *Current HIV/AIDS Reports*. 2012;9:344–50.

28. World Health Organization. The ICD-10 classification of mental and behavioural

disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.

29. Association AP. Diagnostic and statistical manual of mental disorders. 5th Edition. Washington, DC: American Psychiatric Pub; 2013.

30. Sales JM, Swartzendruber A, Phillips AL. Trauma-Informed HIV Prevention and Treatment. *Curr HIV/AIDS Rep*. 2016;13:374–82.

31. Burnham KE, Cruess DG, Kalichman MO, *et al.* Trauma symptoms, internalized stigma, social support, and sexual risk behavior among HIV-positive gay and bisexual MSM who have sought sex partners online. *AIDS care*. 2016;28:347–53.

32. Rzeszutek M, Oniszczenko W, Firląg-Burkacka E. Gender differences in posttraumatic stress symptoms and social support in a sample of HIV-positive individuals. *Women & health*. 2017;57:792–803.

33. Rostom A, Dubé C, Cranney A, *et al.* Appendix D. Quality Assessment Forms. Agency for Healthcare Research and Quality (US); 2004 https://www.ncbi.nlm.nih.gov/books/NBK35156/ (Accessed 21 October 2018).

34. Stata C, Station C. TX. Stata Press 2016

35. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine. 2002;21(11):1539-58.

36. Egger M, Smith GD, Schneider M, *et al.* Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1997; 315: 629–34.

37. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for

publication bias. *Biometrics.* 1994; 50: 1088–101.

38. Fabian KE, Huh D, Kemp CG, *et al.* Moderating Factors in an Anti-stigma Intervention for African American Women with HIV in the United States: A Secondary Analysis of the UNITY Trial. *AIDS and Behavior*. 2019;19:1-11.
39. Chen CD, Yan H, Li SY, *et al.* Post-traumatic stress disorder and it associated factors among people living with HIV in Wuhan city. *Chin J Public Health*. 2018;1-4.
40. Spies G, Konkiewitz EC, Seedat S. Incidence and persistence of depression among women living with and without HIV in South Africa: A longitudinal study. *AIDS Behav*. 2018;22(10):3155–65.
41. Verhey R, Chibanda D, Gibson L, *et al.* Validation of the posttraumatic stress disorder checklist - 5 (PCL-5) in a primary care population with high HIV prevalence in Zimbabwe. *BMC Psychiatry.* 2018;18:109.
42. Gao M, Xiao C, Zhang X, *et al.* Social capital and PTSD among PLWHA in China: the mediating role of resilience and internalized stigma. *Psychology, health & medicine*. 2018;23:698–706.
43. McLean CP, Gay NG, Metzger DA, *et al.* Psychiatric Symptoms and Barriers to Care in HIV-Infected Individuals Who Are Lost to Care. *J Int Assoc Provid AIDS Care.* 2017;16:423–9.
44. Rubin LH, Pyra M, Cook JA, *et al.* Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected

women. *Journal of neurovirology.* 2016;22:159–69.

45. John M, Greene M, Hessol NA, *et al.* Geriatric assessments and association with VACS index among HIV-infected older adults in San Francisco. *Journal of acquired immune deficiency syndromes (1999).* 2016;72:534.
46. Zhang X, Wang T, Liu M, *et al.* Post-traumatic stress disorder among people living with HIV/AIDS and its influence factors. *Chongqing Medicine.* 2016;232–5.
47. Battaglia TA, Gunn CM, McCoy ME, *et al.* Beliefs About Anal Cancer among HIV-Infected Women: Barriers and Motivators to Participation in Research. *Womens Health Issues*. 2015;25:720–6.
48. Hansrod F, Spies G, Seedat S. Type and severity of intimate partner violence and its relationship with PTSD in HIV-infected women. *Psychology, health & medicine.* 2015;20:697–709.
49. Brownley JR, Fallot RD, Berley RW, *et al.* Trauma history in African-American women living with HIV: effects on psychiatric symptom severity and religious coping. *AIDS care.* 2015;27:964–71.
50. Malee K, Mellins CA, Huo Y, *et al.* Prevalence, incidence and persistence of psychiatric and substance use disorders among mothers living with HIV. *Journal of acquired immune deficiency syndromes (1999).* 2014;65:526.
51. Glémaud M, Illa L, Echenique M, *et al.* Abuse and mental health concerns among HIV-infected Haitian women living in the United States. Journal of the Association of Nurses in *AIDS Care.* 2014;25:S62–9.

52. Gore-Felton C, Ginzburg K, Chartier M, *et al.* Attachment style and coping in relation to posttraumatic stress disorder symptoms among adults living with HIV/AIDS. *Journal of behavioral medicine.* 2013;36:51–60.

53. Glover DA, Williams JK, Kisler KA. Using novel methods to examine stress among HIV-positive African American men who have sex with men and women. *J Behav Med*. 2013;36:283–94.

54. Dévieux JG, Malow RM, Attonito JM, *et al.* Post-traumatic stress disorder symptomatology and alcohol use among HIV-seropositive adults in Haiti. *AIDS care*. 2013;25(10):1210-8.

55. Gard TL, Hoover DR, Shi Q, *et al.* The impact of HIV status, HIV disease progression, and post-traumatic stress symptoms on the health-related quality of life of Rwandan women genocide survivors. *Quality of Life Research*. 2013;22(8):2073-84.

56. Peterson K, Togun T, Klis S, *et al.* Depression and posttraumatic stress disorder among HIV-infected Gambians on antiretroviral therapy. *AIDS patient care and STDs*. 2012;26:589–96.

57. Kinyanda E, Hoskins S, Nakku J, *et al.* Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. *BMC psychiatry*. 2011;11:205.

58. Bogart LM, Wagner GJ, Galvan FH, *et al.* Perceived discrimination and mental health symptoms among Black men with HIV. *Cultural Diversity and Ethnic*

Minority Psychology. 2011;17:295.

59. Martin L, Kagee A. Lifetime and HIV-related PTSD among persons recently diagnosed with HIV. *AIDS Behav*. 2011;15:125–31.

60. Reisner SL, Falb KL, Mimiaga MJ. Early life traumatic stressors and the mediating role of PTSD in incident HIV infection among US men, comparisons by sexual orientation and race/ethnicity: results from the NESARC, 2004–2005. *Journal of Acquired Immune Deficiency Syndromes*. 2011;57:340–50.

61. Theuninck AC, Lake N, Gibson S. HIV-related posttraumatic stress disorder: Investigating the traumatic events. *AIDS Patient care and STDS*. 2010;24:485–91.

62. Joska JA, Fincham DS, Stein DJ, *et al.* Clinical correlates of HIV-associated neurocognitive disorders in South Africa. *AIDS Behav*. 2010;14:371–8.

63. Adewuya AO, Afolabi MO, Ola BA, *et al.* Post-traumatic stress disorder (PTSD) after stigma related events in HIV infected individuals in Nigeria. *Social Psychiatry and Psychiatric Epidemiology*. 2009;44:761.

64. Spies G, Kader K, Kidd M, *et al.* Validity of the K-10 in detecting DSM-IV-defined depression and anxiety disorders among HIV-infected individuals. *AIDS care*. 2009;21:1163–8.

65. Fincham D, Smit J, Carey P, *et al.* The relationship between behavioural inhibition, anxiety disorders, depression and CD4 counts in HIV-positive adults: a cross-sectional controlled study. *AIDS care.* 2008;20:1279–83.

66. Zanjani F, Saboe K, Oslin D. Age difference in rates of mental health/substance

abuse and behavioral care in HIV-positive adults. *AIDS patient care and STDs*. 2007;21:347–55.

67. Israelski DM, Prentiss DE, Lubega S, *et al.* Psychiatric co-morbidity in vulnerable populations receiving primary care for HIV/AIDS. *AIDS care*. 2007;19:220–5.
68. Boarts JM, Sledjeski EM, Bogart LM, *et al.* The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS Behav.* 2006;10:253–61.
69. Leserman J, Whetten K, Lowe K, *et al.* How trauma, recent stressful events, and PTSD affect functional health status and health utilization in HIV-infected patients in the south. *Psychosomatic medicine*. 2005;67:500–7.
70. Olley BO, Gxamza F, Seedat S, *et al.* Psychopathology and coping in recently diagnosed HIV/AIDS patients-the role of gender. *South African Medical Journal*. 2003;93:928–31.
71. Vitiello B, Burnam MA, Bing EG, *et al.* Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry*. 2003;160:547–54.
72. Martinez A, Israelski D, Walker C, *et al.* Posttraumatic stress disorder in women attending human immunodeficiency virus outpatient clinics. *AIDS patient care and STDs.* 2002;16:283–91.
73. Koenen KC, Ratanatharathorn A, Ng L, *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med.* 2017;47:2260–74.

74. Abbey G, Thompson SBN, Hickish T, *et al.* A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology*. 2015;24:371–81.

75. Siqveland J, Hussain A, Lindstrøm JC, *et al.* Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. *Frontiers in Psychiatry.* 2017;8:164.

76. Kelly B, Raphael B, Judd F, *et al.* Posttraumatic stress disorder in response to HIV infection. *General Hospital Psychiatry*. 1998;20:345–52.

77. Bing EG, Burnam MA, Longshore D, *et al.* Psychiatric disorders and drug use among human immunodeficiency virus–infected adults in the United States. *Archives of general psychiatry.* 2001;58:721–8.

78. Pringsheim T, Jette N, Frolkis A, *et al.* The prevalence of Parkinson's disease: A systematic review and meta-analysis. *Movement disorders.* 2014;29:1583–90.

79. Wang T, Fu H, Kaminga AC, *et al*. Prevalence of depression or depressive symptoms among people living with HIV/AIDS in China: a systematic review and meta-analysis. *BMC psychiatry.* 2018 Dec;18(1):160.

80. Turan B, Budhwani H, Fazeli PL, *et al.* How Does Stigma Affect People Living with HIV? The Mediating Roles of Internalized and Anticipated HIV Stigma in the Effects of Perceived Community Stigma on Health and Psychosocial Outcomes. *AIDS Behav*. 2017;21:283–91.

81. Kamen C, Vorasarun C, Canning T, *et al.* The impact of stigma and social support

on development of post-traumatic growth among persons living with HIV. *Journal of clinical psychology in medical settings*. 2016;23:126–34.

82. Lowther K, Selman L, Harding R, *et al.* Experience of persistent psychological symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): a systematic review. *International journal of nursing studies*. 2014;51(8):1171-89.
83. Li Z, Morano JP, Khoshnood K, *et al.* HIV-related stigma among people living with HIV/AIDS in rural Central China. *BMC Health Serv Res*. 2018;18:453.
84. Li L, Liang L-J, Lin C, *et al.* HIV prevention intervention to reduce HIV-related stigma: evidence from China. *AIDS (London, England)*. 2010;24:115.
85. Shavitt S, Cho YI, Johnson TP, *et al.* Culture Moderates the Relation Between Perceived Stress, Social Support, and Mental and Physical Health. *Journal of Cross-Cultural Psychology*. 2016;47:956–80.
86. Lauber C, Rössler W. Stigma towards people with mental illness in developing countries in Asia. *International Review of Psychiatry*. 2007;19:157–78.
87. Seeman N, Tang S, Brown AD, *et al.* World survey of mental illness stigma. *Journal of Affective Disorders.* 2016;190:115–21.
88. Reisner SL, Mimiaga MJ, Safren SA, *et al.* Stressful or traumatic life events, post-traumatic stress disorder (PTSD) symptoms, and HIV sexual risk taking among men who have sex with men. *AIDS care*. 2009;21:1481–9.
89. Luo Z, Feng T, Fu H, *et al.* Lifetime prevalence of suicidal ideation among men

who have sex with men: a meta-analysis. *BMC psychiatry*. 2017;17:406.

90. Hagan H, Jordan AE, Neurer J, *et al.* Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS*. 2015;29:2335–45.

91. Ayers S, Wright DB, Ford E. Hyperarousal symptoms after traumatic and nontraumatic births. *Journal of Reproductive and Infant Psychology*. 2015;33:282–93.

92. Melsen WG, Bootsma MC, Rovers MM, *et al*. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clinical Microbiology and Infection*. 2014;20(2):123-9.

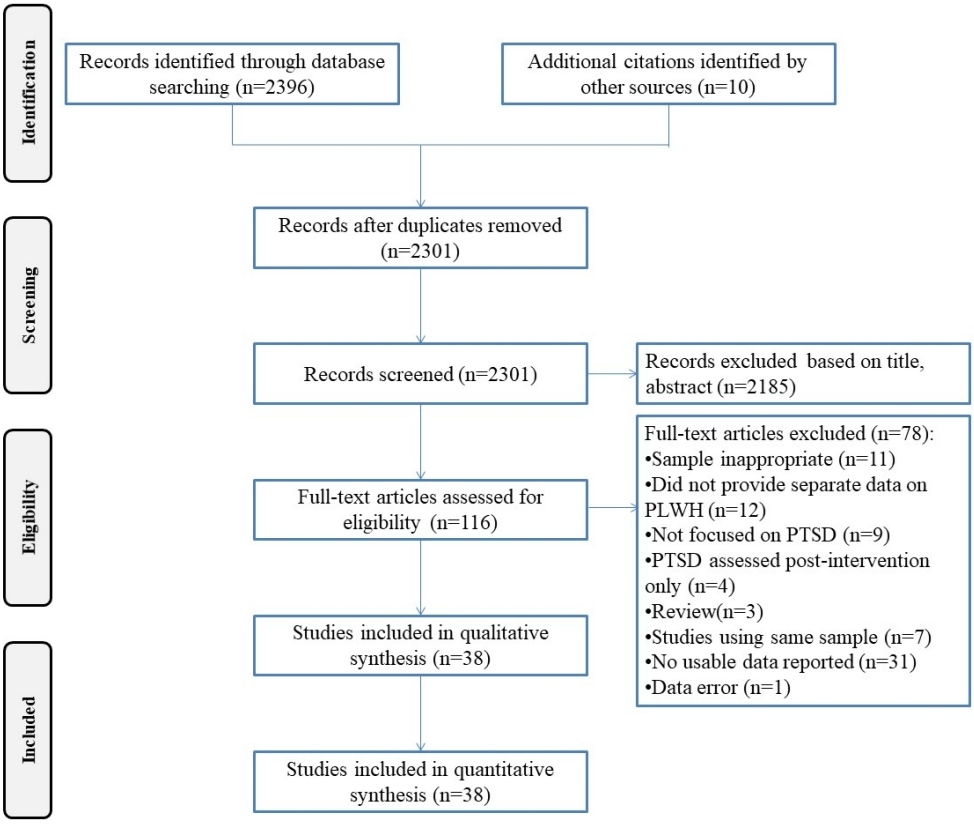

Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

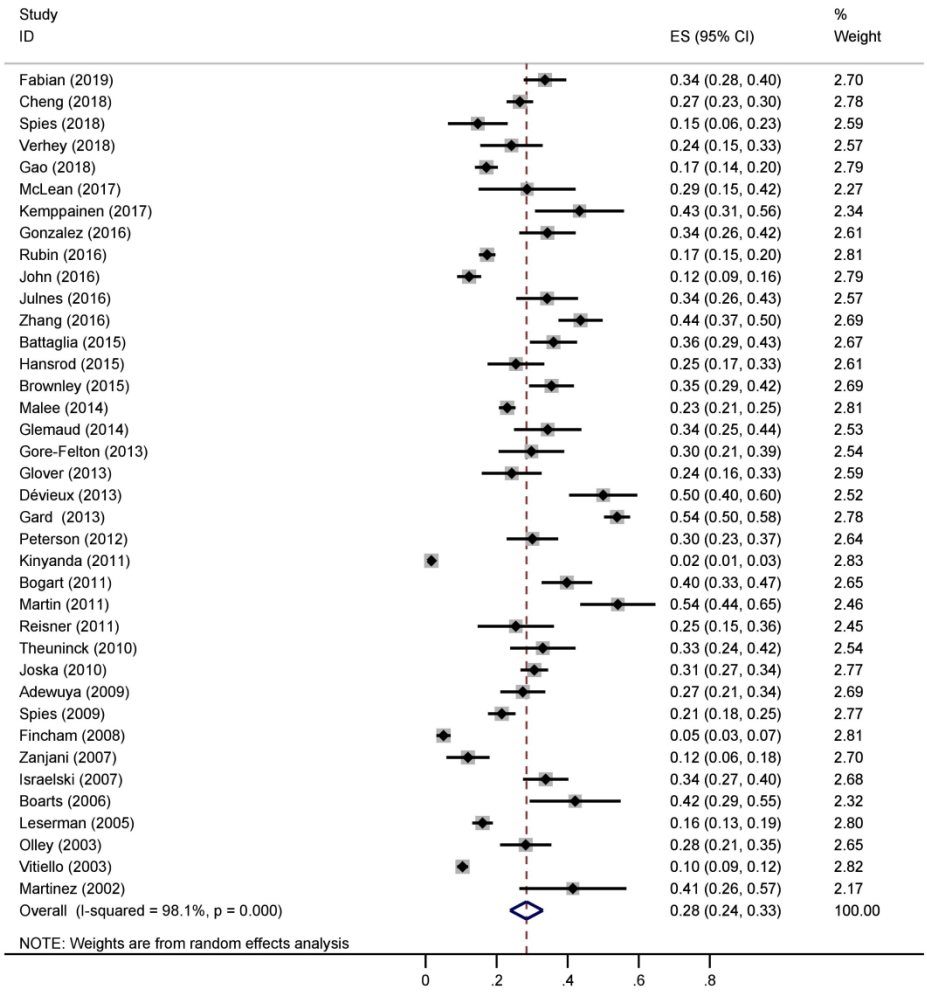

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

281x304mm (300 x 300 DPI)

Appendix 1 – Search strategy

ID	Search terms
PubMed	
#1	("stress disorders, post-traumatic"[Mesh] OR PTSD*[tiab] OR posttrauma*[tiab] OR "post trauma*" [tiab]OR post-trauma*[tiab] OR trauma* [tiab] OR psychotrauma*[tiab] OR stress*[tiab])
#2	("HIV Infections"[Mesh] OR "HIV" [MeSH] OR "human immunodeficiency virus" [tiab] OR "human immuno deficiency virus" [tiab] OR "human immune deficiency virus" [tiab] OR "human immunedeficiency virus" [tiab] OR "AIDS" [tiab] OR "acquired immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency syndromes" [tiab] OR "acquired immuno deficiency syndrome" [tiab] OR "acquired immuno deficiency syndromes" [tiab] OR "acquired immune deficiency syndrome" [tiab] OR "acquired immune deficiency syndromes" [tiab] OR "acquired immunedeficiency syndrome" [tiab] OR "acquired immunedeficiency syndromes" [tiab])
#3	(((((((("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Cross-Sectional Studies"[Mesh])) OR Prevalence) OR Epidemiology) OR Cross-Sectional Studies) OR "Longitudinal Studies"[Mesh]) OR "Cohort Studies"[Mesh]) OR Cohort Studies) OR Longitudinal Studies))
#4	#1 AND #2 AND #3

Search Filters

a. Human studies
b. Language – English/Chinese
c. Publication dates – From 2000/01/01 to 2019/11/31

Appendix 2 – Risk of bias and quality of included studies

Country	Year	Citation	1	2	3	4	5	6	7	8	9	10	11	Quality
USA	2019	Fabian 2019	yes	yes	no	unclear	unclear	no	no	yes	no	yes	yes	moderate
China	2018	Cheng 2018	yes	yes	yes	unclear	unclear	yes	no	no	no	no	no	moderate
South Africa	2018	Spies 2018	yes	yes	no	no	unclear	yes	no	yes	no	no	no	moderate
Zimbabwe	2018	Verhey 2018	yes	yes	yes	no	unclear	yes	yes	no	no	yes	no	moderate
China	2018	Gao 2018	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
USA	2017	McLean 2017	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2017	Kemppainen 2017	yes	yes	no	no	unclear	no	no	no	no	no	no	low
USA	2016	Gonzalez 2016	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2016	Rubin 2016	yes	yes	yes	no	no	no	yes	yes	yes	yes	no	moderate
USA	2016	John 2016	yes	no	yes	yes	no	yes	no	no	no	no	no	moderate
USA	2016	Julnes 2016	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
China	2016	Zhang 2016	yes	yes	no	no	no	no	no	no	no	yes	no	low
USA	2015	Battaglia 2015	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
South Africa	2015	Hansrod 2015	yes	yes	yes	no	unclear	yes	no	yes	no	no	no	moderate
USA	2015	Brownley 2015	yes	yes	yes	unclear	unclear	no	no	no	no	yes	no	moderate
USA	2014	Malee 2014	yes	yes	yes	no	unclear	no	yes	yes	yes	yes	yes	high
USA	2014	Glémaud 2014	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low

USA	2013	Gore-Felton 2013	yes	yes	no	no	unclear	yes	no	no	no	no	no	low
USA	2013	Glover 2013	yes	yes	no	unclear	unclear	yes	yes	yes	yes	yes	yes	high
Haiti	2013	Dévieux 2013	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
Rwanda	2013	Gard 2013	yes	yes	yes	unclear	no	no	yes	yes	no	yes	no	moderate
Gambia	2012	Peterson 2012	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	no	high
Uganda	2011	Kinyanda 2011	yes	yes	yes	yes	unclear	no	yes	yes	no	yes	no	moderate
USA	2011	Bogart 2011	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
UK	2011	Martin 2011	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
USA	2011	Reisner 2011	yes	yes	yes	no	unclear	no	yes	yes	yes	no	no	moderate
UK	2010	Theuninck 2010	yes	no	no	no	no	no	no	no	no	no	no	low
South Africa	2010	Joska 2010	yes	yes	no	unclear	unclear	yes	no	yes	yes	no	no	moderate
Nigeria	2009	Adewuya 2009	yes	yes	no	no	unclear	no	no	yes	no	yes	no	moderate
South Africa	2009	Spies 2009	yes	yes	no	no	unclear	yes	no	yes	no	yes	no	moderate
South Africa	2008	Fincham 2008	yes	yes	yes	yes	unclear	no	yes	yes	yes	no	no	moderate
USA	2007	Zanjani 2007	yes	yes	yes	no	unclear	no	no	yes	yes	no	no	moderate
USA	2007	Israelski 2007	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low
USA	2006	Boarts 2006	yes	no	no	no	unclear	yes	yes	yes	no	no	yes	moderate
USA	2005	Leserman 2005	yes	yes	no	yes	no	no	yes	yes	yes	yes	no	high
South Africa	2003	Olley 2003	yes	yes	no	yes	unclear	no	no	yes	no	no	no	moderate

USA	2003	Vitiello 2003	yes	no	no	no	unclear	no	yes	no	no	yes	yes	moderate
USA	2002	Martinez 2002	yes	yes	no	yes	unclear	no	yes	no	no	yes	no	moderate

Risk of bias was assessed using the Agency for Healthcare Research and Quality (AHRQ). The checklist included 11 items. Each item was coded with a "yeses/No/Unclear": "No" or "Unclear" was scored "0", and "yeses" was scored "1". Total score out of 11 where 8-11, 4-7, and 0-3 depict high, moderate and low quality, respectively.

MOOSE Checklist

Items	Page #	Comments
TITLE Identify the study as a meta-analysis (or systematic review)	3	
ABSTRACT Use the journal's structured format	3,4	
INTRODUCTION		
· The clinical problem	5,6	
· The hypothesis	5	
· A statement of objectives that includes the study population, the condition of interest, the exposure or intervention, and the outcome(s) considered	7	
SOURCES		
· Qualifications of searchers (eg, librarians and investigators)	8	1 psychiatrist
· Search strategy, including time period included in the synthesis and keywords	7,8	
· Effort to include all available studies, including contact with authors	8	
· Databases and registries searched	7	
· Search software used, name and version, including special features used (eg, explosion)	-	
· Use of hand searching (eg, reference lists of obtained articles)	8	
· List of citations located and those excluded, including justification	figure 1	
· Method of addressing articles published in languages other than English	7	
· Method of handling abstracts and unpublished studies	-	Not applicable
· Description of any contact with authors	-	
STUDY SELECTION		
· Types of study designs considered	8	Observational
· Relevance or appropriateness of studies gathered for assessing the hypothesis to be tested	7,8	
· Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7,8	
· Documentation of how data were classified and coded (eg, multiple raters, blinding, etc)	8,9	
· Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	-	Not applicable
· Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	9,10	
· Assessment of heterogeneity	10	
· Statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	10	
RESULTS		
· A graph summarizing individual study estimates and the overall estimate	Figure 1,2	
· A table giving descriptive information for each included study	Tables 1	
· Results of sensitivity testing (eg, subgroup analysis)	17,18	
· Indication of statistical uncertainty of findings	17	
DISCUSSION		
· Strengths and weaknesses	22-27	
· Potential biases in the review process (eg, publication bias)	27	
· Justification for exclusion (eg, exclusion of non–English-language citations)	-	
· Assessment of quality of included studies	26	
· Consideration of alternative explanations for observed results	27	
· Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	28	
· Guidelines for future research	27,28	
· Disclosure of funding source	29	

BMJ Open

A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

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TITLE PAGE

Title: A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

Running head: Posttraumatic stress disorder, HIV, Prevalence, Meta-analysis

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A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

ABSTRACT

Objectives Although people living with HIV (PLWH) have been disproportionately affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among PLWH is unknown. This study aimed to systematically review the prevalence of PTSD among PLWH worldwide and explore variation in prevalence across sociodemographic and methodological factors.

Design A meta-analysis using a random-effect model was conducted to pool the prevalence estimated from individual studies, and subgroup analyses were used to analyse heterogeneities.

Setting, participants and measures Observational studies providing PTSD prevalence data in an adult HIV population were searched from January 2000 to November 2019. Measurements were not restricted, although the definition of PTSD had to align with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.

Results A total of 38 articles were included among 2406 records identified initially. The estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant heterogeneity was detected in the proportion of PLWH who reported PTSD across studies, which was partially explained by geographic area, population group,

measurement and sampling method (p<0.05).

Conclusion PTSD among PLWH is common worldwide. This review highlights that PTSD should be routinely screened for and that more effective prevention strategies and treatment packages targeting PTSD are needed in PLWH.

Strengths and limitations of this study

- This is the first meta-analysis providing comprehensive assessment on the prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
- Several subgroup analyses were conducted to examine the influence of diverse sociodemographic backgrounds as well as methodological heterogeneity.
- This review was conducted with specific definitions of PTSD as part of the inclusion criteria to help in acquiring high level of evidence, which also limited the number of eligible studies.
- A lack of studies carried out on the topic in low-income and middle-income countries could underestimate the burden of HIV-PTSD prevalence of the world.
- We did not undertake a search of grey literature, restricting our sample to articles published in peer-reviewed journals.

INTRODUCTION

Globally, there were more than 36 million people living with HIV (PLWH) by the end of 2017.[1] Although increasingly expanded access to antiretroviral therapy (ART) has led to a prolonged life span, a large portion of PLWH still suffer a significant burden due to psychiatric disorders.[2 3] Posttraumatic stress disorder (PTSD) is a mental health condition following exposure to a life-threatening event, or extreme or repeated exposure to traumatic events.[4] A growing body of literature indicates that HIV-infected people have a heightened risk for PTSD. [5-6] PLWH are more likely to report a history of traumatic and stressful life experiences than the general population, including childhood sexual/physical abuse and intimate partner violence. [7–9] PTSD may precede an HIV-positive diagnosis due to previous traumatic experiences. In addition, being diagnosed with HIV, a life-threatening illness, is a potentially traumatic event in and of itself, and PTSD may emerge as a result of this diagnosis. Infection with HIV not only causes a progressive destruction of the immune system, which increases the susceptibility to malignancies that threaten a person's life, but being labeled and associated with HIV stigma, taking multiple daily medications and experiencing repeated unpleasant side effects also constitute potentially traumatic events.[10] These high rates of potential trauma exposure during the course of the illness may also increase the likelihood of developing PTSD.

Generally, the concept of PTSD has been broadly applied to military veterans, survivors of disasters and accidents, and victims of violent assaults. PTSD as a serious

and costly health problem in the general population is well recognized, and not only impairs a person's physical health, but also greatly influences social functioning.[11] The co-occurrence of PTSD and HIV-infection creates even more challenges regarding both the treatment of PTSD and the management of HIV. PTSD can negatively impact medication adherence and impair immune functioning,[12–15] both of which are especially critical for PLWH. HIV-infected patients with PTSD have been found to be at increased risk of somatization and physical disorders.[16] The illness experience of PTSD, such as persistent avoidance and re-experiencing the traumatic event, may also compromise quality of life and cause significant distress in PLWH.[7 17] Subsequently, prolonged and untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.[18] There is also evidence suggesting that reductions in PTSD symptom severity are related to improved HIV-risk related outcomes.[19] Given that PTSD elevates HIV-risk behaviors[20 21] and the possibility of HIV transmission also increases along with disease progression, PLWH suffering from PTSD are an important group to understand and with whom to intervene.

Valid data on PTSD prevalence among PLWH is essential. Evidence on the extent of PTSD among PLWH is needed to raise awareness and recommend clinical management. Although a number of studies have investigated the prevalence of PTSD in PLWH, findings have been inconsistent.[22] While studies have reported varied incidence, few efforts have been made to aggregate existing research using meta-analysis techniques. There was one published meta-analysis estimating the pooled

prevalence of PTSD among women living with HIV in 2012.[23] But the lack of studies with other groups lowered the generalizability and global relevance of their findings. Moreover, the meta-analysis was conducted in 2012, and the increase of publications about PTSD among PLWH since then[24–26] suggests that a timely update is urgently needed. Indeed, several reviews provide a useful overview of the possible prevalence of PTSD among PLWH;[22 27] however, a number of gaps remain. First, to date, there has been no attempt to achieve a better understanding of the epidemiology of PTSD in PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second, economically and politically, while precise estimates of prevalence can support efficient allocation of resources, factors that might influence PTSD prevalence, such as population characteristics and socio-cultural context have been neglected.

Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in PLWH differs based between population groups, country income groups and study characteristics. This information can then be used to inform further practice and research for this highly co-morbid group.

METHODS

Search strategy

Systematic searches were conducted through 5 electronic English databases (Medline, Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence

among PLWH from January 2000 to November 2019. The search terms were: posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV, acquired immunodeficiency syndrome, AIDS, OR PLWH$; AND epidemiology, occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the precise search strategy). The reference lists of review articles and retrieved full-text articles were also examined for additional papers that were eligible for this review.

Eligibility criteria

Studies were included for this meta-analysis if they met the following predetermined selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2) observational study where prevalence figures for PTSD were stated or can be calculated in an adult HIV population; and (3) underlined that PTSD cases were identified in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.[28 29] Studies were excluded if (1) they only recruited those who had mental distress; (2) they specifically targeted only youth under 18 or children affected by HIV. No restriction was applied regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed closely, and if repeated data were observed, only the earlier publication with one set of complete data was included.

Data extraction and analysis

Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.) following PRISMA recommendations. C.T and X.X. searched the English papers and

J.M. screened the Chinese language papers. After duplicates were deleted, each investigator read titles and abstracts closely to capture all potential studies. Full-text articles were obtained and reviewed for all criteria. Any discrepancies were resolved by discussion with the research team. The PRISMA flow chart shows the results of the systematic search (figure 1)

Data extraction

Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data independently from included papers: first author, year of publication, country of study, sampling method, sample size, number of patients with PTSD, measurements and outcome data. The third investigator (H.W.) helped to verify all extracted data and resolve any uncertainties. To facilitate detection of sample/methodological heterogeneity, countries were categorized according to their income level, and measurements were classified into diagnostic questionnaire and clinical interview based on the approach to diagnosing PTSD. To minimize selection bias, we reviewed the articles included in the meta-analysis to ensure they met eligibility criteria. Gender and sexual orientation were considered because of underlying differences in the epidemics of HIV and trauma.[30–32] Specifically, populations were grouped as women and men, and samples of HIV-infected men were further classified into men who have sex with men (MSM) and non-MSM males.

Assessment of methodological quality

We used the quality assessment forms for cross-sectional/prevalence studies

recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ) [33] to assess the reliability of the eligible studies. The checklist included 11 items. Each item was coded with a "Yes/No/Unclear": "No" or "Unclear" was scored "0", and "Yes" was scored "1". Consistent with previous meta-analysis studies using the AHRQ assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low quality, respectively.

Meta-analysis

In this study, all statistical analyses were performed using Stata 12.0 software (STATA Corporation, College Station, TX) [34]. Heterogeneity was tested and quantified by the chi-square Q statistic and the I^2 statistic. The prevalence of PTSD among PLWH were combined and reported as proportions with corresponding 95% Confidence Intervals (CI). The pooled prevalence was estimated using a random-effects model when heterogeneity was statistically significant (I^2 >50%, $p \leqslant 0.10$). Otherwise, a fix-effects model was used. [35]As sources of heterogeneity may arise from socio-demographic and methodological factors, subgroup analyses were performed by (1) economic levels of the study country, (2) gender/sexual orientation, (3) sampling method and (4) assessment method for PTSD, when enough data was available. Chi-square (χ^2) tests were further used to investigate whether there were significant differences between groups. We only performed these subgroup analyses when data were extractable and sufficient. Separate sensitivity analyses were used for studies with low quality to examine the stability of the pooled prevalence. Publication bias was assessed using the

Egger's and the Begg's tests. [36-37] Significance level of p values < 0.05 were employed for all analyses.

Patient and public involvement

Patients and the public were not involved in this study.

Ethics approval

As this study is a systematic review based on published studies, ethical approval is not required.

RESULTS

Search results

A total of 2396 records were identified by the electronic bibliographic database searches. Ten additional manuscripts were identified through other sources (e.g., reference lists of review papers). From an initial screen of 2301 records after duplicates were removed, 2185 records were excluded on basis of title or abstract because those studies were not relevant to this review (n=2107) or were reviews/commentary (n= 78). The remaining 116 full articles were selected for the eligibility assessment. Of those, 7 were excluded for repeated data, 9 were excluded for targeting PLWH who received psychological intervention or suffered from genocide/natural disaster, and 62 were excluded for not reporting the PTSD prevalence among PLWH. Finally, a total of 38 studies [14 24 25 38-72] met inclusion criteria and were included in this meta-analysis. Search results are elaborated in Figure 1.

Study characteristics

Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a generally moderate to high level of data quality (online supplementary appendix 2). Table 1 shows the characteristics of the included studies. These studies were published between 2002[72] and 2019. [38] Geographically, over half (n=21, 55.3%) of the 38 included studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%), Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%) conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not report their sampling methods, convenience sampling methods were adopted in most studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41 to 1489), of which 2742 were identified with PTSD.

Table 1 Characteristics of the included studies

First author	Year of publication	Location of study	Sampling methods	Sample size*	No. of patients with PTSD	Measurements	Data Collection	Quality
Fabian[38]	2019	USA	convenience sampling	238	80	PCL-C	self-report questionnaire	moderate
Cheng[39]	2018	China	unclear	535	142	PCL-C	self-report questionnaire	moderate
Spies[40]	2018	South Africa	convenience sampling	68	10	DTS	self-report questionnaire	moderate
Verhey[41]	2018	Zimbabwe	random sampling	91	22	CAPS	clinical interview	moderate
Gao[42]	2018	China	convenience sampling	520	89	PCL-C	self-report questionnaire	moderate
McLean[43]	2017	USA	convenience sampling	42	12	PSS	clinical interview	moderate
Kemppainen[25]	2017	USA	convenience sampling	60	26	PCL-C	self-report questionnaire	low
Gonzalez[24]	2016	USA	convenience sampling	137	47	PDS	self-report questionnaire	moderate
Rubin[44]	2016	USA	convenience sampling	1004	174	PCL-C	self-report questionnaire	moderate

John[45]	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
Julnes[14]	2016	USA	convenience sampling	114	39	CDQ	self-report questionnaire	moderate
Zhang[46]	2016	China	convenience sampling	243	106	PCL-C	self-report questionnaire	low
Battaglia[47]	2015	USA	convenience sampling	200	72	PTSD checklist	self-report questionnaire	moderate
Hansrod[48]	2015	South Africa	convenience sampling	114	29	MINI	clinical interview	moderate
Brownley[49]	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
Malee[50]	2014	USA	convenience sampling	1223	281	CDQ	self-report questionnaire	high
Glémaud[51]	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
Gore-Felton[52]	2013	USA	convenience sampling	94	28	PCL-C	self-report questionnaire	low
Glover[53]	2013	USA	convenience sampling	99	24	PDS	self-report questionnaire	high
Dévieux[54]	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate

Gard[55]	2013	Rwanda	unclear	705	380	HTS	self-report questionnaire	moderate
Peterson[56]	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
Kinyanda[57]	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
Bogart[58]	2011	USA	convenience sampling	181	72	PDS	self-report questionnaire	moderate
Martin[59]	2011	UK	convenience sampling	85	46	CIDI	clinical interview	moderate
Reisner[60]	2011	USA	convenience sampling	63	16	AUDADIS-IV	clinical interview	moderate
Theuninck[61]	2010	UK	convenience sampling	100	33	PCL-C	self-report questionnaire	low
Joska[62]	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
Adewuya[63]	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
Spies[64]	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
Fincham[65]	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate

Zanjani[66]	2007	USA	random sampling	109	13	MINI	clinical interview	moderate
Israelski[67]	2007	USA	unclear	210	71	PCL-C	self-report questionnaire	low
Boarts[68]	2006	USA	convenience sampling	57	24	PDS	self-report questionnaire	moderate
Leserman[69]	2005	USA	consecutive sampling	611	98	PTSD checklist	self-report questionnaire	high
Olley[70]	2003	South Africa	consecutive sampling	149	42	MINI	clinical interview	moderate
Vitiello[71]	2003	USA	probability sample	1489	155	CIDI	clinical interview	moderate
Martinez[72]	2002	USA	consecutive sampling	41	17	PCL-C	self-report questionnaire	moderate

* Total number of adults living with HIV

PCL-C Posttraumatic Stress Disorder Checklist-Civilian Version; *DTS* Davidson Trauma Scale; *CAPS* Clinician Administered Post-traumatic Stress Scale; *CDQ* Client Diagnostic Questionnaire; *PDS* Posttraumatic Stress Diagnostic Scale – Self-report version; *PSS* Posttraumatic Stress Symptom Scale; *PRIME MD PHQ* Primary Care Evaluation of Mental Disorders Patient Health Questionnaire; *AUDADIS-IV* The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; *MINI* Mini-International Neuropsychiatric

Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV

Prevalence of PTSD in PLWH

The reported prevalence of PTSD in PLWH ranged from 1.6% [57] to 54.1% [59]. The overall pooled prevalence was 28% (95%CI: 24% to 33%), estimated by a random effects model, as significant heterogeneity ($p \leqslant 0.001$, $I^2=98.1\%$) was observed among the included studies. Meta-analyses are shown as forest plots (Fig. 2).

Publication bias and sensitivity analysis

Possible publication bias was indicated according to the results of Egger's linear test (t= 6.84, p<0.05) and Begg's rank test (z=0.58, p=0.56). However, low sensitivity was suggested with the pooled prevalence of PTSD changed slightly from 28% (95%CI: 24% to 33%) to 27% (95%CI: 22% to 32%) after excluding low-quality articles.

Subgroup Analyses

The results of subgroup analyses are shown in Table 2. The prevalence of PTSD in PLWH differed significantly by geographic area, population group, sampling and measurement method. Specifically, the proportion of PLWH with PTSD in high-income countries tended to be higher (pooled rate= 29%, 95%CI 25% to 34%) than middle-income countries (pooled rate= 27%, 95%CI 16% to 37%) and low-income countries (pooled rate= 26%, 95%CI 7% to 45%). Studies using clinical interviews reported lower rates of PTSD (pooled rate= 22%, 95%CI 16% to 27%) compared with those using self-report questionnaires (pooled rate= 31%, 95%CI 27% to 36%). The pooled PTSD prevalence among women living with HIV, MSM living with HIV and non-MSM men living with HIV were 35% (95%CI: 28% to 43%), 33% (95%CI: 29% to 38%) and 20%

(95%CI: 17% to 23%), respectively. Also, studies conducted with convenience sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to 24%).

Table 2 Subgroup analyses of the prevalence of PTSD in PLWH

Subgroup		Number of studies	Positive PTSD screening (Diagnosis)	Sample size (Tested)	Pooled prevalence of PTSD (95%CI)	Heterogeneity (I^2)	Between group difference	
							χ^2	P value
Geographic area	High-income countries	23	1483	6832	0.29(0.25-0.34)	94.70%	107.32	<0.001
	Middle-income countries	10	1077	3755	0.27(0.16-0.37)	98.60%		
	Low-income countries	5	182	1156	0.26(0.07-0.45)	98.30%		
Population group	Women living with HIV	15	1282	4190	0.35(0.28-0.43)	96.10%	26.99	<0.001
	MSM living with HIV	3	129	380	0.33(0.29-0.38)	73.70%		
	non-MSM male living with HIV	4	165	754	0.20(0.17-0.23)	89.10%		
Sampling	Consecutive sampling	7	280	2387	0.17(0.10-0.24)	97.30%	206.01	<0.001
	Convenience sampling	20	1260	4746	0.32(0.27-0.37)	91.60%		

Data collection	Self-report questionnaire	25	2197	7812	0.31(0.27-0.36)	95.70%	297.01	<0.001
	Clinical interview	13	545	3931	0.22(0.16-0.27)	97.20%		

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to provide the pooled estimated prevalence of PTSD among PLWH. A comprehensive search of the literature assessing the rate of comorbidity between PTSD and HIV-infection was performed, and 38 studies met the predefined criteria and were included in the meta-analysis. A total of 11743 participants were involved, of which 2742 were identified with PTSD. The estimated pooled prevalence was 28% (95% CI: 24% to 33%), which suggests a considerable burden of PTSD in the HIV-infected population. High heterogeneity across studies was detected, and factors such as differences in region, population characteristics, sampling, and measurement were associated with the prevalence.

As indicated, the PTSD prevalence among PLWH found in this study (28%) not only far exceeded that among the general population (3.9%), [73] but was also much higher than the prevalence of PTSD among other vulnerable groups in some previous studies. For example, the prevalence for cancer-related PTSD was 5.1%-15.3%;[74] in persons with chronic pain, the estimated mean prevalence of PTSD was 9.7%. [75] The pooled prevalence of PTSD among PLWH found in this study heightened the high rate of co-morbidity between HIV infection and PTSD, which is consistent with previous demonstrations. [8 76] For PLWH, although depressive symptoms have been the focus of many studies, and 36% of PLWH were likely to have depression according to nationally representative data in the U.S., [77] this pooled estimated prevalence of PTSD among PLWH showed that PTSD is also a common mental disorder among individuals living

with HIV/AIDS. Therefore, the results of our study significantly underscore the importance of early assessment and trauma-directed psychological interventions for PLWH.

Undoubtedly, heterogeneity between studies is expected in such a relatively large topic of review. In this review, the estimated PTSD prevalence in PLWH varied widely (1.6%-54.1%) across studies and countries, which is also a common problem in the epidemiology of psychological and mental health disorders. [78 79] Consistent with the findings of previous research, [59] the majority of studies which have determined the incidence of HIV-related PTSD have been conducted in developed countries (n=23). Compared with lower-income countries, higher-income countries reported relatively higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among PLWH may be explained by the cross-cultural differences in attitudes towards HIV infection. Turan et al.[80] found that the level of perceived HIV-related stigma in the community experienced by PLWH may cause adverse health and psychosocial outcomes. Social isolation and stigma might exacerbate symptoms of PTSD. [81] In high-income countries, PLWH may experience "compound" or "layered" stigma, where stigmatizing beliefs are not only associated with HIV infection but also related to sexual orientation, commercial sexual behaviors, etc. [82] Although, HIV-related stigma is highly burdensome in some mid-income countries, such as China, [83 84] the reported prevalence of PLWH with PTSD was lower compared to higher-income countries. The differences between collectivism and individualism rooted in eastern and western culture may be an

explanation. [85] It is worth noting that social context may not only influence the susceptibility of mental health disorders, but also constitutes an important factor in perceived stigma among individuals with mental illness. Compared to high-income countries, stigmatizing beliefs about the causes and presence of mental illness are still widespread in low- and middle-income countries, [86 87] which may lead to less disease reporting. Caution must be applied, since there is a lack of studies investigating HIV-related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular, detection of prevalence is associated with the representativeness and size of sample. In the context of low- and middle-income countries, it could be argued that lower HIV testing rates may underestimate the PTSD prevalence and impact generalizability. Thus, more epidemiological studies are warranted to better understand and clarify the difference in PTSD prevalence among PLWH globally.

Subgroup analyses indicated that the prevalence of PTSD differed significantly when gender and sexual orientation were taken into consideration. Specifically, women living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence in PTSD, in which being female is a risk factor associated with PTSD development. [16] As suggested by the aforementioned findings, HIV-infected MSM may experience higher levels of stigma and trauma related to their sexual orientation. [30 88] Compared with heterosexual counterparts, MSM reported higher risk for suicidal ideation, [89] which also indicates greater psychological stress and mental health problems (i.e. PTSD and

depression). The findings that MSM and female HIV-infected individuals are at higher risk of developing PTSD may indicate that related health promotion campaigns should be directed to these groups. Clinicians should also take into consideration the PTSD susceptibility in different groups of HIV-infected populations during diagnoses. Notably, most eligible studies did not provide separate the prevalence regarding the gender of participants, and only 3 studies identified PTSD prevalence among MSM living with HIV. Given that these data are from a small number of studies and/or participants, this finding should be interpreted with caution. Nonetheless, given the high prevalence of PTSD in this group, future efforts should be made to obtain more prevalence data on PTSD among MSM living with HIV.

In our study, we assessed methodological differences that may result in heterogeneity. Factors including sampling strategies (convenience vs consecutive) and measurement (self-report vs clinical interview) were evaluated by subgroup analyses. Among 38 studies providing estimated prevalence of PTSD, 7 reported participants were consecutively enrolled via self-referral from flyers describing the study or advertisements from HIV health care providers, and generated a lower pooled rate (17%) compared with the other 20 studies using convenience sampling (32%), though both sampling methods were non-probabilistic. An increase in reporting rate due to convenience sampling has also been found in another meta-analysis synthesizing the HCV seroconversion rates in MSM living with HIV. [90] Convenience samples may allow researchers to select participants who are more likely to have PTSD symptoms and lead

to over-estimation, but given that only 4 studies were rated as high quality and limited description of study methods was detected in some studies, the reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness of calculating pooled prevalence estimates could be questioned, and the pooled prevalence estimate regarding the varied recruitment approaches of the studies should be interpreted with caution.

In this review, a total of 14 different tools were used to assess PTSD symptoms among PLWH across studies. Overall, the prevalence of PTSD screened by self-report instruments (31%) was higher than that assessed by clinical interview (22%). Though both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD), clinical interviews most likely do a much better job of assessing symptoms carefully – for example, not counting symptoms that do not meet clinically meaningful thresholds, and self-report measures may inflate the prevalence estimates; [91] alternatively, subjects may be more comfortable reporting symptoms using self-report questionnaires (presumably paper or online surveys rather than face-to-face interviews). Screening or diagnosing with survey instruments is a common and practical method, especially in resource-limited regions. We found that, though a number of measures have been used to assess PTSD among PLWH, there is no tool designed for this population specifically. As the sensitivity and specificity of the measures may impact accurate PTSD detection, further research is required to identify a standardized measure accordingly to improve validity.

Certain limitations should be acknowledged in this meta-analysis. First, though minimal potential for publication bias was presumed as all data drawn for this review were from studies reporting estimated point prevalence without intervention, publication bias cannot be ruled out for there are a number of studies published in languages other than English and Chinese that were not included in this review. Second, the heterogeneity was high in the whole sample and most subgroups. Heterogeneity importantly influences the reliability and accuracy of a meta-analysis, and the only reliable method for acquiring correct inferences is careful selection of appropriate studies. [92] Even though strict eligibility criteria were employed in addressing PTSD prevalence in this study, it should be noted that getting HIV is only one possible traumatic event, and therefore it is possible that the PTSD experienced by participants in the selected studies was due to an event other than finding out they were HIV positive. Accordingly, we suggests that further studies assessing PTSD among PLWH include more detail on the specific traumas experienced by study participants. In addition, we have analysed the influences of region, population group, recruitment venue, and measurement method, which explained some of the heterogeneity. However, the results should be interpreted with caution. Third, though some studies have indicated that several sociodemographic factors such as age may be associated with PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified by age due to the lack of detailed information reported in the published studies. As the quality of reporting could increase the susceptibility to bias, it is imperative for

researchers to report their findings of observational studies in accordance with the appropriate guidelines, such as the STROBE checklist.

CONCLUSIONS

This review contributes to evidence on the quantitatively pooled prevalence of PTSD among PLWH. Stratified subgroups including geographic area, population group, sampling and measurement method were found to be significant factors accounting for the varied prevalence of PTSD among PLWH. More effective intervention strategies targeting PTSD among PLWH are urgently needed. Future efforts should be made to obtain countries' own PTSD prevalence data among PLWH as well as specific vulnerable minorities, which will provide a basis for public health policy, health-care planning, and resource allocation for PTSD intervention initiatives. Our study also suggests that more research using robust and comprehensive methodology is needed to provide rigorous evidence for designing the targeted psychological interventions.

Figure 1 Flow chart of study inclusion

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

Contributors: Conception of the work: HW and CT. Systematic review and article evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT, LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the authors. All the authors fulfill the ICMJE criteria for authorship.

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REFERENCES

1. UNAIDS. UNAIDS Data 2018. http://www.unaids.org/en/resources/documents/2018/unaids-data-2018 (Accessed 18 March 2019).
2. Niu L, Luo D, Liu Y, *et al.* The mental health of people living with HIV in China, 1998–2014: a systematic review. *PLoS One*. 2016;11:e0153489.
3. Adams C, Zacharia S, Masters L, *et al*. Mental health problems in people living with HIV: changes in the last two decades: the London experience 1990–2014. *AIDS care*. 2016;28:56–9.
4. Friedman MJ, Resick PA, Bryant RA, *et al.* Considering PTSD for DSM-5. *Depression and anxiety.* 2011;28:750–69.
5. Young C. Understanding HIV-related posttraumatic stress disorder in South Africa: a review and conceptual framework. *African Journal of AIDS Research*.

2011;10:139–48.

6. Sherr L, Nagra N, Kulubya G, *et al.* HIV infection associated post-traumatic stress disorder and post-traumatic growth–a systematic review. *Psychology, health & medicine*. 2011;16:612–29.
7. Cavanaugh CE, Hansen NB, Sullivan TP. HIV sexual risk behavior among low-income women experiencing intimate partner violence: The role of posttraumatic stress disorder. *AIDS Behav.* 2010;14:318–27.
8. Neigh GN, Rhodes ST, Valdez A, *et al.* PTSD co-morbid with HIV: Separate but equal, or two parts of a whole? *Neurobiology of disease*. 2016;92:116–23.
9. Borwein A, Salters KA, Palmer AK, *et al.* High rates of lifetime and recent violence observed among harder-to-reach women living with HIV. *AIDS care*. 2014;26:587–94.
10. Luo S, Lin C, Ji G, *et al.* Post-traumatic Stress Disorder Symptoms Among People Living with HIV/AIDS in Rural China. *AIDS Behav*. 2017;21:3202–8.
11. Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *The Journal of clinical psychiatry*. 2000;61(Suppl 5):4-14.
12. Pence BW. The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS. *Journal of Antimicrobial Chemotherapy.* 2009;63:636–40.
13. Ebrahimzadeh Z, Goodarzi MA, Joulaei H. Predicting the Antiretroviral Medication Adherence and CD4 Measure in Patients with HIV/AIDS Based on the Post

Traumatic Stress Disorder and Depression. *Iranian Journal of Public Health*. 2019;48:139–46.

14. Julnes PS, Auh S, Krakora R, *et al.* The association between post-traumatic stress disorder and markers of inflammation and immune activation in HIV-infected individuals with controlled viremia. *Psychosomatics.* 2016;57:423–30.
15. Lynn C, Chenneville T, Bradley-Klug K, *et al.* Depression, anxiety, and posttraumatic stress as predictors of immune functioning: differences between youth with behaviorally and perinatally acquired HIV. *AIDS care*. 2019 Mar 4:1–10.
16. Brief DJ, Bollinger AR, Vielhauer MJ, *et al.* Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*. 2004;16:97–120.
17. Nightingale VR, Sher TG, Mattson M, *et al.* The effects of traumatic stressors and HIV-related trauma symptoms on health and health related quality of life. *AIDS Behav*. 2011;15:1870–8.
18. Koegler E, Kennedy CE. A scoping review of the associations between mental health and factors related to HIV acquisition and disease progression in conflict-affected populations. *Confl Health*. 2018;12:20.
19. Pearson CR, Kaysen D, Huh D, *et al.* Randomized Control Trial of Culturally Adapted Cognitive Processing Therapy for PTSD Substance Misuse and HIV Sexual Risk Behavior for Native American Women. *AIDS Behav*. 2019;23:695–706.
20. Tull MT, Weiss NH, McDermott MJ. Post-traumatic stress disorder and impulsive

and risky behavior: Overview and discussion of potential mechanisms. *Comprehensive guide to post-traumatic stress disorders*. 2016;803–16.

21. Weiss NH, Tull MT, Borne MER, *et al.* Posttraumatic stress disorder symptom severity and HIV-risk behaviors among substance-dependent inpatients. *AIDS care*. 2013;25:1219–26.
22. Applebaum AJ, Bedoya CA, Hendriksen ES, *et al.* Future directions for interventions targeting PTSD in HIV-infected adults. *Journal of the Association of Nurses in AIDS Care*. 2015;26:127–38.
23. Machtinger E, Wilson T, Haberer JE, *et al.* Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS Behav*. 2012;16:2091–100.
24. Gonzalez A, Locicero B, Mahaffey B, *et al.* Internalized HIV stigma and mindfulness: associations with PTSD symptom severity in trauma-exposed adults with HIV/AIDS. *Behavior modification*. 2016;40:144–63.
25. Kemppainen JK, MacKain S, Alexander M, *et al.* Posttraumatic stress disorder and stressful life events among rural women with HIV disease. *Journal of the Association of Nurses in AIDS Care*. 2017;28:216–25.
26. Rubin LH, Cook JA, Springer G, *et al.* Perceived and post-traumatic stress are associated with decreased learning, memory, and fluency in HIV-infected women. *AIDS (London, England)*. 2017;31:2393–1401.
27. Seedat S. Interventions to improve psychological functioning and health outcomes of HIV-infected individuals with a history of trauma or PTSD. *Current HIV/AIDS*

Reports. 2012;9:344–50.

28. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
29. Association AP. Diagnostic and statistical manual of mental disorders. 5th Edition. Washington, DC: American Psychiatric Pub; 2013.
30. Sales JM, Swartzendruber A, Phillips AL. Trauma-Informed HIV Prevention and Treatment. *Curr HIV/AIDS Rep*. 2016;13:374–82.
31. Burnham KE, Cruess DG, Kalichman MO, *et al.* Trauma symptoms, internalized stigma, social support, and sexual risk behavior among HIV-positive gay and bisexual MSM who have sought sex partners online. *AIDS care*. 2016;28:347–53.
32. Rzeszutek M, Oniszczenko W, Firląg-Burkacka E. Gender differences in posttraumatic stress symptoms and social support in a sample of HIV-positive individuals. *Women & health*. 2017;57:792–803.
33. Rostom A, Dubé C, Cranney A, *et al.* Appendix D. Quality Assessment Forms. Agency for Healthcare Research and Quality (US); 2004 https://www.ncbi.nlm.nih.gov/books/NBK35156/ (Accessed 21 October 2018).
34. Stata C, Station C. TX. Stata Press 2016
35. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine. 2002;21(11):1539-58.
36. Egger M, Smith GD, Schneider M, *et al.* Bias in meta-analysis

detected by a simple, graphical test. *BMJ.* 1997; 315: 629–34.

37. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics.* 1994; 50: 1088–101.

38. Fabian KE, Huh D, Kemp CG, *et al.* Moderating Factors in an Anti-stigma Intervention for African American Women with HIV in the United States: A Secondary Analysis of the UNITY Trial. *AIDS and Behavior*. 2019;19:1-11.

39. Chen CD, Yan H, Li SY, *et al.* Post-traumatic stress disorder and it associated factors among people living with HIV in Wuhan city. *Chin J Public Health*. 2018;1-4.

40. Spies G, Konkiewitz EC, Seedat S. Incidence and persistence of depression among women living with and without HIV in South Africa: A longitudinal study. *AIDS Behav*. 2018;22(10):3155–65.

41. Verhey R, Chibanda D, Gibson L, *et al.* Validation of the posttraumatic stress disorder checklist - 5 (PCL-5) in a primary care population with high HIV prevalence in Zimbabwe. *BMC Psychiatry.* 2018;18:109.

42. Gao M, Xiao C, Zhang X, *et al.* Social capital and PTSD among PLWHA in China: the mediating role of resilience and internalized stigma. *Psychology, health & medicine*. 2018;23:698–706.

43. McLean CP, Gay NG, Metzger DA, *et al.* Psychiatric Symptoms and Barriers to Care in HIV-Infected Individuals Who Are Lost to Care. *J Int Assoc Provid AIDS Care.* 2017;16:423–9.

44. Rubin LH, Pyra M, Cook JA, *et al.* Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women. *Journal of neurovirology.* 2016;22:159–69.

45. John M, Greene M, Hessol NA, *et al.* Geriatric assessments and association with VACS index among HIV-infected older adults in San Francisco. *Journal of acquired immune deficiency syndromes (1999).* 2016;72:534.

46. Zhang X, Wang T, Liu M, *et al.* Post-traumatic stress disorder among people living with HIV/AIDS and its influence factors. *Chongqing Medicine.* 2016;232–5.

47. Battaglia TA, Gunn CM, McCoy ME, *et al.* Beliefs About Anal Cancer among HIV-Infected Women: Barriers and Motivators to Participation in Research. *Womens Health Issues*. 2015;25:720–6.

48. Hansrod F, Spies G, Seedat S. Type and severity of intimate partner violence and its relationship with PTSD in HIV-infected women. *Psychology, health & medicine.* 2015;20:697–709.

49. Brownley JR, Fallot RD, Berley RW, *et al.* Trauma history in African-American women living with HIV: effects on psychiatric symptom severity and religious coping. *AIDS care.* 2015;27:964–71.

50. Malee K, Mellins CA, Huo Y, *et al.* Prevalence, incidence and persistence of psychiatric and substance use disorders among mothers living with HIV. *Journal of acquired immune deficiency syndromes (1999).* 2014;65:526.

51. Glémaud M, Illa L, Echenique M, *et al.* Abuse and mental health concerns among

HIV-infected Haitian women living in the United States. Journal of the Association of Nurses in *AIDS Care.* 2014;25:S62–9.

52. Gore-Felton C, Ginzburg K, Chartier M, *et al.* Attachment style and coping in relation to posttraumatic stress disorder symptoms among adults living with HIV/AIDS. *Journal of behavioral medicine.* 2013;36:51–60.
53. Glover DA, Williams JK, Kisler KA. Using novel methods to examine stress among HIV-positive African American men who have sex with men and women. *J Behav Med*. 2013;36:283–94.
54. Dévieux JG, Malow RM, Attonito JM, *et al.* Post-traumatic stress disorder symptomatology and alcohol use among HIV-seropositive adults in Haiti. *AIDS care*. 2013;25(10):1210-8.
55. Gard TL, Hoover DR, Shi Q, *et al.* The impact of HIV status, HIV disease progression, and post-traumatic stress symptoms on the health-related quality of life of Rwandan women genocide survivors. *Quality of Life Research*. 2013;22(8):2073-84.
56. Peterson K, Togun T, Klis S, *et al.* Depression and posttraumatic stress disorder among HIV-infected Gambians on antiretroviral therapy. *AIDS patient care and STDs*. 2012;26:589–96.
57. Kinyanda E, Hoskins S, Nakku J, *et al.* Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda. *BMC psychiatry*. 2011;11:205.

58. Bogart LM, Wagner GJ, Galvan FH, *et al.* Perceived discrimination and mental health symptoms among Black men with HIV. *Cultural Diversity and Ethnic Minority Psychology*. 2011;17:295.

59. Martin L, Kagee A. Lifetime and HIV-related PTSD among persons recently diagnosed with HIV. *AIDS Behav*. 2011;15:125–31.

60. Reisner SL, Falb KL, Mimiaga MJ. Early life traumatic stressors and the mediating role of PTSD in incident HIV infection among US men, comparisons by sexual orientation and race/ethnicity: results from the NESARC, 2004–2005. *Journal of Acquired Immune Deficiency Syndromes*. 2011;57:340–50.

61. Theuninck AC, Lake N, Gibson S. HIV-related posttraumatic stress disorder: Investigating the traumatic events. *AIDS Patient care and STDS*. 2010;24:485–91.

62. Joska JA, Fincham DS, Stein DJ, *et al.* Clinical correlates of HIV-associated neurocognitive disorders in South Africa. *AIDS Behav*. 2010;14:371–8.

63. Adewuya AO, Afolabi MO, Ola BA, *et al.* Post-traumatic stress disorder (PTSD) after stigma related events in HIV infected individuals in Nigeria. *Social Psychiatry and Psychiatric Epidemiology*. 2009;44:761.

64. Spies G, Kader K, Kidd M, *et al.* Validity of the K-10 in detecting DSM-IV-defined depression and anxiety disorders among HIV-infected individuals. *AIDS care*. 2009;21:1163–8.

65. Fincham D, Smit J, Carey P, *et al.* The relationship between behavioural inhibition, anxiety disorders, depression and CD4 counts in HIV-positive adults: a cross-

sectional controlled study. *AIDS care.* 2008;20:1279–83.

66. Zanjani F, Saboe K, Oslin D. Age difference in rates of mental health/substance abuse and behavioral care in HIV-positive adults. *AIDS patient care and STDs*. 2007;21:347–55.

67. Israelski DM, Prentiss DE, Lubega S, *et al.* Psychiatric co-morbidity in vulnerable populations receiving primary care for HIV/AIDS. *AIDS care*. 2007;19:220–5.

68. Boarts JM, Sledjeski EM, Bogart LM, *et al.* The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS Behav.* 2006;10:253–61.

69. Leserman J, Whetten K, Lowe K, *et al.* How trauma, recent stressful events, and PTSD affect functional health status and health utilization in HIV-infected patients in the south. *Psychosomatic medicine*. 2005;67:500–7.

70. Olley BO, Gxamza F, Seedat S, *et al.* Psychopathology and coping in recently diagnosed HIV/AIDS patients-the role of gender. *South African Medical Journal*. 2003;93:928–31.

71. Vitiello B, Burnam MA, Bing EG, *et al.* Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry.* 2003;160:547–54.

72. Martinez A, Israelski D, Walker C, *et al.* Posttraumatic stress disorder in women attending human immunodeficiency virus outpatient clinics. *AIDS patient care and STDs.* 2002;16:283–91.

73. Koenen KC, Ratanatharathorn A, Ng L, *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med.* 2017;47:2260–74.

74. Abbey G, Thompson SBN, Hickish T, *et al.* A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology*. 2015;24:371–81.

75. Siqveland J, Hussain A, Lindstrøm JC, *et al.* Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. *Frontiers in Psychiatry.* 2017;8:164.

76. Kelly B, Raphael B, Judd F, *et al.* Posttraumatic stress disorder in response to HIV infection. *General Hospital Psychiatry*. 1998;20:345–52.

77. Bing EG, Burnam MA, Longshore D, *et al.* Psychiatric disorders and drug use among human immunodeficiency virus–infected adults in the United States. *Archives of general psychiatry.* 2001;58:721–8.

78. Pringsheim T, Jette N, Frolkis A, *et al.* The prevalence of Parkinson's disease: A systematic review and meta-analysis. *Movement disorders.* 2014;29:1583–90.

79. Wang T, Fu H, Kaminga AC, *et al*. Prevalence of depression or depressive symptoms among people living with HIV/AIDS in China: a systematic review and meta-analysis. *BMC psychiatry.* 2018 Dec;18(1):160.

80. Turan B, Budhwani H, Fazeli PL, *et al.* How Does Stigma Affect People Living with HIV? The Mediating Roles of Internalized and Anticipated HIV Stigma in the Effects of Perceived Community Stigma on Health and Psychosocial Outcomes.

AIDS Behav. 2017;21:283–91.

81. Kamen C, Vorasarun C, Canning T, *et al.* The impact of stigma and social support on development of post-traumatic growth among persons living with HIV. *Journal of clinical psychology in medical settings*. 2016;23:126–34.
82. Lowther K, Selman L, Harding R, *et al.* Experience of persistent psychological symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): a systematic review. *International journal of nursing studies*. 2014;51(8):1171-89.
83. Li Z, Morano JP, Khoshnood K, *et al.* HIV-related stigma among people living with HIV/AIDS in rural Central China. *BMC Health Serv Res*. 2018;18:453.
84. Li L, Liang L-J, Lin C, *et al.* HIV prevention intervention to reduce HIV-related stigma: evidence from China. *AIDS (London, England)*. 2010;24:115.
85. Shavitt S, Cho YI, Johnson TP, *et al.* Culture Moderates the Relation Between Perceived Stress, Social Support, and Mental and Physical Health. *Journal of Cross-Cultural Psychology*. 2016;47:956–80.
86. Lauber C, Rössler W. Stigma towards people with mental illness in developing countries in Asia. *International Review of Psychiatry*. 2007;19:157–78.
87. Seeman N, Tang S, Brown AD, *et al.* World survey of mental illness stigma. *Journal of Affective Disorders.* 2016;190:115–21.
88. Reisner SL, Mimiaga MJ, Safren SA, *et al.* Stressful or traumatic life events, post-traumatic stress disorder (PTSD) symptoms, and HIV sexual risk taking among men

who have sex with men. *AIDS care*. 2009;21:1481–9.

89. Luo Z, Feng T, Fu H, *et al.* Lifetime prevalence of suicidal ideation among men who have sex with men: a meta-analysis. *BMC psychiatry*. 2017;17:406.

90. Hagan H, Jordan AE, Neurer J, *et al.* Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS*. 2015;29:2335–45.

91. Ayers S, Wright DB, Ford E. Hyperarousal symptoms after traumatic and nontraumatic births. *Journal of Reproductive and Infant Psychology*. 2015;33:282–93.

92. Melsen WG, Bootsma MC, Rovers MM, *et al*. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clinical Microbiology and Infection*. 2014;20(2):123-9.

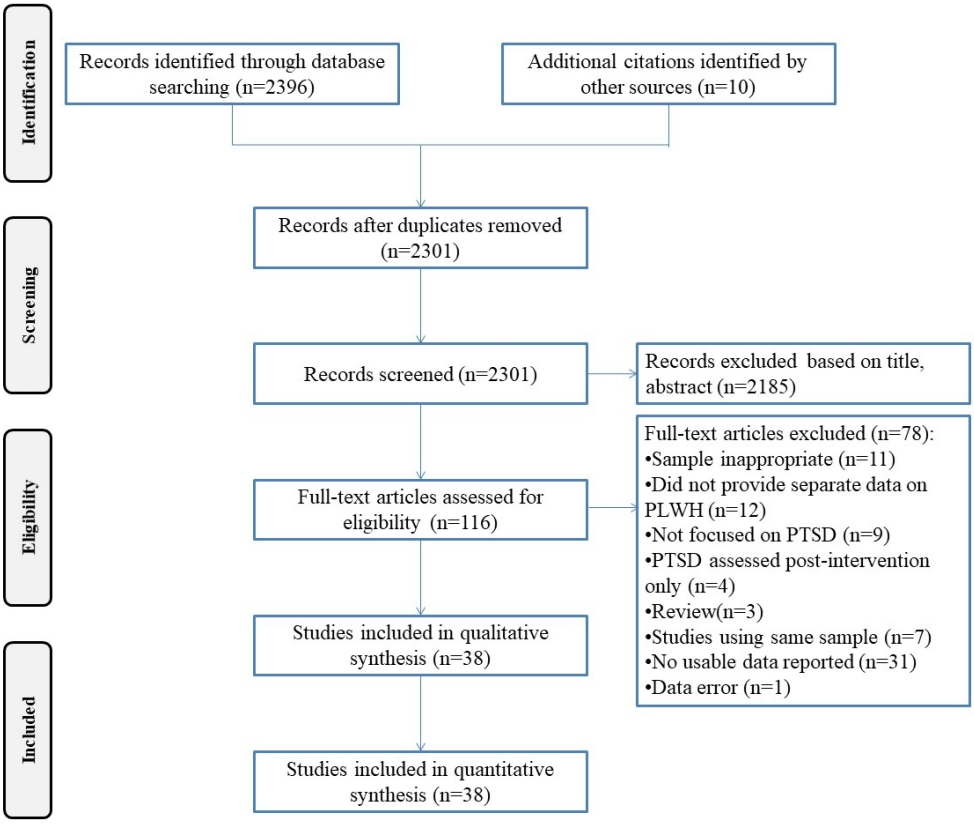

Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

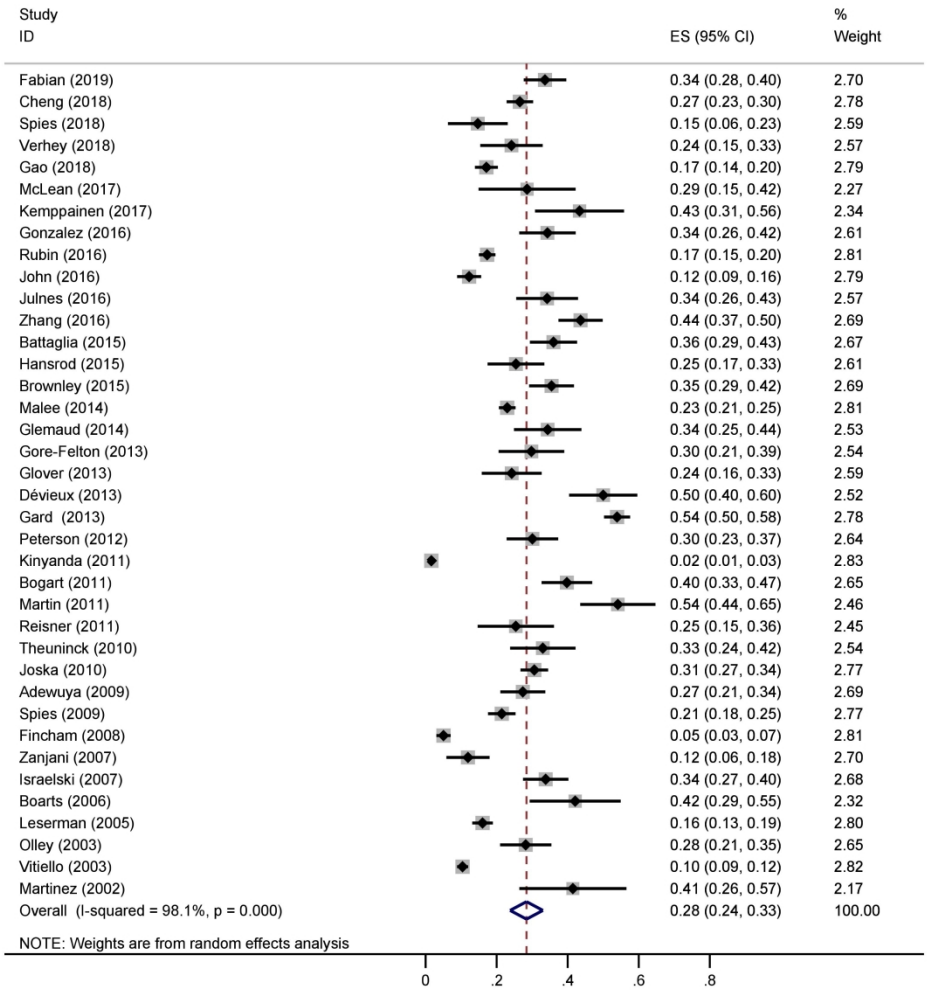

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

281x304mm (300 x 300 DPI)

Appendix 1 – Search strategy

ID	Search terms
PubMed	
#1	("stress disorders, post-traumatic"[Mesh] OR PTSD*[tiab] OR posttrauma*[tiab] OR "post trauma*" [tiab]OR post-trauma*[tiab] OR trauma* [tiab] OR psychotrauma*[tiab] OR stress*[tiab])
#2	("HIV Infections"[Mesh] OR "HIV" [MeSH] OR "human immunodeficiency virus" [tiab] OR "human immuno deficiency virus" [tiab] OR "human immune deficiency virus" [tiab] OR "human immunedeficiency virus" [tiab] OR "AIDS" [tiab] OR "acquired immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency syndromes" [tiab] OR "acquired immuno deficiency syndrome" [tiab] OR "acquired immuno deficiency syndromes" [tiab] OR "acquired immune deficiency syndrome" [tiab] OR "acquired immune deficiency syndromes" [tiab] OR "acquired immunedeficiency syndrome" [tiab] OR "acquired immunedeficiency syndromes" [tiab])
#3	(((((((("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Cross-Sectional Studies"[Mesh])) OR Prevalence) OR Epidemiology) OR Cross-Sectional Studies) OR "Longitudinal Studies"[Mesh]) OR "Cohort Studies"[Mesh]) OR Cohort Studies) OR Longitudinal Studies))
#4	#1 AND #2 AND #3

Search Filters

a. Human studies
b. Language – English/Chinese
c. Publication dates – From 2000/01/01 to 2019/11/31

Appendix 2 – Risk of bias and quality of included studies

Country	Year	Citation	1	2	3	4	5	6	7	8	9	10	11	Quality
USA	2019	Fabian 2019	yes	yes	no	unclear	unclear	no	no	yes	no	yes	yes	moderate
China	2018	Cheng 2018	yes	yes	yes	unclear	unclear	yes	no	no	no	no	no	moderate
South Africa	2018	Spies 2018	yes	yes	no	no	unclear	yes	no	yes	no	no	no	moderate
Zimbabwe	2018	Verhey 2018	yes	yes	yes	no	unclear	yes	yes	no	no	yes	no	moderate
China	2018	Gao 2018	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
USA	2017	McLean 2017	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2017	Kemppainen 2017	yes	yes	no	no	unclear	no	no	no	no	no	no	low
USA	2016	Gonzalez 2016	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2016	Rubin 2016	yes	yes	yes	no	no	no	yes	yes	yes	yes	no	moderate
USA	2016	John 2016	yes	no	yes	yes	no	yes	no	no	no	no	no	moderate
USA	2016	Julnes 2016	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
China	2016	Zhang 2016	yes	yes	no	no	no	no	no	no	no	yes	no	low
USA	2015	Battaglia 2015	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
South Africa	2015	Hansrod 2015	yes	yes	yes	no	unclear	yes	no	yes	no	no	no	moderate
USA	2015	Brownley 2015	yes	yes	yes	unclear	unclear	no	no	no	no	yes	no	moderate
USA	2014	Malee 2014	yes	yes	yes	no	unclear	no	yes	yes	yes	yes	yes	high
USA	2014	Glémaud 2014	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low

USA	2013	Gore-Felton 2013	yes	yes	no	no	unclear	yes	no	no	no	no	no	low
USA	2013	Glover 2013	yes	yes	no	unclear	unclear	yes	yes	yes	yes	yes	yes	high
Haiti	2013	Dévieux 2013	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
Rwanda	2013	Gard 2013	yes	yes	yes	unclear	no	no	yes	yes	no	yes	no	moderate
Gambia	2012	Peterson 2012	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	no	high
Uganda	2011	Kinyanda 2011	yes	yes	yes	yes	unclear	no	yes	yes	no	yes	no	moderate
USA	2011	Bogart 2011	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
UK	2011	Martin 2011	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
USA	2011	Reisner 2011	yes	yes	yes	no	unclear	no	yes	yes	yes	no	no	moderate
UK	2010	Theuninck 2010	yes	no	no	no	no	no	no	no	no	no	no	low
South Africa	2010	Joska 2010	yes	yes	no	unclear	unclear	yes	no	yes	yes	no	no	moderate
Nigeria	2009	Adewuya 2009	yes	yes	no	no	unclear	no	no	yes	no	yes	no	moderate
South Africa	2009	Spies 2009	yes	yes	no	no	unclear	yes	no	yes	no	yes	no	moderate
South Africa	2008	Fincham 2008	yes	yes	yes	yes	unclear	no	yes	yes	yes	no	no	moderate
USA	2007	Zanjani 2007	yes	yes	yes	no	unclear	no	no	yes	yes	no	no	moderate
USA	2007	Israelski 2007	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low
USA	2006	Boarts 2006	yes	no	no	no	unclear	yes	yes	yes	no	no	yes	moderate
USA	2005	Leserman 2005	yes	yes	no	yes	no	no	yes	yes	yes	yes	no	high
South Africa	2003	Olley 2003	yes	yes	no	yes	unclear	no	no	yes	no	no	no	moderate

USA	2003	Vitiello 2003	yes	no	no	no	unclear	no	yes	no	no	yes	yes	moderate
USA	2002	Martinez 2002	yes	yes	no	yes	unclear	no	yes	no	no	yes	no	moderate

Risk of bias was assessed using the Agency for Healthcare Research and Quality (AHRQ). The checklist included 11 items. Each item was coded with a "yeses/No/Unclear": "No" or "Unclear" was scored "0", and "yeses" was scored "1". Total score out of 11 where 8-11, 4-7, and 0-3 depict high, moderate and low quality, respectively.

MOOSE Checklist

Items	Page #	Comments
TITLE Identify the study as a meta-analysis (or systematic review)	3	
ABSTRACT Use the journal's structured format	3,4	
INTRODUCTION		
· The clinical problem	5,6	
· The hypothesis	5	
· A statement of objectives that includes the study population, the condition of interest, the exposure or intervention, and the outcome(s) considered	7	
SOURCES		
· Qualifications of searchers (eg, librarians and investigators)	8	1 psychiatrist
· Search strategy, including time period included in the synthesis and keywords	7,8	
· Effort to include all available studies, including contact with authors	8	
· Databases and registries searched	7	
· Search software used, name and version, including special features used (eg, explosion)	-	
· Use of hand searching (eg, reference lists of obtained articles)	8	
· List of citations located and those excluded, including justification	figure 1	
· Method of addressing articles published in languages other than English	7	
· Method of handling abstracts and unpublished studies	-	Not applicable
· Description of any contact with authors	-	
STUDY SELECTION		
· Types of study designs considered	8	Observational
· Relevance or appropriateness of studies gathered for assessing the hypothesis to be tested	7,8	
· Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7,8	
· Documentation of how data were classified and coded (eg, multiple raters, blinding, etc)	8,9	
· Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	-	Not applicable
· Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	9,10	
· Assessment of heterogeneity	10	
· Statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	10	
RESULTS		
· A graph summarizing individual study estimates and the overall estimate	Figure 1,2	
· A table giving descriptive information for each included study	Tables 1	
· Results of sensitivity testing (eg, subgroup analysis)	17,18	
· Indication of statistical uncertainty of findings	17	
DISCUSSION		
· Strengths and weaknesses	22-27	
· Potential biases in the review process (eg, publication bias)	27	
· Justification for exclusion (eg, exclusion of non–English-language citations)	-	
· Assessment of quality of included studies	26	
· Consideration of alternative explanations for observed results	27	
· Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	28	
· Guidelines for future research	27,28	
· Disclosure of funding source	29	

BMJ Open

A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

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TITLE PAGE

Title: A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

Running head: Posttraumatic stress disorder, HIV, Prevalence, Meta-analysis

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A global estimate of the prevalence of posttraumatic stress disorder among adults living with HIV: A systematic review and meta-analysis

ABSTRACT

Objectives Although people living with HIV (PLWH) have been disproportionately affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among PLWH is unknown. This study aimed to systematically review the prevalence of PTSD among PLWH worldwide and explore variation in prevalence across sociodemographic and methodological factors.

Design A meta-analysis using a random-effect model was conducted to pool the prevalence estimated from individual studies, and subgroup analyses were used to analyse heterogeneities.

Setting, participants and measures Observational studies providing PTSD prevalence data in an adult HIV population were searched from January 2000 to November 2019. Measurements were not restricted, although the definition of PTSD had to align with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.

Results A total of 38 articles were included among 2406 records identified initially. The estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant heterogeneity was detected in the proportion of PLWH who reported PTSD across studies, which was partially explained by geographic area, population group,

measurement and sampling method (p<0.05).

Conclusion PTSD among PLWH is common worldwide. This review highlights that PTSD should be routinely screened for and that more effective prevention strategies and treatment packages targeting PTSD are needed in PLWH.

Strengths and limitations of this study

- This is the first meta-analysis providing comprehensive assessment on the prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
- Several subgroup analyses were conducted to examine the influence of diverse sociodemographic backgrounds as well as methodological heterogeneity.
- This review was conducted with specific definitions of PTSD as part of the inclusion criteria to help in acquiring high level of evidence, which also limited the number of eligible studies.
- A lack of studies carried out on the topic in low-income and middle-income countries could underestimate the burden of HIV-PTSD prevalence of the world.
- We did not undertake a search of grey literature, restricting our sample to articles published in peer-reviewed journals.

INTRODUCTION

Globally, there were more than 36 million people living with HIV (PLWH) by the end of 2017.[1] Although increasingly expanded access to antiretroviral therapy (ART) has led to a prolonged life span, a large portion of PLWH still suffer a significant burden due to psychiatric disorders.[2 3] Posttraumatic stress disorder (PTSD) is a mental health condition following exposure to a life-threatening event, or extreme or repeated exposure to traumatic events.[4] A growing body of literature indicates that PLWH have a heightened risk for PTSD. [5-6] PLWH are more likely to report a history of traumatic and stressful life experiences than the general population, including childhood sexual/physical abuse and intimate partner violence. [7–9] PTSD may precede an HIV-positive diagnosis due to previous traumatic experiences. In addition, being diagnosed with HIV, a life-threatening illness, is a potentially traumatic event in and of itself, and PTSD may emerge as a result of this diagnosis. Infection with HIV not only causes a progressive destruction of the immune system, which increases the susceptibility to malignancies that threaten a person's life, but being labeled and associated with HIV stigma, taking multiple daily medications and experiencing repeated unpleasant side effects also constitute potentially traumatic events.[10] These high rates of potential trauma exposure during the course of the illness may also increase the likelihood of developing PTSD.

Generally, the concept of PTSD has been broadly applied to military veterans, survivors of disasters and accidents, and victims of violent assaults. PTSD as a serious

and costly health problem in the general population is well recognized, and not only impairs a person's physical health, but also greatly influences social functioning.[11] The co-occurrence of PTSD and HIV-infection creates even more challenges regarding both the treatment of PTSD and the management of HIV. PTSD can negatively impact medication adherence and impair immune functioning,[12–15] both of which are especially critical for PLWH. PLWH with PTSD have been found to be at increased risk of somatization and physical disorders.[16] The illness experience of PTSD, such as persistent avoidance and re-experiencing the traumatic event, may also compromise quality of life and cause significant distress in PLWH.[7 17] Subsequently, prolonged and untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.[18] There is also evidence suggesting that reductions in PTSD symptom severity are related to improved HIV-risk related outcomes.[19] Given that PTSD elevates HIV-risk behaviors[20 21] and the possibility of HIV transmission also increases along with disease progression, PLWH suffering from PTSD are an important group to understand and with whom to intervene.

Valid data on PTSD prevalence among PLWH is essential. Evidence on the extent of PTSD among PLWH is needed to raise awareness and recommend clinical management. Although a number of studies have investigated the prevalence of PTSD in PLWH, findings have been inconsistent.[22] While studies have reported varied incidence, few efforts have been made to aggregate existing research using meta-analysis techniques. There was one published meta-analysis estimating the pooled

prevalence of PTSD among women living with HIV in 2012.[23] But the lack of studies with other groups lowered the generalizability and global relevance of their findings. Moreover, the meta-analysis was conducted in 2012, and the increase of publications about PTSD among PLWH since then[24–26] suggests that a timely update is urgently needed. Indeed, several reviews provide a useful overview of the possible prevalence of PTSD among PLWH;[22 27] however, a number of gaps remain. First, to date, there has been no attempt to achieve a better understanding of the epidemiology of PTSD in PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second, economically and politically, while precise estimates of prevalence can support efficient allocation of resources, factors that might influence PTSD prevalence, such as population characteristics and socio-cultural context have been neglected.

Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in PLWH differs based between population groups, country income groups and study characteristics. This information can then be used to inform further practice and research for this highly co-morbid group.

METHODS

Search strategy

Systematic searches were conducted through 5 electronic English databases (Medline, Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence

among PLWH from January 2000 to November 2019. The search terms were: posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV, acquired immunodeficiency syndrome, AIDS, OR PLWH$; AND epidemiology, occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the precise search strategy). The reference lists of review articles and retrieved full-text articles were also examined for additional papers that were eligible for this review.

Eligibility criteria

Studies were included for this meta-analysis if they met the following predetermined selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2) observational study where prevalence figures for PTSD were stated or can be calculated in an adult HIV population; and (3) underlined that PTSD cases were identified in accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD) diagnostic criteria.[28 29] Studies were excluded if (1) they only recruited those who had mental distress; (2) they specifically targeted only youth under 18 or children affected by HIV. No restriction was applied regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed closely, and if repeated data were observed, only the earlier publication with one set of complete data was included.

Data extraction and analysis

Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.) following PRISMA recommendations. C.T and X.X. searched the English papers and

J.M. screened the Chinese language papers. After duplicates were deleted, each investigator read titles and abstracts closely to capture all potential studies. Full-text articles were obtained and reviewed for all criteria. Any discrepancies were resolved by discussion with the research team. The PRISMA flow chart shows the results of the systematic search (figure 1)

Data extraction

Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data independently from included papers: first author, year of publication, country of study, sampling method, sample size, number of patients with PTSD, measurements and outcome data. The third investigator (H.W.) helped to verify all extracted data and resolve any uncertainties. To facilitate detection of sample/methodological heterogeneity, countries were categorized according to their income level, and measurements were classified into diagnostic questionnaire and clinical interview based on the approach to diagnosing PTSD. To minimize selection bias, we reviewed the articles included in the meta-analysis to ensure they met eligibility criteria. Gender and sexual orientation were considered because of underlying differences in the epidemics of HIV and trauma.[30–32] Specifically, populations were grouped as women and men, and samples of HIV-infected men were further classified into men who have sex with men (MSM) and non-MSM males.

Assessment of methodological quality

We used the quality assessment forms for cross-sectional/prevalence studies

recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ) [33] to assess the reliability of the eligible studies. The checklist included 11 items. Each item was coded with a "Yes/No/Unclear": "No" or "Unclear" was scored "0", and "Yes" was scored "1". Consistent with previous meta-analysis studies using the AHRQ assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low quality, respectively.

Meta-analysis

In this study, all statistical analyses were performed using Stata 12.0 software (STATA Corporation, College Station, TX) [34]. Heterogeneity was tested and quantified by the chi-square Q statistic and the I^2 statistic. The prevalence of PTSD among PLWH were combined and reported as proportions with corresponding 95% Confidence Intervals (CI). The pooled prevalence was estimated using a random-effects model when heterogeneity was statistically significant (I^2 >50%, $p \leqslant 0.10$). Otherwise, a fix-effects model was used. [35]As sources of heterogeneity may arise from socio-demographic and methodological factors, subgroup analyses were performed by (1) economic levels of the study country, (2) gender/sexual orientation, (3) sampling method and (4) assessment method for PTSD, when enough data was available. Chi-square (χ^2) tests were further used to investigate whether there were significant differences between groups. We only performed these subgroup analyses when data were extractable and sufficient. Separate sensitivity analyses were used for studies with low quality to examine the stability of the pooled prevalence. Publication bias was assessed using the

Egger's and the Begg's tests. [36-37] Significance level of p values < 0.05 were employed for all analyses.

Patient and public involvement

Patients and the public were not involved in this study.

Ethics approval

As this study is a systematic review based on published studies, ethical approval is not required.

RESULTS

Search results

A total of 2396 records were identified by the electronic bibliographic database searches. Ten additional manuscripts were identified through other sources (e.g., reference lists of review papers). From an initial screen of 2301 records after duplicates were removed, 2185 records were excluded on basis of title or abstract because those studies were not relevant to this review (n=2107) or were reviews/commentary (n= 78). The remaining 116 full articles were selected for the eligibility assessment. Of those, 7 were excluded for repeated data, 9 were excluded for targeting PLWH who received psychological intervention or suffered from genocide/natural disaster, and 62 were excluded for not reporting the PTSD prevalence among PLWH. Finally, a total of 38 studies [14 24 25 38-72] met inclusion criteria and were included in this meta-analysis. Search results are elaborated in Figure 1.

Study characteristics

Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a generally moderate to high level of data quality (online supplementary appendix 2). Table 1 shows the characteristics of the included studies. These studies were published between 2002[72] and 2019. [38] Geographically, over half (n=21, 55.3%) of the 38 included studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%), Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%) conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not report their sampling methods, convenience sampling methods were adopted in most studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41 to 1489), of which 2742 were identified with PTSD.

Table 1 Characteristics of the included studies

First author	Year of publication	Location of study	Sampling methods	Sample size*	No. of patients with PTSD	Measurements	Data Collection	Quality
Fabian[38]	2019	USA	convenience sampling	238	80	PCL-C	self-report questionnaire	moderate
Cheng[39]	2018	China	unclear	535	142	PCL-C	self-report questionnaire	moderate
Spies[40]	2018	South Africa	convenience sampling	68	10	DTS	self-report questionnaire	moderate
Verhey[41]	2018	Zimbabwe	random sampling	91	22	CAPS	clinical interview	moderate
Gao[42]	2018	China	convenience sampling	520	89	PCL-C	self-report questionnaire	moderate
McLean[43]	2017	USA	convenience sampling	42	12	PSS	clinical interview	moderate
Kemppainen[25]	2017	USA	convenience sampling	60	26	PCL-C	self-report questionnaire	low
Gonzalez[24]	2016	USA	convenience sampling	137	47	PDS	self-report questionnaire	moderate
Rubin[44]	2016	USA	convenience sampling	1004	174	PCL-C	self-report questionnaire	moderate

John[45]	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
Julnes[14]	2016	USA	convenience sampling	114	39	CDQ	self-report questionnaire	moderate
Zhang[46]	2016	China	convenience sampling	243	106	PCL-C	self-report questionnaire	low
Battaglia[47]	2015	USA	convenience sampling	200	72	PTSD checklist	self-report questionnaire	moderate
Hansrod[48]	2015	South Africa	convenience sampling	114	29	MINI	clinical interview	moderate
Brownley[49]	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
Malee[50]	2014	USA	convenience sampling	1223	281	CDQ	self-report questionnaire	high
Glémaud[51]	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
Gore-Felton[52]	2013	USA	convenience sampling	94	28	PCL-C	self-report questionnaire	low
Glover[53]	2013	USA	convenience sampling	99	24	PDS	self-report questionnaire	high
Dévieux[54]	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate

Gard[55]	2013	Rwanda	unclear	705	380	HTS	self-report questionnaire	moderate
Peterson[56]	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
Kinyanda[57]	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
Bogart[58]	2011	USA	convenience sampling	181	72	PDS	self-report questionnaire	moderate
Martin[59]	2011	UK	convenience sampling	85	46	CIDI	clinical interview	moderate
Reisner[60]	2011	USA	convenience sampling	63	16	AUDADIS-IV	clinical interview	moderate
Theuninck[61]	2010	UK	convenience sampling	100	33	PCL-C	self-report questionnaire	low
Joska[62]	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
Adewuya[63]	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
Spies[64]	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
Fincham[65]	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate

Zanjani[66]	2007	USA	random sampling	109	13	MINI	clinical interview	moderate
Israelski[67]	2007	USA	unclear	210	71	PCL-C	self-report questionnaire	low
Boarts[68]	2006	USA	convenience sampling	57	24	PDS	self-report questionnaire	moderate
Leserman[69]	2005	USA	consecutive sampling	611	98	PTSD checklist	self-report questionnaire	high
Olley[70]	2003	South Africa	consecutive sampling	149	42	MINI	clinical interview	moderate
Vitiello[71]	2003	USA	probability sample	1489	155	CIDI	clinical interview	moderate
Martinez[72]	2002	USA	consecutive sampling	41	17	PCL-C	self-report questionnaire	moderate

* Total number of adults living with HIV

PCL-C Posttraumatic Stress Disorder Checklist-Civilian Version; *DTS* Davidson Trauma Scale; *CAPS* Clinician Administered Post-traumatic Stress Scale; *CDQ* Client Diagnostic Questionnaire; *PDS* Posttraumatic Stress Diagnostic Scale – Self-report version; *PSS* Posttraumatic Stress Symptom Scale; *PRIME MD PHQ* Primary Care Evaluation of Mental Disorders Patient Health Questionnaire; *AUDADIS-IV* The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; *MINI* Mini-International Neuropsychiatric

Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV

Prevalence of PTSD in PLWH

The reported prevalence of PTSD in PLWH ranged from 1.6% [57] to 54.1% [59]. The overall pooled prevalence was 28% (95%CI: 24% to 33%), estimated by a random effects model, as significant heterogeneity ($p \leqslant 0.001$, $I^2=98.1\%$) was observed among the included studies. Meta-analyses are shown as forest plots (Fig. 2).

Publication bias and sensitivity analysis

Possible publication bias was indicated according to the results of Egger's linear test (t= 6.84, p<0.05) and Begg's rank test (z=0.58, p=0.56). However, low sensitivity was suggested with the pooled prevalence of PTSD changed slightly from 28% (95%CI: 24% to 33%) to 27% (95%CI: 22% to 32%) after excluding low-quality articles.

Subgroup Analyses

The results of subgroup analyses are shown in Table 2. The prevalence of PTSD in PLWH differed significantly by geographic area, population group, sampling and measurement method. Specifically, the proportion of PLWH with PTSD in high-income countries tended to be higher (pooled rate= 29%, 95%CI 25% to 34%) than middle-income countries (pooled rate= 27%, 95%CI 16% to 37%) and low-income countries (pooled rate= 26%, 95%CI 7% to 45%). Studies using clinical interviews reported lower rates of PTSD (pooled rate= 22%, 95%CI 16% to 27%) compared with those using self-report questionnaires (pooled rate= 31%, 95%CI 27% to 36%). The pooled PTSD prevalence among women living with HIV, MSM living with HIV and non-MSM men living with HIV were 35% (95%CI: 28% to 43%), 33% (95%CI: 29% to 38%) and 20%

(95%CI: 17% to 23%), respectively. Also, studies conducted with convenience sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to 24%).

Table 2 Subgroup analyses of the prevalence of PTSD in PLWH

Subgroup		Number of studies	Positive PTSD screening (Diagnosis)	Sample size (Tested)	Pooled prevalence of PTSD (95%CI)	Heterogeneity (I^2)	Between group difference	
							χ^2	P value
Geographic area	High-income countries	23	1483	6832	0.29(0.25-0.34)	94.70%	107.32	<0.001
	Middle-income countries	10	1077	3755	0.27(0.16-0.37)	98.60%		
	Low-income countries	5	182	1156	0.26(0.07-0.45)	98.30%		
Population group	Women living with HIV	15	1282	4190	0.35(0.28-0.43)	96.10%	26.99	<0.001
	MSM living with HIV	3	129	380	0.33(0.29-0.38)	73.70%		
	non-MSM male living with HIV	4	165	754	0.20(0.17-0.23)	89.10%		
Sampling	Consecutive sampling	7	280	2387	0.17(0.10-0.24)	97.30%	206.01	<0.001
	Convenience sampling	20	1260	4746	0.32(0.27-0.37)	91.60%		

Data collection	Self-report questionnaire	25	2197	7812	0.31(0.27-0.36)	95.70%	297.01	<0.001
	Clinical interview	13	545	3931	0.22(0.16-0.27)	97.20%		

DISCUSSION

To the best of our knowledge, this is the first meta-analysis to provide the pooled estimated prevalence of PTSD among PLWH. A comprehensive search of the literature assessing the rate of comorbidity between PTSD and HIV-infection was performed, and 38 studies met the predefined criteria and were included in the meta-analysis. A total of 11743 participants were involved, of which 2742 were identified with PTSD. The estimated pooled prevalence was 28% (95% CI: 24% to 33%), which suggests a considerable burden of PTSD in the HIV-infected population. High heterogeneity across studies was detected, and factors such as differences in region, population characteristics, sampling, and measurement were associated with the prevalence.

As indicated, the PTSD prevalence among PLWH found in this study (28%) not only far exceeded that among the general population (3.9%), [73] but was also much higher than the prevalence of PTSD among other vulnerable groups in some previous studies. For example, the prevalence for cancer-related PTSD was 5.1%-15.3%;[74] in persons with chronic pain, the estimated mean prevalence of PTSD was 9.7%. [75] The pooled prevalence of PTSD among PLWH found in this study heightened the high rate of co-morbidity between HIV infection and PTSD, which is consistent with previous demonstrations. [8 76] For PLWH, although depressive symptoms have been the focus of many studies, and 36% of PLWH were likely to have depression according to nationally representative data in the U.S., [77] this pooled estimated prevalence of PTSD among PLWH showed that PTSD is also a common mental disorder among individuals living

with HIV/AIDS. Therefore, the results of our study significantly underscore the importance of early assessment and trauma-directed psychological interventions for PLWH.

Undoubtedly, heterogeneity between studies is expected in such a relatively large topic of review. In this review, the estimated PTSD prevalence in PLWH varied widely (1.6%-54.1%) across studies and countries, which is also a common problem in the epidemiology of psychological and mental health disorders. [78 79] Consistent with the findings of previous research, [59] the majority of studies which have determined the incidence of HIV-related PTSD have been conducted in developed countries (n=23). Compared with lower-income countries, higher-income countries reported relatively higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among PLWH may be explained by the cross-cultural differences in attitudes towards HIV infection. Turan et al.[80] found that the level of perceived HIV-related stigma in the community experienced by PLWH may cause adverse health and psychosocial outcomes. Social isolation and stigma might exacerbate symptoms of PTSD. [81] In high-income countries, PLWH may experience "compound" or "layered" stigma, where stigmatizing beliefs are not only associated with HIV infection but also related to sexual orientation, commercial sexual behaviors, etc. [82] Although, HIV-related stigma is highly burdensome in some mid-income countries, such as China, [83 84] the reported prevalence of PLWH with PTSD was lower compared to higher-income countries. The differences between collectivism and individualism rooted in eastern and western culture may be an

explanation. [85] It is worth noting that social context may not only influence the susceptibility of mental health disorders, but also constitutes an important factor in perceived stigma among individuals with mental illness. Compared to high-income countries, stigmatizing beliefs about the causes and presence of mental illness are still widespread in low- and middle-income countries, [86 87] which may lead to less disease reporting. Caution must be applied, since there is a lack of studies investigating HIV-related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular, detection of prevalence is associated with the representativeness and size of sample. In the context of low- and middle-income countries, it could be argued that lower HIV testing rates may underestimate the PTSD prevalence and impact generalizability. Thus, more epidemiological studies are warranted to better understand and clarify the difference in PTSD prevalence among PLWH globally.

Subgroup analyses indicated that the prevalence of PTSD differed significantly when gender and sexual orientation were taken into consideration. Specifically, women living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence in PTSD, in which being female is a risk factor associated with PTSD development. [16] As suggested by the aforementioned findings, MSM living with HIV may experience higher levels of stigma and trauma related to their sexual orientation. [30 88] Compared with heterosexual counterparts, MSM reported higher risk for suicidal ideation, [89] which also indicates greater psychological stress and mental health problems (i.e. PTSD and

depression). The findings that MSM and female HIV-infected individuals are at higher risk of developing PTSD may indicate that related health promotion campaigns should be directed to these groups. Clinicians should also take into consideration the PTSD susceptibility in different groups of HIV-infected populations during diagnoses. Notably, most eligible studies did not provide separate the prevalence regarding the gender of participants, and only 3 studies identified PTSD prevalence among MSM living with HIV. Given that these data are from a small number of studies and/or participants, this finding should be interpreted with caution. Nonetheless, given the high prevalence of PTSD in this group, future efforts should be made to obtain more prevalence data on PTSD among MSM living with HIV.

In our study, we assessed methodological differences that may result in heterogeneity. Factors including sampling strategies (convenience vs consecutive) and measurement (self-report vs clinical interview) were evaluated by subgroup analyses. Among 38 studies providing estimated prevalence of PTSD, 7 reported participants were consecutively enrolled via self-referral from flyers describing the study or advertisements from HIV health care providers, and generated a lower pooled rate (17%) compared with the other 20 studies using convenience sampling (32%), though both sampling methods were non-probabilistic. An increase in reporting rate due to convenience sampling has also been found in another meta-analysis synthesizing the HCV seroconversion rates in MSM living with HIV. [90] Convenience samples may allow researchers to select participants who are more likely to have PTSD symptoms and lead

to over-estimation, but given that only 4 studies were rated as high quality and limited description of study methods was detected in some studies, the reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness of calculating pooled prevalence estimates could be questioned, and the pooled prevalence estimate regarding the varied recruitment approaches of the studies should be interpreted with caution.

In this review, a total of 14 different tools were used to assess PTSD symptoms among PLWH across studies. Overall, the prevalence of PTSD screened by self-report instruments (31%) was higher than that assessed by clinical interview (22%). Though both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD), clinical interviews most likely do a much better job of assessing symptoms carefully – for example, not counting symptoms that do not meet clinically meaningful thresholds, and self-report measures may inflate the prevalence estimates; [91] alternatively, subjects may be more comfortable reporting symptoms using self-report questionnaires (presumably paper or online surveys rather than face-to-face interviews). Screening or diagnosing with survey instruments is a common and practical method, especially in resource-limited regions. We found that, though a number of measures have been used to assess PTSD among PLWH, there is no tool designed for this population specifically. As the sensitivity and specificity of the measures may impact accurate PTSD detection, further research is required to identify a standardized measure accordingly to improve validity.

Certain limitations should be acknowledged in this meta-analysis. First, though minimal potential for publication bias was presumed as all data drawn for this review were from studies reporting estimated point prevalence without intervention, publication bias cannot be ruled out for there are a number of studies published in languages other than English and Chinese that were not included in this review. Second, the heterogeneity was high in the whole sample and most subgroups. Heterogeneity importantly influences the reliability and accuracy of a meta-analysis, and the only reliable method for acquiring correct inferences is careful selection of appropriate studies. [92] Even though strict eligibility criteria were employed in addressing PTSD prevalence in this study, it should be noted that getting HIV is only one possible traumatic event, and therefore it is possible that the PTSD experienced by participants in the selected studies was due to an event other than finding out they were HIV positive. Accordingly, we suggest that further studies assessing PTSD among PLWH include more detail on the specific traumas experienced by study participants. In addition, we have analysed the influences of region, population group, recruitment venue, and measurement method, which explained some of the heterogeneity. However, the results should be interpreted with caution. Third, though some studies have indicated that several sociodemographic factors such as age may be associated with PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified by age due to the lack of detailed information reported in the published studies. As the quality of reporting could increase the susceptibility to bias, it is imperative for

researchers to report their findings of observational studies in accordance with the appropriate guidelines, such as the STROBE checklist.

CONCLUSIONS

This review contributes to evidence on the quantitatively pooled prevalence of PTSD among PLWH. Stratified subgroups including geographic area, population group, sampling and measurement method were found to be significant factors accounting for the varied prevalence of PTSD among PLWH. More effective intervention strategies targeting PTSD among PLWH are urgently needed. Future efforts should be made to obtain countries' own PTSD prevalence data among PLWH as well as specific vulnerable minorities, which will provide a basis for public health policy, health-care planning, and resource allocation for PTSD intervention initiatives. Our study also suggests that more research using robust and comprehensive methodology is needed to provide rigorous evidence for designing the targeted psychological interventions.

Figure 1 Flow chart of study inclusion

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

Contributors: Conception of the work: HW and CT. Systematic review and article evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT, LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the authors. All the authors fulfill the ICMJE criteria for authorship.

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REFERENCES

1. UNAIDS. UNAIDS Data 2018. http://www.unaids.org/en/resources/documents/2018/unaids-data-2018 (Accessed 18 March 2019).
2. Niu L, Luo D, Liu Y, *et al.* The mental health of people living with HIV in China, 1998–2014: a systematic review. *PLoS One*. 2016;11:e0153489.
3. Adams C, Zacharia S, Masters L, *et al*. Mental health problems in people living with HIV: changes in the last two decades: the London experience 1990–2014. *AIDS care*. 2016;28:56–9.
4. Friedman MJ, Resick PA, Bryant RA, *et al.* Considering PTSD for DSM-5. *Depression and anxiety.* 2011;28:750–69.
5. Young C. Understanding HIV-related posttraumatic stress disorder in South Africa:

a review and conceptual framework. *African Journal of AIDS Research*. 2011;10:139–48.

6. Sherr L, Nagra N, Kulubya G, *et al.* HIV infection associated post-traumatic stress disorder and post-traumatic growth–a systematic review. *Psychology, health & medicine*. 2011;16:612–29.
7. Cavanaugh CE, Hansen NB, Sullivan TP. HIV sexual risk behavior among low-income women experiencing intimate partner violence: The role of posttraumatic stress disorder. *AIDS Behav.* 2010;14:318–27.
8. Neigh GN, Rhodes ST, Valdez A, *et al.* PTSD co-morbid with HIV: Separate but equal, or two parts of a whole? *Neurobiology of disease*. 2016;92:116–23.
9. Borwein A, Salters KA, Palmer AK, *et al.* High rates of lifetime and recent violence observed among harder-to-reach women living with HIV. *AIDS care*. 2014;26:587–94.
10. Luo S, Lin C, Ji G, *et al.* Post-traumatic Stress Disorder Symptoms Among People Living with HIV/AIDS in Rural China. *AIDS Behav*. 2017;21:3202–8.
11. Kessler RC. Posttraumatic stress disorder: the burden to the individual and to society. *The Journal of clinical psychiatry*. 2000;61(Suppl 5):4-14.
12. Pence BW. The impact of mental health and traumatic life experiences on antiretroviral treatment outcomes for people living with HIV/AIDS. *Journal of Antimicrobial Chemotherapy.* 2009;63:636–40.
13. Ebrahimzadeh Z, Goodarzi MA, Joulaei H. Predicting the Antiretroviral Medication

Adherence and CD4 Measure in Patients with HIV/AIDS Based on the Post Traumatic Stress Disorder and Depression. *Iranian Journal of Public Health*. 2019;48:139–46.

14. Julnes PS, Auh S, Krakora R, *et al.* The association between post-traumatic stress disorder and markers of inflammation and immune activation in HIV-infected individuals with controlled viremia. *Psychosomatics*. 2016;57:423–30.
15. Lynn C, Chenneville T, Bradley-Klug K, *et al.* Depression, anxiety, and posttraumatic stress as predictors of immune functioning: differences between youth with behaviorally and perinatally acquired HIV. *AIDS care*. 2019 Mar 4:1–10.
16. Brief DJ, Bollinger AR, Vielhauer MJ, *et al.* Understanding the interface of HIV, trauma, post-traumatic stress disorder, and substance use and its implications for health outcomes. *AIDS care*. 2004;16:97–120.
17. Nightingale VR, Sher TG, Mattson M, *et al.* The effects of traumatic stressors and HIV-related trauma symptoms on health and health related quality of life. *AIDS Behav*. 2011;15:1870–8.
18. Koegler E, Kennedy CE. A scoping review of the associations between mental health and factors related to HIV acquisition and disease progression in conflict-affected populations. *Confl Health*. 2018;12:20.
19. Pearson CR, Kaysen D, Huh D, *et al.* Randomized Control Trial of Culturally Adapted Cognitive Processing Therapy for PTSD Substance Misuse and HIV Sexual Risk Behavior for Native American Women. *AIDS Behav*. 2019;23:695–706.

20. Tull MT, Weiss NH, McDermott MJ. Post-traumatic stress disorder and impulsive and risky behavior: Overview and discussion of potential mechanisms. *Comprehensive guide to post-traumatic stress disorders*. 2016;803–16.

21. Weiss NH, Tull MT, Borne MER, *et al.* Posttraumatic stress disorder symptom severity and HIV-risk behaviors among substance-dependent inpatients. *AIDS care*. 2013;25:1219–26.

22. Applebaum AJ, Bedoya CA, Hendriksen ES, *et al.* Future directions for interventions targeting PTSD in HIV-infected adults. *Journal of the Association of Nurses in AIDS Care*. 2015;26:127–38.

23. Machtinger E, Wilson T, Haberer JE, *et al.* Psychological trauma and PTSD in HIV-positive women: a meta-analysis. *AIDS Behav*. 2012;16:2091–100.

24. Gonzalez A, Locicero B, Mahaffey B, *et al.* Internalized HIV stigma and mindfulness: associations with PTSD symptom severity in trauma-exposed adults with HIV/AIDS. *Behavior modification*. 2016;40:144–63.

25. Kemppainen JK, MacKain S, Alexander M, *et al.* Posttraumatic stress disorder and stressful life events among rural women with HIV disease. *Journal of the Association of Nurses in AIDS Care*. 2017;28:216–25.

26. Rubin LH, Cook JA, Springer G, *et al.* Perceived and post-traumatic stress are associated with decreased learning, memory, and fluency in HIV-infected women. *AIDS (London, England)*. 2017;31:2393–1401.

27. Seedat S. Interventions to improve psychological functioning and health outcomes

of HIV-infected individuals with a history of trauma or PTSD. *Current HIV/AIDS Reports*. 2012;9:344–50.

28. World Health Organization. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization; 1992.
29. Association AP. Diagnostic and statistical manual of mental disorders. 5th Edition. Washington, DC: American Psychiatric Pub; 2013.
30. Sales JM, Swartzendruber A, Phillips AL. Trauma-Informed HIV Prevention and Treatment. *Curr HIV/AIDS Rep*. 2016;13:374–82.
31. Burnham KE, Cruess DG, Kalichman MO, *et al.* Trauma symptoms, internalized stigma, social support, and sexual risk behavior among HIV-positive gay and bisexual MSM who have sought sex partners online. *AIDS care*. 2016;28:347–53.
32. Rzeszutek M, Oniszczenko W, Firląg-Burkacka E. Gender differences in posttraumatic stress symptoms and social support in a sample of HIV-positive individuals. *Women & health*. 2017;57:792–803.
33. Rostom A, Dubé C, Cranney A, *et al.* Appendix D. Quality Assessment Forms. Agency for Healthcare Research and Quality (US); 2004 https://www.ncbi.nlm.nih.gov/books/NBK35156/ (Accessed 21 October 2018).
34. Stata C, Station C. TX. Stata Press 2016
35. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Statistics in medicine. 2002;21(11):1539-58.

36. Egger M, Smith GD, Schneider M, *et al.* Bias in meta-analysis detected by a simple, graphical test. *BMJ.* 1997; 315: 629–34.

37. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics.* 1994; 50: 1088–101.

38. Fabian KE, Huh D, Kemp CG, *et al.* Moderating Factors in an Anti-stigma Intervention for African American Women with HIV in the United States: A Secondary Analysis of the UNITY Trial. *AIDS and Behavior*. 2019;19:1-11.

39. Chen CD, Yan H, Li SY, *et al.* Post-traumatic stress disorder and it associated factors among people living with HIV in Wuhan city. *Chin J Public Health*. 2018;1-4.

40. Spies G, Konkiewitz EC, Seedat S. Incidence and persistence of depression among women living with and without HIV in South Africa: A longitudinal study. *AIDS Behav*. 2018;22(10):3155–65.

41. Verhey R, Chibanda D, Gibson L, *et al.* Validation of the posttraumatic stress disorder checklist - 5 (PCL-5) in a primary care population with high HIV prevalence in Zimbabwe. *BMC Psychiatry.* 2018;18:109.

42. Gao M, Xiao C, Zhang X, *et al.* Social capital and PTSD among PLWHA in China: the mediating role of resilience and internalized stigma. *Psychology, health & medicine*. 2018;23:698–706.

43. McLean CP, Gay NG, Metzger DA, *et al.* Psychiatric Symptoms and Barriers to Care in HIV-Infected Individuals Who Are Lost to Care. *J Int Assoc Provid AIDS*

Care. 2017;16:423–9.

44. Rubin LH, Pyra M, Cook JA, *et al.* Post-traumatic stress is associated with verbal learning, memory, and psychomotor speed in HIV-infected and HIV-uninfected women. *Journal of neurovirology.* 2016;22:159–69.

45. John M, Greene M, Hessol NA, *et al.* Geriatric assessments and association with VACS index among HIV-infected older adults in San Francisco. *Journal of acquired immune deficiency syndromes (1999).* 2016;72:534.

46. Zhang X, Wang T, Liu M, *et al.* Post-traumatic stress disorder among people living with HIV/AIDS and its influence factors. *Chongqing Medicine.* 2016;232–5.

47. Battaglia TA, Gunn CM, McCoy ME, *et al.* Beliefs About Anal Cancer among HIV-Infected Women: Barriers and Motivators to Participation in Research. *Womens Health Issues*. 2015;25:720–6.

48. Hansrod F, Spies G, Seedat S. Type and severity of intimate partner violence and its relationship with PTSD in HIV-infected women. *Psychology, health & medicine.* 2015;20:697–709.

49. Brownley JR, Fallot RD, Berley RW, *et al.* Trauma history in African-American women living with HIV: effects on psychiatric symptom severity and religious coping. *AIDS care.* 2015;27:964–71.

50. Malee K, Mellins CA, Huo Y, *et al.* Prevalence, incidence and persistence of psychiatric and substance use disorders among mothers living with HIV. *Journal of acquired immune deficiency syndromes (1999).* 2014;65:526.

51. Glémaud M, Illa L, Echenique M, *et al.* Abuse and mental health concerns among HIV-infected Haitian women living in the United States. Journal of the Association of Nurses in *AIDS Care.* 2014;25:S62–9.

52. Gore-Felton C, Ginzburg K, Chartier M, *et al.* Attachment style and coping in relation to posttraumatic stress disorder symptoms among adults living with HIV/AIDS. *Journal of behavioral medicine.* 2013;36:51–60.

53. Glover DA, Williams JK, Kisler KA. Using novel methods to examine stress among HIV-positive African American men who have sex with men and women. *J Behav Med*. 2013;36:283–94.

54. Dévieux JG, Malow RM, Attonito JM, *et al.* Post-traumatic stress disorder symptomatology and alcohol use among HIV-seropositive adults in Haiti. *AIDS care*. 2013;25(10):1210-8.

55. Gard TL, Hoover DR, Shi Q, *et al.* The impact of HIV status, HIV disease progression, and post-traumatic stress symptoms on the health-related quality of life of Rwandan women genocide survivors. *Quality of Life Research*. 2013;22(8):2073-84.

56. Peterson K, Togun T, Klis S, *et al.* Depression and posttraumatic stress disorder among HIV-infected Gambians on antiretroviral therapy. *AIDS patient care and STDs*. 2012;26:589–96.

57. Kinyanda E, Hoskins S, Nakku J, *et al.* Prevalence and risk factors of major depressive disorder in HIV/AIDS as seen in semi-urban Entebbe district, Uganda.

BMC psychiatry. 2011;11:205.

58. Bogart LM, Wagner GJ, Galvan FH, *et al.* Perceived discrimination and mental health symptoms among Black men with HIV. *Cultural Diversity and Ethnic Minority Psychology*. 2011;17:295.

59. Martin L, Kagee A. Lifetime and HIV-related PTSD among persons recently diagnosed with HIV. *AIDS Behav*. 2011;15:125–31.

60. Reisner SL, Falb KL, Mimiaga MJ. Early life traumatic stressors and the mediating role of PTSD in incident HIV infection among US men, comparisons by sexual orientation and race/ethnicity: results from the NESARC, 2004–2005. *Journal of Acquired Immune Deficiency Syndromes*. 2011;57:340–50.

61. Theuninck AC, Lake N, Gibson S. HIV-related posttraumatic stress disorder: Investigating the traumatic events. *AIDS Patient care and STDS*. 2010;24:485–91.

62. Joska JA, Fincham DS, Stein DJ, *et al.* Clinical correlates of HIV-associated neurocognitive disorders in South Africa. *AIDS Behav*. 2010;14:371–8.

63. Adewuya AO, Afolabi MO, Ola BA, *et al.* Post-traumatic stress disorder (PTSD) after stigma related events in HIV infected individuals in Nigeria. *Social Psychiatry and Psychiatric Epidemiology*. 2009;44:761.

64. Spies G, Kader K, Kidd M, *et al.* Validity of the K-10 in detecting DSM-IV-defined depression and anxiety disorders among HIV-infected individuals. *AIDS care*. 2009;21:1163–8.

65. Fincham D, Smit J, Carey P, *et al.* The relationship between behavioural inhibition,

anxiety disorders, depression and CD4 counts in HIV-positive adults: a cross-sectional controlled study. *AIDS care.* 2008;20:1279–83.

66. Zanjani F, Saboe K, Oslin D. Age difference in rates of mental health/substance abuse and behavioral care in HIV-positive adults. *AIDS patient care and STDs*. 2007;21:347–55.
67. Israelski DM, Prentiss DE, Lubega S, *et al.* Psychiatric co-morbidity in vulnerable populations receiving primary care for HIV/AIDS. *AIDS care*. 2007;19:220–5.
68. Boarts JM, Sledjeski EM, Bogart LM, *et al.* The differential impact of PTSD and depression on HIV disease markers and adherence to HAART in people living with HIV. *AIDS Behav.* 2006;10:253–61.
69. Leserman J, Whetten K, Lowe K, *et al.* How trauma, recent stressful events, and PTSD affect functional health status and health utilization in HIV-infected patients in the south. *Psychosomatic medicine*. 2005;67:500–7.
70. Olley BO, Gxamza F, Seedat S, *et al.* Psychopathology and coping in recently diagnosed HIV/AIDS patients-the role of gender. *South African Medical Journal*. 2003;93:928–31.
71. Vitiello B, Burnam MA, Bing EG, *et al.* Use of psychotropic medications among HIV-infected patients in the United States. *American Journal of Psychiatry.* 2003;160:547–54.
72. Martinez A, Israelski D, Walker C, *et al.* Posttraumatic stress disorder in women attending human immunodeficiency virus outpatient clinics. *AIDS patient care and*

STDs. 2002;16:283–91.

73. Koenen KC, Ratanatharathorn A, Ng L, *et al.* Posttraumatic stress disorder in the World Mental Health Surveys. *Psychol Med.* 2017;47:2260–74.
74. Abbey G, Thompson SBN, Hickish T, *et al.* A meta-analysis of prevalence rates and moderating factors for cancer-related post-traumatic stress disorder. *Psychooncology*. 2015;24:371–81.
75. Siqveland J, Hussain A, Lindstrøm JC, *et al.* Prevalence of Posttraumatic Stress Disorder in Persons with Chronic Pain: A Meta-analysis. *Frontiers in Psychiatry.* 2017;8:164.
76. Kelly B, Raphael B, Judd F, *et al.* Posttraumatic stress disorder in response to HIV infection. *General Hospital Psychiatry*. 1998;20:345–52.
77. Bing EG, Burnam MA, Longshore D, *et al.* Psychiatric disorders and drug use among human immunodeficiency virus–infected adults in the United States. *Archives of general psychiatry.* 2001;58:721–8.
78. Pringsheim T, Jette N, Frolkis A, *et al.* The prevalence of Parkinson's disease: A systematic review and meta-analysis. *Movement disorders.* 2014;29:1583–90.
79. Wang T, Fu H, Kaminga AC, *et al*. Prevalence of depression or depressive symptoms among people living with HIV/AIDS in China: a systematic review and meta-analysis. *BMC psychiatry.* 2018 Dec;18(1):160.
80. Turan B, Budhwani H, Fazeli PL, *et al.* How Does Stigma Affect People Living with HIV? The Mediating Roles of Internalized and Anticipated HIV Stigma in the

Effects of Perceived Community Stigma on Health and Psychosocial Outcomes. *AIDS Behav*. 2017;21:283–91.

81. Kamen C, Vorasarun C, Canning T, *et al.* The impact of stigma and social support on development of post-traumatic growth among persons living with HIV. *Journal of clinical psychology in medical settings*. 2016;23:126–34.
82. Lowther K, Selman L, Harding R, *et al.* Experience of persistent psychological symptoms and perceived stigma among people with HIV on antiretroviral therapy (ART): a systematic review. *International journal of nursing studies*. 2014;51(8):1171-89.
83. Li Z, Morano JP, Khoshnood K, *et al.* HIV-related stigma among people living with HIV/AIDS in rural Central China. *BMC Health Serv Res*. 2018;18:453.
84. Li L, Liang L-J, Lin C, *et al.* HIV prevention intervention to reduce HIV-related stigma: evidence from China. *AIDS (London, England)*. 2010;24:115.
85. Shavitt S, Cho YI, Johnson TP, *et al.* Culture Moderates the Relation Between Perceived Stress, Social Support, and Mental and Physical Health. *Journal of Cross-Cultural Psychology*. 2016;47:956–80.
86. Lauber C, Rössler W. Stigma towards people with mental illness in developing countries in Asia. *International Review of Psychiatry*. 2007;19:157–78.
87. Seeman N, Tang S, Brown AD, *et al.* World survey of mental illness stigma. *Journal of Affective Disorders.* 2016;190:115–21.
88. Reisner SL, Mimiaga MJ, Safren SA, *et al.* Stressful or traumatic life events, post-

traumatic stress disorder (PTSD) symptoms, and HIV sexual risk taking among men who have sex with men. *AIDS care*. 2009;21:1481–9.

89. Luo Z, Feng T, Fu H, *et al.* Lifetime prevalence of suicidal ideation among men who have sex with men: a meta-analysis. *BMC psychiatry*. 2017;17:406.
90. Hagan H, Jordan AE, Neurer J, *et al.* Incidence of sexually transmitted hepatitis C virus infection in HIV-positive men who have sex with men. *AIDS*. 2015;29:2335–45.
91. Ayers S, Wright DB, Ford E. Hyperarousal symptoms after traumatic and nontraumatic births. *Journal of Reproductive and Infant Psychology*. 2015;33:282–93.
92. Melsen WG, Bootsma MC, Rovers MM, *et al*. The effects of clinical and statistical heterogeneity on the predictive values of results from meta-analyses. *Clinical Microbiology and Infection*. 2014;20(2):123-9.

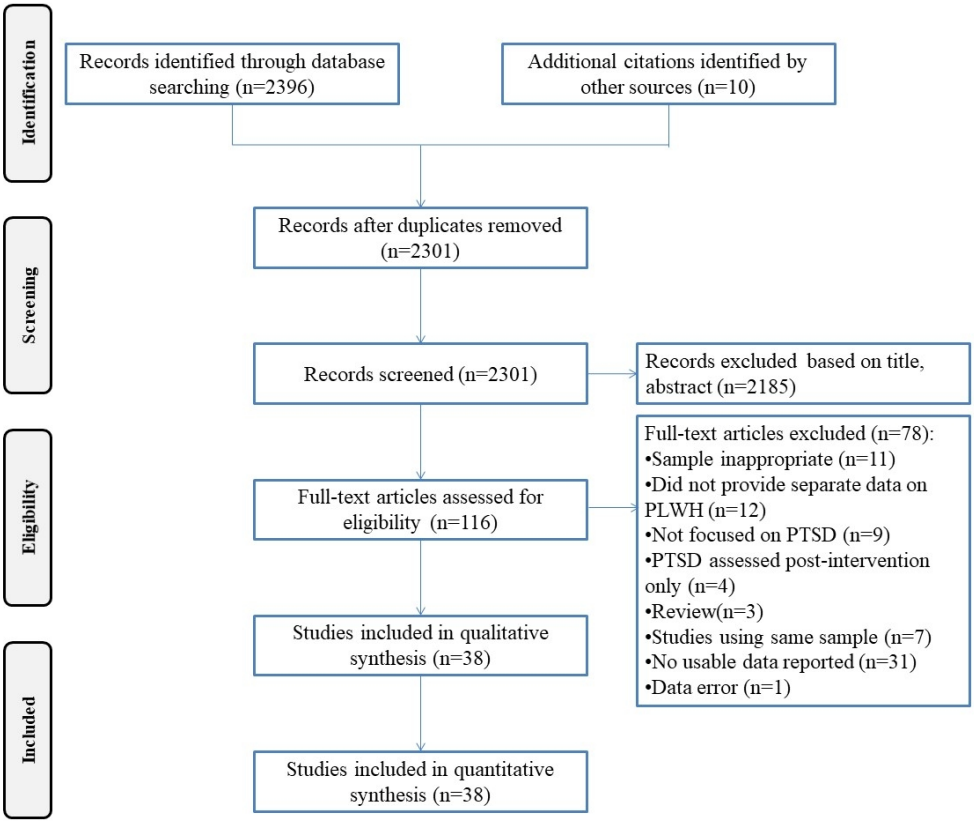

Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

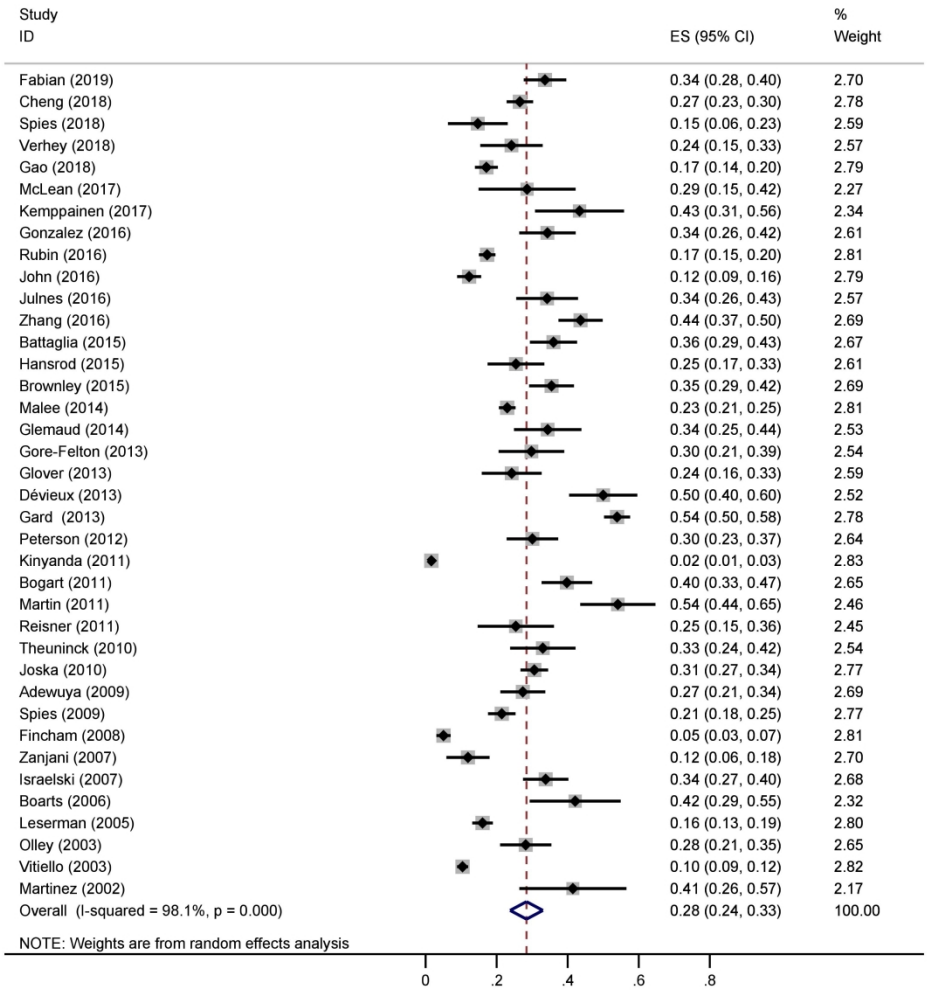

Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

281x304mm (300 x 300 DPI)

Appendix 1 – Search strategy

ID	Search terms
PubMed	
#1	("stress disorders, post-traumatic"[Mesh] OR PTSD*[tiab] OR posttrauma*[tiab] OR "post trauma*" [tiab]OR post-trauma*[tiab] OR trauma* [tiab] OR psychotrauma*[tiab] OR stress*[tiab])
#2	("HIV Infections"[Mesh] OR "HIV" [MeSH] OR "human immunodeficiency virus" [tiab] OR "human immuno deficiency virus" [tiab] OR "human immune deficiency virus" [tiab] OR "human immunedeficiency virus" [tiab] OR "AIDS" [tiab] OR "acquired immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency syndromes" [tiab] OR "acquired immuno deficiency syndrome" [tiab] OR "acquired immuno deficiency syndromes" [tiab] OR "acquired immune deficiency syndrome" [tiab] OR "acquired immune deficiency syndromes" [tiab] OR "acquired immunedeficiency syndrome" [tiab] OR "acquired immunedeficiency syndromes" [tiab])
#3	(((((((("Prevalence"[Mesh] OR "Epidemiology"[Mesh] OR "Cross-Sectional Studies"[Mesh])) OR Prevalence) OR Epidemiology) OR Cross-Sectional Studies) OR "Longitudinal Studies"[Mesh]) OR "Cohort Studies"[Mesh]) OR Cohort Studies) OR Longitudinal Studies))
#4	#1 AND #2 AND #3

Search Filters

a. Human studies
b. Language – English/Chinese
c. Publication dates – From 2000/01/01 to 2019/11/31

Appendix 2 – Risk of bias and quality of included studies

Country	Year	Citation	1	2	3	4	5	6	7	8	9	10	11	Quality
USA	2019	Fabian 2019	yes	yes	no	unclear	unclear	no	no	yes	no	yes	yes	moderate
China	2018	Cheng 2018	yes	yes	yes	unclear	unclear	yes	no	no	no	no	no	moderate
South Africa	2018	Spies 2018	yes	yes	no	no	unclear	yes	no	yes	no	no	no	moderate
Zimbabwe	2018	Verhey 2018	yes	yes	yes	no	unclear	yes	yes	no	no	yes	no	moderate
China	2018	Gao 2018	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
USA	2017	McLean 2017	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2017	Kemppainen 2017	yes	yes	no	no	unclear	no	no	no	no	no	no	low
USA	2016	Gonzalez 2016	yes	yes	yes	no	unclear	yes	yes	yes	no	yes	no	moderate
USA	2016	Rubin 2016	yes	yes	yes	no	no	no	yes	yes	yes	yes	no	moderate
USA	2016	John 2016	yes	no	yes	yes	no	yes	no	no	no	no	no	moderate
USA	2016	Julnes 2016	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
China	2016	Zhang 2016	yes	yes	no	no	no	no	no	no	no	yes	no	low
USA	2015	Battaglia 2015	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
South Africa	2015	Hansrod 2015	yes	yes	yes	no	unclear	yes	no	yes	no	no	no	moderate
USA	2015	Brownley 2015	yes	yes	yes	unclear	unclear	no	no	no	no	yes	no	moderate
USA	2014	Malee 2014	yes	yes	yes	no	unclear	no	yes	yes	yes	yes	yes	high
USA	2014	Glémaud 2014	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low

USA	2013	Gore-Felton 2013	yes	yes	no	no	unclear	yes	no	no	no	no	no	low
USA	2013	Glover 2013	yes	yes	no	unclear	unclear	yes	yes	yes	yes	yes	yes	high
Haiti	2013	Dévieux 2013	yes	yes	yes	no	unclear	no	no	yes	no	no	no	moderate
Rwanda	2013	Gard 2013	yes	yes	yes	unclear	no	no	yes	yes	no	yes	no	moderate
Gambia	2012	Peterson 2012	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	no	high
Uganda	2011	Kinyanda 2011	yes	yes	yes	yes	unclear	no	yes	yes	no	yes	no	moderate
USA	2011	Bogart 2011	yes	yes	yes	no	unclear	no	yes	yes	no	no	no	moderate
UK	2011	Martin 2011	yes	yes	yes	no	unclear	no	no	no	no	yes	no	moderate
USA	2011	Reisner 2011	yes	yes	yes	no	unclear	no	yes	yes	yes	no	no	moderate
UK	2010	Theuninck 2010	yes	no	no	no	no	no	no	no	no	no	no	low
South Africa	2010	Joska 2010	yes	yes	no	unclear	unclear	yes	no	yes	yes	no	no	moderate
Nigeria	2009	Adewuya 2009	yes	yes	no	no	unclear	no	no	yes	no	yes	no	moderate
South Africa	2009	Spies 2009	yes	yes	no	no	unclear	yes	no	yes	no	yes	no	moderate
South Africa	2008	Fincham 2008	yes	yes	yes	yes	unclear	no	yes	yes	yes	no	no	moderate
USA	2007	Zanjani 2007	yes	yes	yes	no	unclear	no	no	yes	yes	no	no	moderate
USA	2007	Israelski 2007	yes	yes	yes	unclear	unclear	no	no	no	no	no	no	low
USA	2006	Boarts 2006	yes	no	no	no	unclear	yes	yes	yes	no	no	yes	moderate
USA	2005	Leserman 2005	yes	yes	no	yes	no	no	yes	yes	yes	yes	no	high
South Africa	2003	Olley 2003	yes	yes	no	yes	unclear	no	no	yes	no	no	no	moderate

USA	2003	Vitiello 2003	yes	no	no	no	unclear	no	yes	no	no	yes	yes	moderate
USA	2002	Martinez 2002	yes	yes	no	yes	unclear	no	yes	no	no	yes	no	moderate

Risk of bias was assessed using the Agency for Healthcare Research and Quality (AHRQ). The checklist included 11 items. Each item was coded with a “yeses/No/Unclear”: “No” or “Unclear” was scored “0”, and “yeses” was scored “1”. Total score out of 11 where 8-11, 4-7, and 0-3 depict high, moderate and low quality, respectively.

MOOSE Checklist

Items	Page #	Comments
TITLE Identify the study as a meta-analysis (or systematic review)	3	
ABSTRACT Use the journal's structured format	3,4	
INTRODUCTION		
· The clinical problem	5,6	
· The hypothesis	5	
· A statement of objectives that includes the study population, the condition of interest, the exposure or intervention, and the outcome(s) considered	7	
SOURCES		
· Qualifications of searchers (eg, librarians and investigators)	8	1 psychiatrist
· Search strategy, including time period included in the synthesis and keywords	7,8	
· Effort to include all available studies, including contact with authors	8	
· Databases and registries searched	7	
· Search software used, name and version, including special features used (eg, explosion)	-	
· Use of hand searching (eg, reference lists of obtained articles)	8	
· List of citations located and those excluded, including justification	figure 1	
· Method of addressing articles published in languages other than English	7	
· Method of handling abstracts and unpublished studies	-	Not applicable
· Description of any contact with authors	-	
STUDY SELECTION		
· Types of study designs considered	8	Observational
· Relevance or appropriateness of studies gathered for assessing the hypothesis to be tested	7,8	
· Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	7,8	
· Documentation of how data were classified and coded (eg, multiple raters, blinding, etc)	8,9	
· Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	-	Not applicable
· Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results	9,10	
· Assessment of heterogeneity	10	
· Statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	10	
RESULTS		
· A graph summarizing individual study estimates and the overall estimate	Figure 1,2	
· A table giving descriptive information for each included study	Tables 1	
· Results of sensitivity testing (eg, subgroup analysis)	17,18	
· Indication of statistical uncertainty of findings	17	
DISCUSSION		
· Strengths and weaknesses	22-27	
· Potential biases in the review process (eg, publication bias)	27	
· Justification for exclusion (eg, exclusion of non–English-language citations)	-	
· Assessment of quality of included studies	26	
· Consideration of alternative explanations for observed results	27	
· Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	28	
· Guidelines for future research	27,28	
· Disclosure of funding source	29	