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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

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

Authors:

1. Chulei TANG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

ORCID: 0000-0003-3178-5130

2. Lloyd A Goldsamt, PhD, Senior Research Scientist

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

3. Jingjing MENG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

4. Xueling XIAO, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

5. Li ZHANG, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

6. Ann Bartley Williams, PhD, Professor

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

7. Honghong WANG, RN, MSN, PhD, Professor

Xiangya School of Nursing, Central South University, Changsha, China.

1
2
3
4 **Corresponding author**

5
6 Honghong WANG

7
8 Xiangya School of Nursing, Central South University

9
10 172 Tongzipo road, Changsha 410013, Hunan, China

11
12
13 Email: honghong_wang@hotmail.com

14
15 Telephone number: 0731-82650270

16
17 Fax number: 0731-82650270

18
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5 **A global estimate of the prevalence of posttraumatic stress disorder among adults**
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7 **living with HIV: A systematic review and meta-analysis**
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12
13 **ABSTRACT**
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15 **Objectives** Although HIV-infected patients have been disproportionately affected by
16 posttraumatic stress disorder (PTSD), the global prevalence of PTSD among people
17 living with HIV (PLWH) is unknown. This study aimed to systematically review the
18 prevalence of PTSD among PLWH worldwide and explore variation in prevalence
19 across sociodemographic and methodological factors.
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28 **Design** A meta-analysis using a random-effect model was conducted to pool the
29 prevalence estimated from individual studies, and subgroup analyses were used to
30 analyze heterogeneities.
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36 **Setting, participants and measures** Observational studies providing PTSD prevalence
37 in an adult HIV population were included. Measurements were not restricted except that
38 the definition of PTSD should be in accordance with the Diagnostic and Statistical
39 Manual of Mental Disorders (DSM) or the International Classification of Diseases (ICD)
40 diagnostic criteria.
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49 **Results** A total of 34 articles were included among 2396 records identified initially. The
50 estimated global rate of PTSD in PLWH was 27% (95% CI 23-31%). Significant
51 heterogeneity was detected in the proportion of PLWH who reported PTSD across
52 studies, which was partially explained by geographic area, population group,
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5 measurement and sampling method ($p<0.05$).
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7 **Conclusion** PTSD among PLWH is common worldwide. We strongly suggest that
8
9 PTSD should be routinely screened for and that more effective prevention strategies and
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13 treatment packages targeting PTSD are needed in PLWH.
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16 17 18 **Strengths and limitations of this study** 19

- 20 ● This is the first meta-analysis providing comprehensive assessment on the
21
22 prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
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- 25 ● Several subgroup analyses were conducted to examine the influence of diverse
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27 sociodemographic backgrounds as well as methodological heterogeneity.
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- 30 ● This review was conducted with specified definition of PTSD in inclusion criteria
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32 to help in acquiring high level of evidence, which also limited the number of
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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

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5 both the treatment of PTSD and the management of HIV. PTSD can negatively impact
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7 medication adherence and impair immune functioning,¹²⁻¹⁵ all of which are especially
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9 critical for PLWH. HIV-infected patients with PTSD have been found to be at increased
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11 risk of somatization and physical disorders.¹⁶ The illness experience of PTSD, such as
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13 persistent avoidance and re-experiencing the traumatic event, may also compromise
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15 quality of life and cause significant distress in PLWH.^{7 17} Subsequently, prolonged and
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17 untreated PTSD may lead to exacerbation of both PTSD and HIV progression.¹⁸ There
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19 is also evidence suggesting that reductions in PTSD symptom severity are related to
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21 improved HIV-risk related outcomes.¹⁹ Given that PTSD elevates HIV-risk behaviors²⁰
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23 ²¹ and the possibility of HIV transmission also increases along with disease progression,
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25 PLWH suffering from PTSD are an important group to understand and with whom to
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27 intervene.
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36 Valid data on PTSD prevalence rates among PLWH is essential. Evidence on the
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38 extent of PTSD among PLWH is needed to raise awareness and recommend clinical
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40 management. Although a number of studies have investigated the prevalence of PTSD
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42 in PLWH, findings have been inconsistent.²² While studies have reported varied
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44 incidence, few efforts have been made to aggregate existing research using
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46 meta-analysis techniques. There was one published meta-analysis estimating the pooled
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48 prevalence of PTSD among women living with HIV in 2012.²³ But the lack of studies
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50 with other groups lowered the generalizability and global relevance of their findings.
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52 Moreover, the meta-analysis was conducted in 2012, and an increase of publications
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5 about PTSD among PLWH since then²⁴⁻²⁶ suggests that a timely update is urgently
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8 needed. Indeed, several reviews provide a useful overview of the possible prevalence of
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10 PTSD among PLWH;²²⁻²⁷ however, a number of gaps remain. First, to date, there has
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12 been no attempt to achieve a better understanding of the epidemiology of PTSD in
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14 PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second,
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16 economically and politically, while precise estimates of prevalence can support efficient
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18 allocation of resources, factors that might influence PTSD prevalence rates, such as
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21 population characteristics and socio-cultural context have been neglected.
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26 Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the
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28 worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in
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30 PLWH differs based upon population group, country income groups and study
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32 characteristics. This information can then be used to inform further practice and
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34 research for this highly co-morbid group.
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38 **METHODS**

39 **Search strategy**

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42 Systematic searches were conducted through 5 electronic English databases (Medline,
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44 Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases
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46 (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence
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48 among PLWH up to May 2018. The search terms were: posttrauma*, post trauma*,
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50 post-trauma*, stress disorder*, OR PTSD; AND HIV, acquired immunodeficiency
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52 syndrome, AIDS, OR PLWH\$; AND epidemiology, occurrence, incidence, OR
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5 prevalence. The reference lists of review articles and retrieved full-text articles were
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7 also examined for additional papers that were eligible for this review.
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10 **Eligibility criteria**

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

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46 Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.)
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48 following PRISMA recommendations. C.T and X.X. searched the English papers and
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50 J.M. screened the Chinese language papers. After duplicates were deleted, each
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52 investigator read titles and abstracts closely to capture all potential studies. Full-text
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54 articles were obtained and reviewed for all criteria. Any discrepancies were resolved by
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5 discussion with the research team. The PRISMA flow chart shows the results of the
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7 systematic search (figure 1)
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10 **Data extraction**

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

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46 We used the quality assessment forms for cross-sectional/prevalence studies
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48 recommended by the Agency for Healthcare Research and Quality (AHRQ)³³ to assess
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50 the reliability of the eligible studies. The checklist included 11 items. Each item was
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52 coded with a “Yes/No/Unclear”: “No” or “Unclear” was scored “0”, and “Yes” was
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54 scored “1”. Consistent with previous meta-analyses studies using AHRQ, a total score
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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 ($I^2 > 50\%$, $p \leq 0.10$). 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 2002⁶⁵ 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

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

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5	Zhang ⁴¹	2016	China	convenient sampling	243	106	PCL-C	self-report questionnaire	low
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8	Battaglia ⁴²	2015	USA	convenient sampling	200	72	PTSD checklist	self-report questionnaire	moderate
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11	Hansrod ⁴³	2015	South Africa	convenient sampling	114	29	MINI	clinical interview	moderate
12									
13									
14	Brownley ⁴⁴	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
15									
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18	Malee ⁴⁵	2014	USA	convenient sampling	1223	281	CDQ	self-report questionnaire	high
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20									
21	Glémaud ⁴⁶	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
22									
23									
24	Gore-Felton ⁴⁷	2013	USA	convenient sampling	94	28	PCL-C	self-report questionnaire	low
25									
26									
27	Glover ⁴⁸	2013	USA	convenient sampling	99	24	PDS	self-report questionnaire	high
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29									
30	Peterson ⁴⁹	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
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34	Kinyanda ⁵⁰	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
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37	Bogart ⁵¹	2011	USA	convenient sampling	181	72	PDS	self-report questionnaire	moderate
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5	Martin ⁵²	2011	UK	convenient sampling	85	46	CIDI	clinical interview	moderate
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8	Reisner ⁵³	2011	USA	convenient sampling	63	16	AUDADIS-IV	clinical interview	moderate
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11	Theuninck ⁵⁴	2010	UK	convenient sampling	100	33	PCL-C	self-report questionnaire	low
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14	Joska ⁵⁵	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
15									
16									
17	Adewuya ⁵⁶	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
18									
19									
20	Spies ⁵⁷	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
21									
22									
23									
24	Fincham ⁵⁸	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate
25									
26									
27	Zanjani ⁵⁹	2007	USA	random sampling	109	13	MINI	clinical interview	moderate
28									
29									
30	Israelski ⁶⁰	2007	USA	unclear	210	71	PCL-C	self-report questionnaire	low
31									
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33									
34	Boarts ⁶¹	2006	USA	convenient sampling	57	24	PDS	self-report questionnaire	moderate
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37	Leserman ⁶²	2005	USA	consecutive sampling	611	98	PTSD checklist	self-report questionnaire	high
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5	Olley ⁶³	2003	South Africa	consecutive sampling	149	42	MINI	clinical interview	moderate
6									
7									
8	Vitiello ⁶⁴	2003	USA	probability sample	1489	155	CIDI	clinical interview	moderate
9									
10									
11	Martinez ⁶⁵	2002	USA	consecutive sampling	41	17	PCL-C	self-report questionnaire	moderate
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* Total number of adults living with HIV

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17 *PCL-C* Posttraumatic Stress Disorder Checklist-Civilian Version; *DTS* Davidson Trauma Scale; *CAPS* Clinician Administered

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19 Post-traumatic Stress Scale; *CDQ* Client Diagnostic Questionnaire; *PDS* Posttraumatic Stress Diagnostic Scale – Self-report version; *PSS*

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21 Posttraumatic Stress Symptom Scale; *PRIME MD PHQ* Primary Care Evaluation of Mental Disorders Patient Health Questionnaire;

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23 *AUDADIS-IV* The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV; *MINI* Mini-International Neuropsychiatric

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25 Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV

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27 diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV

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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 ($p \leq 0.001$, $I^2=97.5\%$) 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%

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5 (95%CI: 17% to 23%), respectively. Also, studies conducted with convenience
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8 sampling were more likely to achieve higher PTSD prevalence (pooled rate= 31%,
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10 95%CI 26% to 36%) than those using consecutive sampling (pooled rate= 17%, 95%CI
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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%		

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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

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5 HIV/AIDS. Therefore, the results of our study significantly underscore the importance
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8 of early assessment and trauma-directed psychological interventions for PLWH.
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10 Undoubtedly, heterogeneity between studies is expected in such a relatively large
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12 topic of review. In this review, the estimated PTSD prevalence rates in PLWH varied
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14 widely (1.6%-54.1%) across studies and countries, which is also a common problem in
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16 the epidemiology of psychological and mental health disorders.^{71 72} Consistent with the
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18 findings of previous research,⁵² the majority of studies which have determined the
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20 incidence of HIV-related PTSD have been conducted in developed countries (n=22).
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22 Compared with lower-income countries, higher-income countries reported relatively
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24 higher rates of PTSD. This tendency and the varied prevalence of PTSD among PLWH
25
26 may be explained by the cross-cultural differences in attitudes towards HIV infection.
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28 Turan et al.⁷³ found that the level of perceived HIV-related stigma in the community
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30 experienced by PLWH may cause adverse health and psychosocial outcomes. Social
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32 isolation and stigma might exacerbate symptoms of PTSD.⁷⁴ In high-income countries,
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34 PLWH may experience “compound” or “layered” stigma, where stigmatizing beliefs not
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36 only associated with HIV infection but also related to sexual orientation, commercial
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38 sexual behaviors, etc.⁷⁵ Although, HIV-related stigma is highly burdensome in some
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40 mid-income countries, such as China,^{76 77} the reported prevalence of PLWH with PTSD
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42 was lower compared to higher-income countries. The differences between collectivism
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44 and individualism rooted in eastern and western culture may be an explanation.⁷⁸ It is
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46 worth noting that social context may not only influence the susceptibility of mental
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5 health disorders, but it also constitutes an important factor in perceived stigma among
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7 individuals with mental illness. Compared to high-income countries,
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10 stigmatization-beliefs about the causes and presence of mental illness are still
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13 widespread in low- and middle-income countries,^{79 80} which may lead to less disease
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15 reporting. Caution must be applied, since there is a lack of studies investigating
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18 HIV-related PTSD in lower- (n=4) and middle-income (n=8) countries. In particular,
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21 detection of prevalence is associated with the representativeness and size of sample. In
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24 the context of low- and middle-income countries, it could be argued that lower HIV
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26 testing rate may underestimate the PTSD prevalence and impact generalizability. Thus,
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29 more epidemiological studies are warranted to better understanding and clarify the
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32 difference in PTSD prevalence among PLWH globally.

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

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5 PTSD, in which being female is a risk factor associated with PTSD development.¹⁶ The
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7 findings that MSM and female HIV-infected individuals are at higher risk of developing
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9 PTSD may indicate that related health promotion campaigns should be directed to these
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11 groups. Clinicians should also take into consideration the PTSD susceptibility in
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13 different groups of HIV-infected populations during diagnoses as well. Notably, most
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15 eligible studies did not provide separate prevalence rates regarding the gender of
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17 participants, and only 3 studies identified PTSD prevalence among MSM living with
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19 HIV. Given that these data are from a small number of studies and/or participants, this
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21 finding should be interpreted with caution. Nonetheless, given the high prevalence of
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23 PTSD in this group, future efforts should be made to obtain more prevalence data on
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25 PTSD among MSM.
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34 In our study, we assessed methodological differences that may result in
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36 heterogeneity. Factors including sampling strategies (convenience vs consecutive) and
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38 measurement (self-report vs clinical interview) were evaluated by subgroup analyses.
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40 Among 34 studies providing estimated prevalence of PTSD, 7 reported participants
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42 were consecutively enrolled via self-referral from flyers describing the study or
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44 advertisements from HIV health care providers, and generated a lower pooled
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46 prevalence rate (17%) compared with the other 18 studies using convenience sampling
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48 (31%), though both sampling methods were non-probabilistic. An increase in reporting
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50 rate due to convenience sampling has also been found in another meta-analysis
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52 synthesizing the HCV seroconversion rates in HIV-positive MSM.⁸³ Convenience
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5 samples may allow researchers to select participants who are more likely to have PTSD
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7 symptoms and lead to over-estimation, but given that only 4 studies were rated as high
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9 quality and limited description of study methods was detected in some studies, the
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11 reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the
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13 appropriateness of calculating pooled prevalence estimates could be questioned, and the
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15 pooled prevalence estimate regarding varied recruitment approaches of the studies
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17 should be interpreted with caution.
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23 In this review, a total of 14 different tools were used to assess PTSD symptoms
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25 among PLWH across studies. Overall, the rate of PTSD screened by self-report
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27 instruments (29%) was higher than that assessed by clinical interview (22%). Though
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29 both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD),
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31 clinical interviews most likely do a much better job of assessing symptoms carefully –
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33 for example, not counting symptoms that do not meet clinically meaningful thresholds,
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35 and self-report measures may inflate the prevalence estimates;⁸⁴ alternatively, subjects
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37 may be more comfortable reporting symptoms using self-report questionnaires
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39 (presumably paper or online surveys rather than face-to-face interviews). Screening or
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41 diagnosing with survey instruments is a common and practical method, especially in
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43 resource-limited regions. We found that, though a number of PTSD measures have been
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45 used to assess PTSD among PLWH, there is no tool designed for this population
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47 specifically. As the sensitivity and specificity of the measures may impact accurate
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49 PTSD detection, further research is required to identify a standardized measure
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5 accordingly to improve validity.
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8 Certain limitations should be acknowledged in this meta-analysis. First, though
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10 minimal potential for publication bias was presumed as all data drawn for this review
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12 were from studies reporting estimated point prevalence without intervention,
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14 publication bias cannot be ruled out for there are a number of studies published in
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16 languages other than English and Chinese. Second, the heterogeneity was high in the
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18 whole sample and most subgroups. Considering the eligible studies included in this
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20 meta-analysis were from diverse sociodemographic backgrounds, we have analysed the
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22 influences of region, population group, recruitment venue, and measurement method,
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24 which explained parts of the heterogeneity. Third, though some studies have indicated
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26 that several sociodemographic factors such as age may be associated with PTSD
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28 incidence among PLWH, we were unable to conduct subgroup analyses stratified by age
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30 due to the lack of detailed information reported in the published studies. As the quality
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32 of reporting could increase the susceptibility to bias, it is imperative for the researchers
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34 to report their findings of observational studies in accordance with the appropriate
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36 guidelines, such as the STROBE checklist.
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46 **CONCLUSIONS**

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49 This review contributes to evidence on the quantitatively pooled prevalence of PTSD
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51 among PLWH. Stratified subgroups including geographic area, population group,
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53 sampling and measurement method were found to be significant factors accounting for
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55 the varied prevalence of PTSD among PLWH. More effective intervention strategies
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5 targeting PTSD among PLWH are urgently needed. Future efforts should be made to
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7 obtain countries' own PTSD prevalence data among PLWH as well as specific
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9 vulnerable minorities, which will provide a basis for public health policy, health-care
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11 planning, and resource allocation for PTSD intervention initiatives. Our study also
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13 suggests that more research using robust and comprehensive methodology is needed to
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15 provide rigorous evidence for designing the targeted psychological interventions.
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23 **Figure 1** Flow chart of study inclusion

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25 **Figure 2** Forest plot presenting the prevalence of PTSD in PLWH

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31 **Contributors:** Conception of the work: HW and CT. Systematic review and article
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33 evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT,
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35 LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision
36
37 of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the
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39 authors. All the authors fulfill the ICMJE criteria for authorship.
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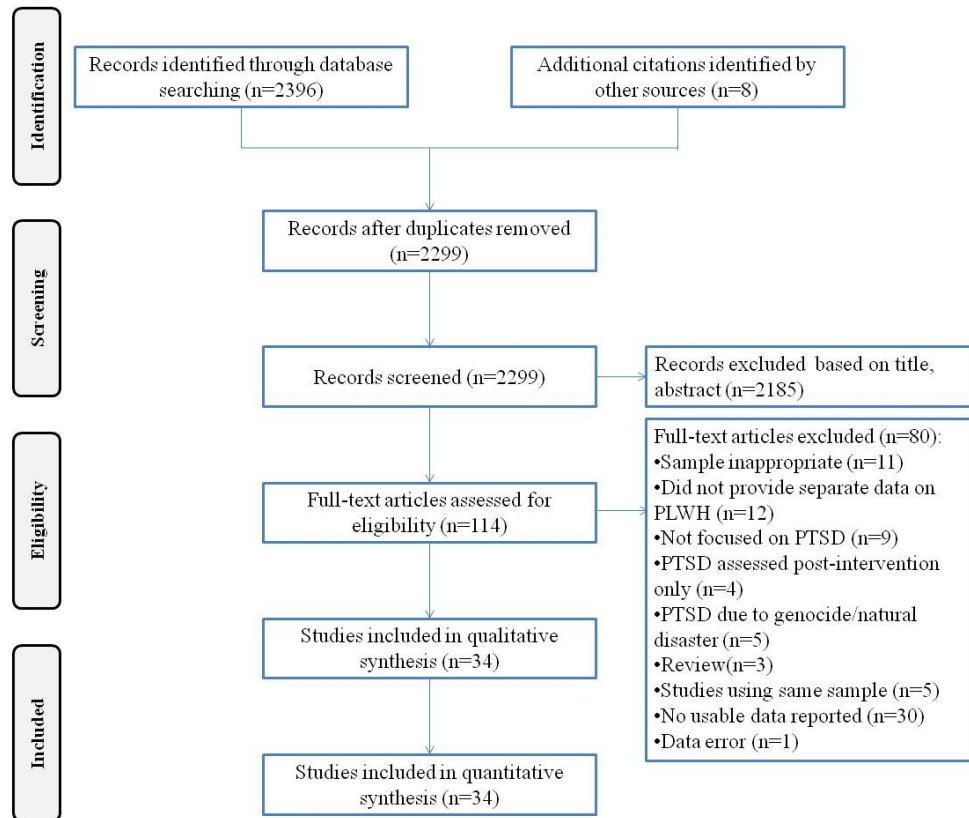


Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

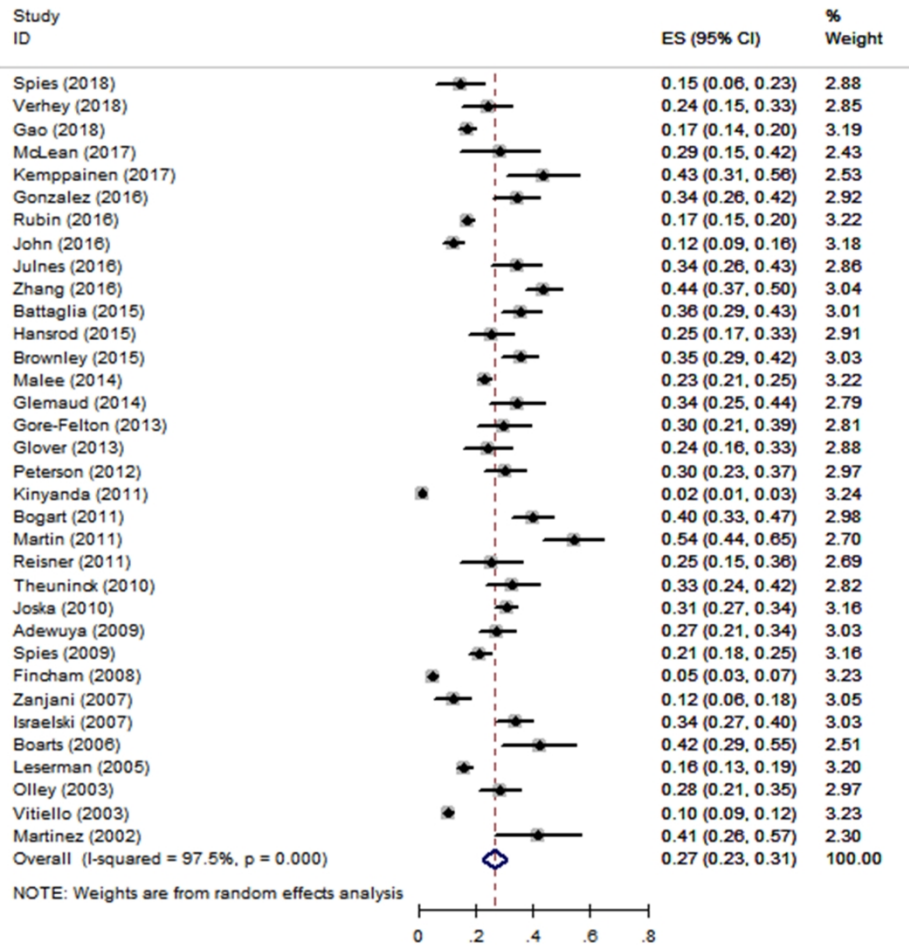


Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

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	
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	21-26	
· Potential biases in the review process (eg, publication bias)	26	
· Justification for exclusion (eg, exclusion of non-English-language citations)	-	
· Assessment of quality of included studies	25	
· 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)	26	
· Guidelines for future research	26,27	
· Disclosure of funding source	27	

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

Authors:

1. Chulei TANG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

ORCID: 0000-0003-3178-5130

2. Lloyd A Goldsamt, PhD, Senior Research Scientist

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

3. Jingjing MENG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

4. Xueling XIAO, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

5. Li ZHANG, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

6. Ann Bartley Williams, PhD, Professor

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

7. Honghong WANG, RN, MSN, PhD, Professor

Xiangya School of Nursing, Central South University, Changsha, China.

1
2
3
4 **Corresponding author**
5

6 Honghong WANG
7

8 Xiangya School of Nursing, Central South University
9

10 172 Tongzipo road, Changsha 410013, Hunan, China
11

12
13 Email: honghong_wang@hotmail.com
14

15 Telephone number: 0731-82650270
16

17 Fax number: 0731-82650270
18
19

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5 **A global estimate of the prevalence of posttraumatic stress disorder among adults**
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7 **living with HIV: A systematic review and meta-analysis**
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13 **ABSTRACT**
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15 **Objectives** Although people living with HIV (PLWH) have been disproportionately
16 affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among
17 PLWH is unknown. This study aimed to systematically review the prevalence of PTSD
18 among PLWH worldwide and explore variation in prevalence across sociodemographic
19 and methodological factors.
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28 **Design** A meta-analysis using a random-effect model was conducted to pool the
29 prevalence estimated from individual studies, and subgroup analyses were used to
30 analyze heterogeneities.
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36 **Setting, participants and measures** Observational studies providing PTSD prevalence
37 data in an adult HIV population were searched from January 2000 to November 2019.
38 Measurements were not restricted, although the definition of PTSD had to align with the
39 Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International
40 Classification of Diseases (ICD) diagnostic criteria.
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49 **Results** A total of 38 articles were included among 2406 records identified initially. The
50 estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant
51 heterogeneity was detected in the proportion of PLWH who reported PTSD across
52 studies, which was partially explained by geographic area, population group,
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5 measurement and sampling method ($p<0.05$).
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7 **Conclusion** PTSD among PLWH is common worldwide. This review highlights that
8 PTSD should be routinely screened for and that more effective prevention strategies and
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10 PTSD should be routinely screened for and that more effective prevention strategies and
11
12 treatment packages targeting PTSD are needed in PLWH.
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17 **Strengths and limitations of this study**

- 18 ● This is the first meta-analysis providing comprehensive assessment on the
19 prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
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21 ● Several subgroup analyses were conducted to examine the influence of diverse
22 sociodemographic backgrounds as well as methodological heterogeneity.
23
24 ● This review was conducted with specific definitions of PTSD as part of the
25 inclusion criteria to help in acquiring high level of evidence, which also limited the
26 number of eligible studies.
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28 ● A lack of studies carried out on the topic in low-income and middle-income
29 countries could underestimate the burden of HIV-PTSD prevalence of the world.
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31 ● We did not undertake a search of grey literature, restricting our sample to articles
32 published in peer-reviewed journals.
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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

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5 and costly health problem in the general population is well recognized, and not only
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8 impairs a person's physical health, but also greatly influences social functioning.¹¹ The
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11 co-occurrence of PTSD and HIV-infection creates even more challenges regarding both
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13 the treatment of PTSD and the management of HIV. PTSD can negatively impact
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15 medication adherence and impair immune functioning,¹²⁻¹⁵ both of which are especially
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17 critical for PLWH. HIV-infected patients with PTSD have been found to be at increased
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19 risk of somatization and physical disorders.¹⁶ The illness experience of PTSD, such as
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21 persistent avoidance and re-experiencing the traumatic event, may also compromise
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23 quality of life and cause significant distress in PLWH.^{7 17} Subsequently, prolonged and
24
25 untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.¹⁸ There
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27 is also evidence suggesting that reductions in PTSD symptom severity are related to
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29 improved HIV-risk related outcomes.¹⁹ Given that PTSD elevates HIV-risk behaviors²⁰
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31 and the possibility of HIV transmission also increases along with disease progression,
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39 PLWH suffering from PTSD are an important group to understand and with whom to
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43 intervene.

44 Valid data on PTSD prevalence rates among PLWH is essential. Evidence on the
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46 extent of PTSD among PLWH is needed to raise awareness and recommend clinical
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48 management. Although a number of studies have investigated the prevalence of PTSD
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50 in PLWH, findings have been inconsistent.²² While studies have reported varied
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52 incidence, few efforts have been made to aggregate existing research using meta-
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54 analysis techniques. There was one published meta-analysis estimating the pooled
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5 prevalence of PTSD among women living with HIV in 2012.²³ But the lack of studies
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8 with other groups lowered the generalizability and global relevance of their findings.
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10 Moreover, the meta-analysis was conducted in 2012, and the increase of publications
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12 about PTSD among PLWH since then²⁴⁻²⁶ suggests that a timely update is urgently
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15 needed. Indeed, several reviews provide a useful overview of the possible prevalence of
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17 PTSD among PLWH;²²⁻²⁷ however, a number of gaps remain. First, to date, there has
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20 been no attempt to achieve a better understanding of the epidemiology of PTSD in
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23 PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second,
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25 economically and politically, while precise estimates of prevalence can support efficient
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27 allocation of resources, factors that might influence PTSD prevalence rates, such as
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30 population characteristics and socio-cultural context have been neglected.
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34 Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the
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36 worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in
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39 PLWH differs based between population groups, country income groups and study
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42 characteristics. This information can then be used to inform further practice and
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45 research for this highly co-morbid group.

46 **METHODS**

47 **Search strategy**

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50 Systematic searches were conducted through 5 electronic English databases (Medline,
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53 Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases
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56 (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence
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5 among PLWH from January 2000 to November 2019. The search terms were:
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7 posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV,
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9 acquired immunodeficiency syndrome, AIDS, OR PLWH\$; AND epidemiology,
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11 occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the
12
13 precise search strategy). The reference lists of review articles and retrieved full-text
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15 articles were also examined for additional papers that were eligible for this review.
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20 21 **Eligibility criteria**

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23 Studies were included for this meta-analysis if they met the following predetermined
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25 selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2)
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27 observational study where prevalence figures for PTSD were stated or can be calculated
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29 in an adult HIV population; and (3) underlined that PTSD cases were identified in
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31 accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or
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33 the International Classification of Diseases (ICD) diagnostic criteria.^{28 29} Studies were
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35 excluded if (1) they only recruited those who had mental distress; (2) they specifically
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37 targeted only youth under 18 or children affected by HIV. No restriction was applied
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39 regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed
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41 closely, and if repeated data were observed, only the earlier publication with one set of
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43 complete data was included.
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50 51 **Data extraction and analysis**

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53 Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.)
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55 following PRISMA recommendations. C.T and X.X. searched the English papers and
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5 J.M. screened the Chinese language papers. After duplicates were deleted, each
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7 investigator read titles and abstracts closely to capture all potential studies. Full-text
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9 articles were obtained and reviewed for all criteria. Any discrepancies were resolved by
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11 discussion with the research team. The PRISMA flow chart shows the results of the
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13 systematic search (figure 1)
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17 **Data extraction**

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19 Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data
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21 independently from included papers: first author, year of publication, country of study,
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23 sampling method, sample size, number of patients with PTSD, measurements and
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25 outcome data. The third investigator (H.W.) helped to verify all extracted data and
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27 resolve any uncertainties. To facilitate detection of sample/methodological
28
29 heterogeneity, countries were categorized according to their income level, and
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31 measurements were classified into diagnostic questionnaire and clinical interview based
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33 on the approach to diagnosing PTSD. Selection bias was examined by reviewing the
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35 articles included in the meta-analysis to ensure they met eligibility criteria. Gender and
36
37 sexual orientation were considered because of underlying differences in the epidemics
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39 of HIV and trauma.³⁰⁻³² Specifically, populations were grouped as women and men, and
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41 samples of HIV-infected men were further classified into men who have sex with men
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43 (MSM) and non-MSM males.
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53 **Assessment of methodological quality**

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55 We used the quality assessment forms for cross-sectional/prevalence studies
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5 recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ)³³ to
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7 assess the reliability of the eligible studies. The checklist included 11 items. Each item
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9 was coded with a “Yes/No/Unclear”: “No” or “Unclear” was scored “0”, and “Yes” was
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11 scored “1”. Consistent with previous meta-analyses studies using the AHRQ
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13 assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low
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15 quality, respectively.
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21 **Meta-analysis**

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23 In this study, all statistical analyses were performed using Stata 12.0 software (STATA
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25 Corporation, College Station, TX)³⁴. Heterogeneity was tested and quantified by the
26
27 chi-square Q statistic and the I^2 statistic. The prevalence rates of PTSD among PLWH
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29 were combined and reported as proportions with corresponding 95% Confidence
30
31 Intervals (CI). The pooled prevalence was estimated using a random-effects model
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33 when heterogeneity was statistically significant ($I^2 > 50\%$, $p \leq 0.10$). Otherwise, a fix-
34
35 effects model was conducted.³⁵ As sources of heterogeneity may arise from socio-
36
37 demographic and methodological factors, subgroup analyses were performed by
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39 dividing subgroups based on (1) economic levels of the study country, (2) gender/sexual
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41 orientation, (3) sampling method and (4) assessment method for PTSD, when enough
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43 data was available. Chi-square (χ^2) tests were further used to investigate whether there
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45 were significant differences between groups. We only performed these subgroup
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47 analyses when data were extractable and sufficient. Separate sensitivity analyses were
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49 used for studies with low quality to examine the stability of the pooled prevalence.
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5 Publication bias was assessed using the Egger's and the Begg's tests.³⁶⁻³⁷ Significance
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7 level of p values < 0.05 were employed for all analyses.
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10 **Patient and public involvement**

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12 Patients and the public were not involved in this study.
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15 **Ethics approval**

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17 As this study is a systematic review based on published studies, ethical approval is not
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19 required.
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23 **RESULTS**

24 **Search results**

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

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5 Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a
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7 generally moderate to high level of data quality (online supplementary appendix 2).
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10 Table 1 shows the characteristics of the included studies. These studies were published
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12 between 2002⁷² and 2019.³⁸ Geographically, over half (n=21, 55.3%) of the 38 included
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14 studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China
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16 (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income
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18 countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%),
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20 Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured
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22 PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%)
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24 conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not
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26 report their sampling methods, convenience sampling methods were adopted in most
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28 studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability
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30 sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41
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32 to 1489), of which 2742 were identified with PTSD.
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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

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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
Dévioux ⁵⁴	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate

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

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5 Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV
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8 diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV
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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 ($p \leq 0.001$, $I^2=98.1\%$) 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

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5 20% (95%CI: 17% to 23%), respectively. Also, studies conducted with convenience
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7 sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI
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9 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to
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11 24%).
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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%		

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

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5 with HIV/AIDS. Therefore, the results of our study significantly underscore the
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7 importance of early assessment and trauma-directed psychological interventions for
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10 PLWH.
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13 Undoubtedly, heterogeneity between studies is expected in such a relatively large
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15 topic of review. In this review, the estimated PTSD prevalence rates in PLWH varied
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17 widely (1.6%-54.1%) across studies and countries, which is also a common problem in
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19 the epidemiology of psychological and mental health disorders.^{78 79} Consistent with the
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21 findings of previous research,⁵⁹ the majority of studies which have determined the
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23 incidence of HIV-related PTSD have been conducted in developed countries (n=23).
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25 Compared with lower-income countries, higher-income countries reported relatively
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27 higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among
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29 PLWH may be explained by the cross-cultural differences in attitudes towards HIV
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31 infection. Turan et al.⁸⁰ found that the level of perceived HIV-related stigma in the
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33 community experienced by PLWH may cause adverse health and psychosocial
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35 outcomes. Social isolation and stigma might exacerbate symptoms of PTSD.⁸¹ In high-
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37 income countries, PLWH may experience “compound” or “layered” stigma, where
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39 stigmatizing beliefs are not only associated with HIV infection but also related to sexual
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41 orientation, commercial sexual behaviors, etc.⁸² Although, HIV-related stigma is highly
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43 burdensome in some mid-income countries, such as China,^{83 84} the reported prevalence
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45 of PLWH with PTSD was lower compared to higher-income countries. The differences
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47 between collectivism and individualism rooted in eastern and western culture may be an
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5 explanation.⁸⁵ It is worth noting that social context may not only influence the
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8 susceptibility of mental health disorders, but also constitutes an important factor in
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10 perceived stigma among individuals with mental illness. Compared to high-income
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12 countries, stigmatizing beliefs about the causes and presence of mental illness are still
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14 widespread in low- and middle-income countries,^{86 87} which may lead to less disease
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16 reporting. Caution must be applied, since there is a lack of studies investigating HIV-
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18 related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular,
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20 detection of prevalence is associated with the representativeness and size of sample. In
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22 the context of low- and middle-income countries, it could be argued that lower HIV
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24 testing rates may underestimate the PTSD prevalence and impact generalizability. Thus,
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26 more epidemiological studies are warranted to better understand and clarify the
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28 difference in PTSD prevalence among PLWH globally.
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36 Subgroup analyses indicated that the prevalence of PTSD differed significantly
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38 when gender and sexual orientation were taken into consideration. Specifically, women
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40 living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both
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42 MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence
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44 in PTSD, in which being female is a risk factor associated with PTSD development.¹⁶
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47 As suggested by the aforementioned findings, HIV-infected MSM may experience
48
49 higher levels of stigma and trauma related to their sexual orientation.^{30 88} Compared
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51 with heterosexual counterparts, MSM reported higher risk for suicidal ideation,⁸⁹ which
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53 also indicates greater psychological stress and mental health problems (i.e. PTSD and
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5 depression). The findings that MSM and female HIV-infected individuals are at higher
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7 risk of developing PTSD may indicate that related health promotion campaigns should
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9 be directed to these groups. Clinicians should also take into consideration the PTSD
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11 susceptibility in different groups of HIV-infected populations during diagnoses.
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15 Notably, most eligible studies did not provide separate prevalence rates regarding the
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17 gender of participants, and only 3 studies identified PTSD prevalence among MSM
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19 living with HIV. Given that these data are from a small number of studies and/or
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21 participants, this finding should be interpreted with caution. Nonetheless, given the high
22
23 prevalence of PTSD in this group, future efforts should be made to obtain more
24
25 prevalence data on PTSD among MSM living with HIV.
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31 In our study, we assessed methodological differences that may result in
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33 heterogeneity. Factors including sampling strategies (convenience vs consecutive) and
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35 measurement (self-report vs clinical interview) were evaluated by subgroup analyses.
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37 Among 38 studies providing estimated prevalence of PTSD, 7 reported participants
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39 were consecutively enrolled via self-referral from flyers describing the study or
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41 advertisements from HIV health care providers, and generated a lower pooled
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43 prevalence rate (17%) compared with the other 20 studies using convenience sampling
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45 (32%), though both sampling methods were non-probabilistic. An increase in reporting
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47 rate due to convenience sampling has also been found in another meta-analysis
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49 synthesizing the HCV seroconversion rates in HIV-positive MSM.⁹⁰ Convenience
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51 samples may allow researchers to select participants who are more likely to have PTSD
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5 symptoms and lead to over-estimation, but given that only 4 studies were rated as high
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7 quality and limited description of study methods was detected in some studies, the
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9 reporting of epidemiology may not be sufficient to draw conclusions. Therefore, the
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11 appropriateness of calculating pooled prevalence estimates could be questioned, and the
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13 pooled prevalence estimate regarding the varied recruitment approaches of the studies
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15 should be interpreted with caution.
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21 In this review, a total of 14 different tools were used to assess PTSD symptoms
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23 among PLWH across studies. Overall, the prevalence rate of PTSD screened by self-
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25 report instruments (31%) was higher than that assessed by clinical interview (22%).
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27 Though both measurements were in accordance with the diagnostic criteria (i.e. DSM or
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29 ICD), clinical interviews most likely do a much better job of assessing symptoms
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31 carefully – for example, not counting symptoms that do not meet clinically meaningful
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33 thresholds, and self-report measures may inflate the prevalence estimates;⁹¹
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35 alternatively, subjects may be more comfortable reporting symptoms using self-report
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37 questionnaires (presumably paper or online surveys rather than face-to-face interviews).
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39 Screening or diagnosing with survey instruments is a common and practical method,
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41 especially in resource-limited regions. We found that, though a number of measures
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43 have been used to assess PTSD among PLWH, there is no tool designed for this
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45 population specifically. As the sensitivity and specificity of the measures may impact
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47 accurate PTSD detection, further research is required to identify a standardized measure
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49 accordingly to improve validity.
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5 Certain limitations should be acknowledged in this meta-analysis. First, though
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7 minimal potential for publication bias was presumed as all data drawn for this review
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9 were from studies reporting estimated point prevalence without intervention,
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11 publication bias cannot be ruled out for there are a number of studies published in
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13 languages other than English and Chinese. Second, the heterogeneity was high in the
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15 whole sample and most subgroups. Heterogeneity importantly influences the reliability
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17 and accuracy of a meta-analysis, and only careful selection of appropriate studies is the
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19 reliable method for acquiring correct inferences.⁹² Even though strict eligibility criteria
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21 were employed in addressing HIV-PTSD prevalence in this study, it should be noted
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23 that getting HIV is only one possible traumatic event. This review suggests the need to
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25 consider traumatic experiences for further studies assessing PTSD among PLWH. In
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27 addition, we have analysed the influences of region, population group, recruitment
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29 venue, and measurement method, which explained some of the heterogeneity. However,
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31 the results should be interpreted with caution. Third, though some studies have
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33 indicated that several sociodemographic factors such as age may be associated with
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35 PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified
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37 by age due to the lack of detailed information reported in the published studies. As the
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39 quality of reporting could increase the susceptibility to bias, it is imperative for
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41 researchers to report their findings of observational studies in accordance with the
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43 appropriate guidelines, such as the STROBE checklist.
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56 CONCLUSIONS

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5 This review contributes to evidence on the quantitatively pooled prevalence of PTSD
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7 among PLWH. Stratified subgroups including geographic area, population group,
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9 sampling and measurement method were found to be significant factors accounting for
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11 the varied prevalence of PTSD among PLWH. More effective intervention strategies
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13 targeting PTSD among PLWH are urgently needed. Future efforts should be made to
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15 obtain countries' own PTSD prevalence data among PLWH as well as specific
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17 vulnerable minorities, which will provide a basis for public health policy, health-care
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19 planning, and resource allocation for PTSD intervention initiatives. Our study also
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21 suggests that more research using robust and comprehensive methodology is needed to
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23 provide rigorous evidence for designing the targeted psychological interventions.
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34 **Figure 1** Flow chart of study inclusion

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36 **Figure 2** Forest plot presenting the prevalence of PTSD in PLWH
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41 **Contributors:** Conception of the work: HW and CT. Systematic review and article
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43 evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT,
44
45 LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision
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47 of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the
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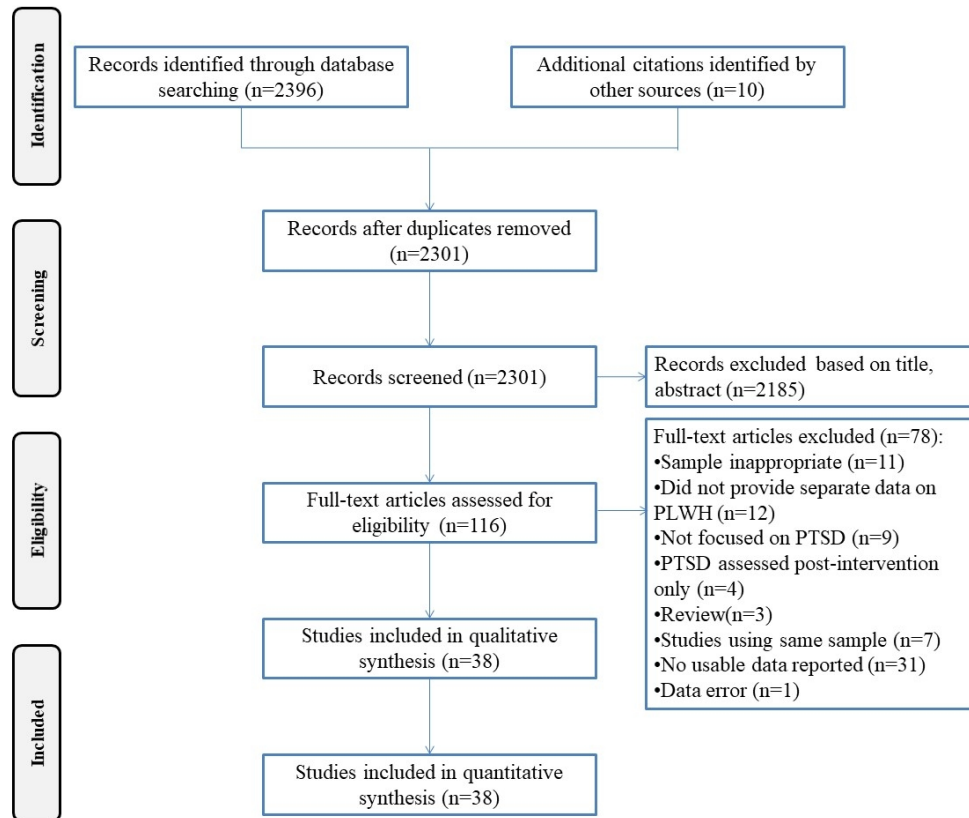


Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

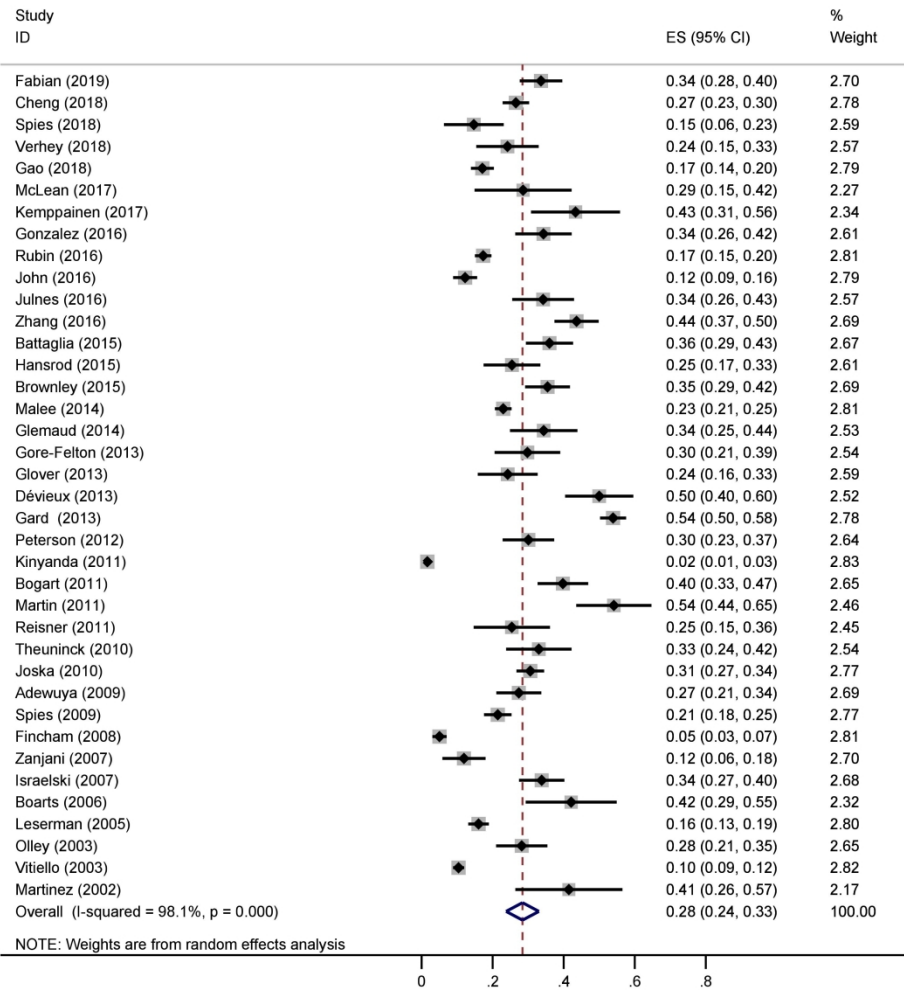


Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

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 immunodeficiency 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 immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency 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

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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	Dévioux 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	Theunink 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	

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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

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

Authors:

1. Chulei TANG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

ORCID: 0000-0003-3178-5130

2. Lloyd A Goldsamt, PhD, Senior Research Scientist

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

3. Jingjing MENG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

4. Xueling XIAO, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

5. Li ZHANG, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

6. Ann Bartley Williams, PhD, Professor

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

7. Honghong WANG, RN, MSN, PhD, Professor

Xiangya School of Nursing, Central South University, Changsha, China.

1
2
3
4 **Corresponding author**

5
6 Honghong WANG

7
8 Xiangya School of Nursing, Central South University

9
10 172 Tongzipo road, Changsha 410013, Hunan, China

11
12
13 Email: honghong_wang@hotmail.com

14
15 Telephone number: 0731-82650270

16
17 Fax number: 0731-82650270

18
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5 **A global estimate of the prevalence of posttraumatic stress disorder among adults**
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7 **living with HIV: A systematic review and meta-analysis**
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12
13 **ABSTRACT**
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15 **Objectives** Although people living with HIV (PLWH) have been disproportionately
16 affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among
17 PLWH is unknown. This study aimed to systematically review the prevalence of PTSD
18 among PLWH worldwide and explore variation in prevalence across sociodemographic
19 and methodological factors.
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28 **Design** A meta-analysis using a random-effect model was conducted to pool the
29 prevalence estimated from individual studies, and subgroup analyses were used to
30 analyse heterogeneities.
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36 **Setting, participants and measures** Observational studies providing PTSD prevalence
37 data in an adult HIV population were searched from January 2000 to November 2019.
38
39 Measurements were not restricted, although the definition of PTSD had to align with the
40 Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International
41 Classification of Diseases (ICD) diagnostic criteria.
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49 **Results** A total of 38 articles were included among 2406 records identified initially. The
50 estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant
51 heterogeneity was detected in the proportion of PLWH who reported PTSD across
52 studies, which was partially explained by geographic area, population group,
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5 measurement and sampling method ($p<0.05$).
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7 **Conclusion** PTSD among PLWH is common worldwide. This review highlights that
8 PTSD should be routinely screened for and that more effective prevention strategies and
9
10 PTSD should be routinely screened for and that more effective prevention strategies and
11
12 treatment packages targeting PTSD are needed in PLWH.
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17 **Strengths and limitations of this study**

- 18 ● This is the first meta-analysis providing comprehensive assessment on the
19 prevalence of posttraumatic stress disorder (PTSD) among adults living with HIV.
20
21 ● Several subgroup analyses were conducted to examine the influence of diverse
22 sociodemographic backgrounds as well as methodological heterogeneity.
23
24 ● This review was conducted with specific definitions of PTSD as part of the
25 inclusion criteria to help in acquiring high level of evidence, which also limited the
26 number of eligible studies.
27
28 ● A lack of studies carried out on the topic in low-income and middle-income
29 countries could underestimate the burden of HIV-PTSD prevalence of the world.
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31 ● We did not undertake a search of grey literature, restricting our sample to articles
32 published in peer-reviewed journals.
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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

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5 and costly health problem in the general population is well recognized, and not only
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8 impairs a person's physical health, but also greatly influences social functioning.¹¹ The
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10 co-occurrence of PTSD and HIV-infection creates even more challenges regarding both
11
12 the treatment of PTSD and the management of HIV. PTSD can negatively impact
13
14 medication adherence and impair immune functioning,¹²⁻¹⁵ both of which are especially
15
16 critical for PLWH. HIV-infected patients with PTSD have been found to be at increased
17
18 risk of somatization and physical disorders.¹⁶ The illness experience of PTSD, such as
19
20 persistent avoidance and re-experiencing the traumatic event, may also compromise
21
22 quality of life and cause significant distress in PLWH.^{7 17} Subsequently, prolonged and
23
24 untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.¹⁸ There
25
26 is also evidence suggesting that reductions in PTSD symptom severity are related to
27
28 improved HIV-risk related outcomes.¹⁹ Given that PTSD elevates HIV-risk behaviors²⁰
29
30 and the possibility of HIV transmission also increases along with disease progression,
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32 PLWH suffering from PTSD are an important group to understand and with whom to
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34 intervene.
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44 Valid data on PTSD prevalence among PLWH is essential. Evidence on the extent
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46 of PTSD among PLWH is needed to raise awareness and recommend clinical
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48 management. Although a number of studies have investigated the prevalence of PTSD
49
50 in PLWH, findings have been inconsistent.²² While studies have reported varied
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52 incidence, few efforts have been made to aggregate existing research using meta-
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54 analysis techniques. There was one published meta-analysis estimating the pooled
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5 prevalence of PTSD among women living with HIV in 2012.²³ But the lack of studies
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8 with other groups lowered the generalizability and global relevance of their findings.
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10 Moreover, the meta-analysis was conducted in 2012, and the increase of publications
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12 about PTSD among PLWH since then²⁴⁻²⁶ suggests that a timely update is urgently
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15 needed. Indeed, several reviews provide a useful overview of the possible prevalence of
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17 PTSD among PLWH;²²⁻²⁷ however, a number of gaps remain. First, to date, there has
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20 been no attempt to achieve a better understanding of the epidemiology of PTSD in
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23 PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second,
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25 economically and politically, while precise estimates of prevalence can support efficient
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27 allocation of resources, factors that might influence PTSD prevalence, such as
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30 population characteristics and socio-cultural context have been neglected.
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34 Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the
35
36 worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in
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39 PLWH differs based between population groups, country income groups and study
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41 characteristics. This information can then be used to inform further practice and
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44 research for this highly co-morbid group.
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46 **METHODS**

47 **Search strategy**

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49 Systematic searches were conducted through 5 electronic English databases (Medline,
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52 Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases
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55 (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence
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5 among PLWH from January 2000 to November 2019. The search terms were:
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7 posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV,
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10 acquired immunodeficiency syndrome, AIDS, OR PLWH\$; AND epidemiology,
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12 occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the
13
14 precise search strategy). The reference lists of review articles and retrieved full-text
15
16 articles were also examined for additional papers that were eligible for this review.
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20 21 **Eligibility criteria**

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23 Studies were included for this meta-analysis if they met the following predetermined
24
25 selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2)
26
27 observational study where prevalence figures for PTSD were stated or can be calculated
28
29 in an adult HIV population; and (3) underlined that PTSD cases were identified in
30
31 accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or
32
33 the International Classification of Diseases (ICD) diagnostic criteria.^{28 29} Studies were
34
35 excluded if (1) they only recruited those who had mental distress; (2) they specifically
36
37 targeted only youth under 18 or children affected by HIV. No restriction was applied
38
39 regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed
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41 closely, and if repeated data were observed, only the earlier publication with one set of
42
43 complete data was included.
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50 51 **Data extraction and analysis**

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53 Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.)
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55 following PRISMA recommendations. C.T and X.X. searched the English papers and
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5 J.M. screened the Chinese language papers. After duplicates were deleted, each
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8 investigator read titles and abstracts closely to capture all potential studies. Full-text
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11 articles were obtained and reviewed for all criteria. Any discrepancies were resolved by
12
13 discussion with the research team. The PRISMA flow chart shows the results of the
14
15 systematic search (figure 1)
16

17 **Data extraction**

18
19
20 Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data
21
22
23 independently from included papers: first author, year of publication, country of study,
24
25
26 sampling method, sample size, number of patients with PTSD, measurements and
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29 outcome data. The third investigator (H.W.) helped to verify all extracted data and
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31
32 resolve any uncertainties. To facilitate detection of sample/methodological
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35 heterogeneity, countries were categorized according to their income level, and
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38 measurements were classified into diagnostic questionnaire and clinical interview based
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41 on the approach to diagnosing PTSD. To minimize selection bias, we reviewed the
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44 articles included in the meta-analysis to ensure they met eligibility criteria. Gender and
45
46
47 sexual orientation were considered because of underlying differences in the epidemics
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49
50 of HIV and trauma.³⁰⁻³² Specifically, populations were grouped as women and men, and
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53 samples of HIV-infected men were further classified into men who have sex with men
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56 (MSM) and non-MSM males.

54 **Assessment of methodological quality**

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57 We used the quality assessment forms for cross-sectional/prevalence studies
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5 recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ)³³ to
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7 assess the reliability of the eligible studies. The checklist included 11 items. Each item
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9 was coded with a “Yes/No/Unclear”: “No” or “Unclear” was scored “0”, and “Yes” was
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11 scored “1”. Consistent with previous meta-analysis studies using the AHRQ
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13 assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low
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15 quality, respectively.
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20 **Meta-analysis**

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23 In this study, all statistical analyses were performed using Stata 12.0 software (STATA
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25 Corporation, College Station, TX)³⁴. Heterogeneity was tested and quantified by the
26
27 chi-square Q statistic and the I^2 statistic. The prevalence of PTSD among PLWH were
28
29 combined and reported as proportions with corresponding 95% Confidence Intervals
30
31 (CI). The pooled prevalence was estimated using a random-effects model when
32
33 heterogeneity was statistically significant ($I^2 > 50\%$, $p \leq 0.10$). Otherwise, a fix-effects
34
35 model was used.³⁵ As sources of heterogeneity may arise from socio-demographic and
36
37 methodological factors, subgroup analyses were performed by (1) economic levels of
38
39 the study country, (2) gender/sexual orientation, (3) sampling method and (4)
40
41 assessment method for PTSD, when enough data was available. Chi-square (χ^2) tests
42
43 were further used to investigate whether there were significant differences between
44
45 groups. We only performed these subgroup analyses when data were extractable and
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47 sufficient. Separate sensitivity analyses were used for studies with low quality to
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49 examine the stability of the pooled prevalence. Publication bias was assessed using the
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5 Egger's and the Begg's tests.³⁶⁻³⁷ Significance level of p values < 0.05 were employed
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7
8 for all analyses.

9 10 **Patient and public involvement**

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12 Patients and the public were not involved in this study.

13 14 15 **Ethics approval**

16
17
18 As this study is a systematic review based on published studies, ethical approval is not
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20
21 required.

22 23 **RESULTS**

24 25 **Search results**

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28 A total of 2396 records were identified by the electronic bibliographic database
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31 searches. Ten additional manuscripts were identified through other sources (e.g.,
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34 reference lists of review papers). From an initial screen of 2301 records after duplicates
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37 were removed, 2185 records were excluded on basis of title or abstract because those
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40 studies were not relevant to this review ($n=2107$) or were reviews/commentary ($n= 78$).
41
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43 The remaining 116 full articles were selected for the eligibility assessment. Of those, 7
44
45
46 were excluded for repeated data, 9 were excluded for targeting PLWH who received
47
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49 psychological intervention or suffered from genocide/natural disaster, and 62 were
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52 excluded for not reporting the PTSD prevalence among PLWH. Finally, a total of 38
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55 studies^{14 24 25 38-72} met inclusion criteria and were included in this meta-analysis. Search
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58 results are elaborated in Figure 1.

59 60 **Study characteristics**

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5 Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a
6
7 generally moderate to high level of data quality (online supplementary appendix 2).
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10 Table 1 shows the characteristics of the included studies. These studies were published
11
12 between 2002⁷² and 2019.³⁸ Geographically, over half (n=21, 55.3%) of the 38 included
13
14 studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China
15
16 (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income
17
18 countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%),
19
20 Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured
21
22 PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%)
23
24 conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not
25
26 report their sampling methods, convenience sampling methods were adopted in most
27
28 studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability
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30 sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41
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32 to 1489), of which 2742 were identified with PTSD.
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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

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5	John ⁴⁵	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
6									
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8	Julnes ¹⁴	2016	USA	convenience sampling	114	39	CDQ	self-report questionnaire	moderate
9									
10									
11	Zhang ⁴⁶	2016	China	convenience sampling	243	106	PCL-C	self-report questionnaire	low
12									
13									
14									
15	Battaglia ⁴⁷	2015	USA	convenience sampling	200	72	PTSD checklist	self-report questionnaire	moderate
16									
17									
18	Hansrod ⁴⁸	2015	South Africa	convenience sampling	114	29	MINI	clinical interview	moderate
19									
20									
21	Brownley ⁴⁹	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
22									
23									
24	Malee ⁵⁰	2014	USA	convenience sampling	1223	281	CDQ	self-report questionnaire	high
25									
26									
27									
28	Glémaud ⁵¹	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
29									
30									
31	Gore-Felton ⁵²	2013	USA	convenience sampling	94	28	PCL-C	self-report questionnaire	low
32									
33									
34	Glover ⁵³	2013	USA	convenience sampling	99	24	PDS	self-report questionnaire	high
35									
36									
37	Dévioux ⁵⁴	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate
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5	Gard ⁵⁵	2013	Rwanda	unclear	705	380	HTS	self-report questionnaire	moderate
6									
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8	Peterson ⁵⁶	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
9									
10									
11	Kinyanda ⁵⁷	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
12									
13									
14									
15	Bogart ⁵⁸	2011	USA	convenience sampling	181	72	PDS	self-report questionnaire	moderate
16									
17									
18	Martin ⁵⁹	2011	UK	convenience sampling	85	46	CIDI	clinical interview	moderate
19									
20									
21	Reisner ⁶⁰	2011	USA	convenience sampling	63	16	AUDADIS-IV	clinical interview	moderate
22									
23									
24	Theuninck ⁶¹	2010	UK	convenience sampling	100	33	PCL-C	self-report questionnaire	low
25									
26									
27									
28	Joska ⁶²	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
29									
30									
31	Adewuya ⁶³	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
32									
33									
34	Spies ⁶⁴	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
35									
36									
37	Fincham ⁶⁵	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate
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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

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5 Interview; *IES-R* Impact of Event Scale-Revised; *HTS* the Harvard trauma scale; *DIS-IV* Diagnostic Interview Schedule for DSM-IV
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7
8 diagnoses; *PTSD checklist* Posttraumatic Stress Disorder Checklist; *CIDI* Clinical Interview for Diagnosis for DSM-IV
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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 ($p \leq 0.001$, $I^2=98.1\%$) 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%

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5 (95%CI: 17% to 23%), respectively. Also, studies conducted with convenience
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8 sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI
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10 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to
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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%		

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

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5 with HIV/AIDS. Therefore, the results of our study significantly underscore the
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7 importance of early assessment and trauma-directed psychological interventions for
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9 PLWH.
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13 Undoubtedly, heterogeneity between studies is expected in such a relatively large
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15 topic of review. In this review, the estimated PTSD prevalence in PLWH varied widely
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17 (1.6%-54.1%) across studies and countries, which is also a common problem in the
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19 epidemiology of psychological and mental health disorders.^{78 79} Consistent with the
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21 findings of previous research,⁵⁹ the majority of studies which have determined the
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23 incidence of HIV-related PTSD have been conducted in developed countries (n=23).
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25 Compared with lower-income countries, higher-income countries reported relatively
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27 higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among
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29 PLWH may be explained by the cross-cultural differences in attitudes towards HIV
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31 infection. Turan et al.⁸⁰ found that the level of perceived HIV-related stigma in the
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33 community experienced by PLWH may cause adverse health and psychosocial
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35 outcomes. Social isolation and stigma might exacerbate symptoms of PTSD.⁸¹ In high-
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37 income countries, PLWH may experience “compound” or “layered” stigma, where
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39 stigmatizing beliefs are not only associated with HIV infection but also related to sexual
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41 orientation, commercial sexual behaviors, etc.⁸² Although, HIV-related stigma is highly
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43 burdensome in some mid-income countries, such as China,^{83 84} the reported prevalence
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45 of PLWH with PTSD was lower compared to higher-income countries. The differences
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47 between collectivism and individualism rooted in eastern and western culture may be an
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5 explanation.⁸⁵ It is worth noting that social context may not only influence the
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8 susceptibility of mental health disorders, but also constitutes an important factor in
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10 perceived stigma among individuals with mental illness. Compared to high-income
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12 countries, stigmatizing beliefs about the causes and presence of mental illness are still
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14 widespread in low- and middle-income countries,^{86 87} which may lead to less disease
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16 reporting. Caution must be applied, since there is a lack of studies investigating HIV-
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18 related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular,
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20 detection of prevalence is associated with the representativeness and size of sample. In
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22 the context of low- and middle-income countries, it could be argued that lower HIV
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24 testing rates may underestimate the PTSD prevalence and impact generalizability. Thus,
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26 more epidemiological studies are warranted to better understand and clarify the
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28 difference in PTSD prevalence among PLWH globally.
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36 Subgroup analyses indicated that the prevalence of PTSD differed significantly
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38 when gender and sexual orientation were taken into consideration. Specifically, women
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40 living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both
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42 MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence
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44 in PTSD, in which being female is a risk factor associated with PTSD development.¹⁶
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47 As suggested by the aforementioned findings, HIV-infected MSM may experience
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49 higher levels of stigma and trauma related to their sexual orientation.^{30 88} Compared
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51 with heterosexual counterparts, MSM reported higher risk for suicidal ideation,⁸⁹ which
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53 also indicates greater psychological stress and mental health problems (i.e. PTSD and
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5 depression). The findings that MSM and female HIV-infected individuals are at higher
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7 risk of developing PTSD may indicate that related health promotion campaigns should
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9 be directed to these groups. Clinicians should also take into consideration the PTSD
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11 susceptibility in different groups of HIV-infected populations during diagnoses.
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15 Notably, most eligible studies did not provide separate the prevalence regarding the
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17 gender of participants, and only 3 studies identified PTSD prevalence among MSM
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19 living with HIV. Given that these data are from a small number of studies and/or
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21 participants, this finding should be interpreted with caution. Nonetheless, given the high
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23 prevalence of PTSD in this group, future efforts should be made to obtain more
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25 prevalence data on PTSD among MSM living with HIV.
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31 In our study, we assessed methodological differences that may result in
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33 heterogeneity. Factors including sampling strategies (convenience vs consecutive) and
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35 measurement (self-report vs clinical interview) were evaluated by subgroup analyses.
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37 Among 38 studies providing estimated prevalence of PTSD, 7 reported participants
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39 were consecutively enrolled via self-referral from flyers describing the study or
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41 advertisements from HIV health care providers, and generated a lower pooled rate
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43 (17%) compared with the other 20 studies using convenience sampling (32%), though
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45 both sampling methods were non-probabilistic. An increase in reporting rate due to
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47 convenience sampling has also been found in another meta-analysis synthesizing the
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49 HCV seroconversion rates in MSM living with HIV.⁹⁰ Convenience samples may allow
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51 researchers to select participants who are more likely to have PTSD symptoms and lead
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5 to over-estimation, but given that only 4 studies were rated as high quality and limited
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7 description of study methods was detected in some studies, the reporting of
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9 epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness
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11 of calculating pooled prevalence estimates could be questioned, and the pooled
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13 prevalence estimate regarding the varied recruitment approaches of the studies should
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15 be interpreted with caution.
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21 In this review, a total of 14 different tools were used to assess PTSD symptoms
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23 among PLWH across studies. Overall, the prevalence of PTSD screened by self-report
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25 instruments (31%) was higher than that assessed by clinical interview (22%). Though
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27 both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD),
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29 clinical interviews most likely do a much better job of assessing symptoms carefully –
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31 for example, not counting symptoms that do not meet clinically meaningful thresholds,
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33 and self-report measures may inflate the prevalence estimates;⁹¹ alternatively, subjects
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35 may be more comfortable reporting symptoms using self-report questionnaires
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37 (presumably paper or online surveys rather than face-to-face interviews). Screening or
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39 diagnosing with survey instruments is a common and practical method, especially in
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41 resource-limited regions. We found that, though a number of measures have been used
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43 to assess PTSD among PLWH, there is no tool designed for this population specifically.
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45 As the sensitivity and specificity of the measures may impact accurate PTSD detection,
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47 further research is required to identify a standardized measure accordingly to improve
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49 validity.
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5 Certain limitations should be acknowledged in this meta-analysis. First, though
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7 minimal potential for publication bias was presumed as all data drawn for this review
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9 were from studies reporting estimated point prevalence without intervention,
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11 publication bias cannot be ruled out for there are a number of studies published in
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13 languages other than English and Chinese that were not included in this review. Second,
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15 the heterogeneity was high in the whole sample and most subgroups. Heterogeneity
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17 importantly influences the reliability and accuracy of a meta-analysis, and the only
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19 reliable method for acquiring correct inferences is careful selection of appropriate
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21 studies.⁹² Even though strict eligibility criteria were employed in addressing PTSD
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23 prevalence in this study, it should be noted that getting HIV is only one possible
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25 traumatic event, and therefore it is possible that the PTSD experienced by participants
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27 in the selected studies was due to an event other than finding out they were HIV
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29 positive. Accordingly, we suggests that further studies assessing PTSD among PLWH
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31 include more detail on the specific traumas experienced by study participants. In
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33 addition, we have analysed the influences of region, population group, recruitment
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35 venue, and measurement method, which explained some of the heterogeneity. However,
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37 the results should be interpreted with caution. Third, though some studies have
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39 indicated that several sociodemographic factors such as age may be associated with
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41 PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified
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43 by age due to the lack of detailed information reported in the published studies. As the
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45 quality of reporting could increase the susceptibility to bias, it is imperative for
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5 researchers to report their findings of observational studies in accordance with the
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7 appropriate guidelines, such as the STROBE checklist.
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10 **CONCLUSIONS**

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12 This review contributes to evidence on the quantitatively pooled prevalence of PTSD
13 among PLWH. Stratified subgroups including geographic area, population group,
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15 sampling and measurement method were found to be significant factors accounting for
16
17 the varied prevalence of PTSD among PLWH. More effective intervention strategies
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19 targeting PTSD among PLWH are urgently needed. Future efforts should be made to
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21 obtain countries' own PTSD prevalence data among PLWH as well as specific
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23 vulnerable minorities, which will provide a basis for public health policy, health-care
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25 planning, and resource allocation for PTSD intervention initiatives. Our study also
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27 suggests that more research using robust and comprehensive methodology is needed to
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29 provide rigorous evidence for designing the targeted psychological interventions.
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41 **Figure 1** Flow chart of study inclusion

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43 **Figure 2** Forest plot presenting the prevalence of PTSD in PLWH

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45 **Contributors:** Conception of the work: HW and CT. Systematic review and article
46
47 evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT,
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49 LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision
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51 of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the
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53 authors. All the authors fulfill the ICMJE criteria for authorship.
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14
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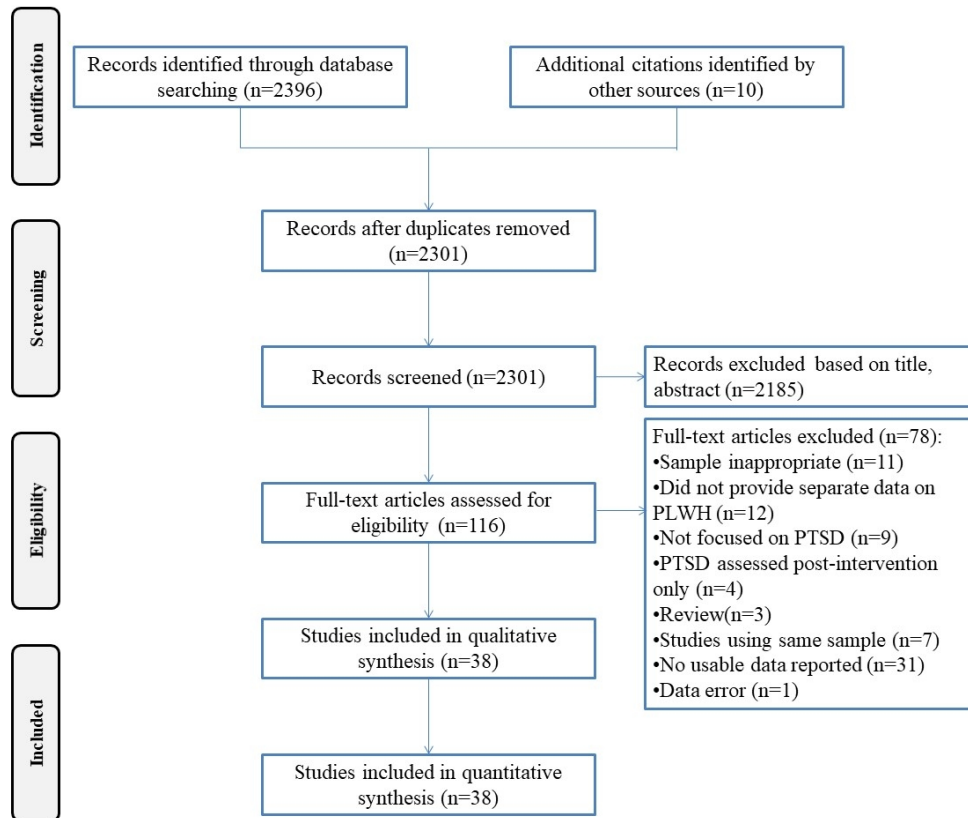


Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

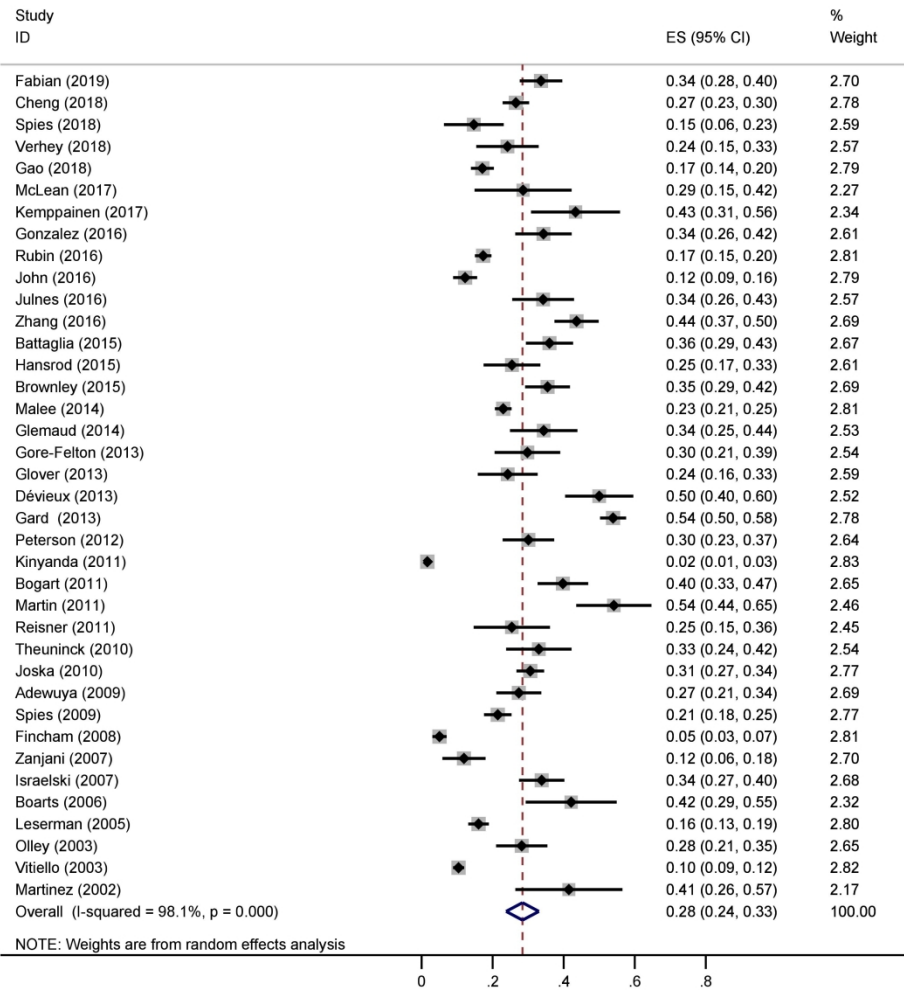


Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

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 immunodeficiency 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 immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency 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

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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	Dévioux 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	Theunink 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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Keywords:	Posttraumatic stress disorder, HIV/AIDS, Prevalence, 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

Authors:

1. Chulei TANG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

ORCID: 0000-0003-3178-5130

2. Lloyd A Goldsamt, PhD, Senior Research Scientist

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

3. Jingjing MENG, BSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

4. Xueling XIAO, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

5. Li ZHANG, MSN, RN

Xiangya School of Nursing, Central South University, Changsha, China

6. Ann Bartley Williams, PhD, Professor

Rory Meyers College of Nursing, New York University, 433 First Avenue, New York 10013, USA

7. Honghong WANG, RN, MSN, PhD, Professor

Xiangya School of Nursing, Central South University, Changsha, China.

1
2
3
4 **Corresponding author**
5

6 Honghong WANG
7

8 Xiangya School of Nursing, Central South University
9

10 172 Tongzipo road, Changsha 410013, Hunan, China
11

12
13 Email: honghong_wang@hotmail.com
14

15 Telephone number: 0731-82650270
16

17 Fax number: 0731-82650270
18
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20
21 **Keywords** Posttraumatic stress disorder, HIV/AIDS, Prevalence, Meta-analysis
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23 **Word count: 3674 words**
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5 **A global estimate of the prevalence of posttraumatic stress disorder among adults**
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7 **living with HIV: A systematic review and meta-analysis**
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13 **ABSTRACT**
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15 **Objectives** Although people living with HIV (PLWH) have been disproportionately
16 affected by posttraumatic stress disorder (PTSD), the global prevalence of PTSD among
17 PLWH is unknown. This study aimed to systematically review the prevalence of PTSD
18 among PLWH worldwide and explore variation in prevalence across sociodemographic
19 and methodological factors.
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28 **Design** A meta-analysis using a random-effect model was conducted to pool the
29 prevalence estimated from individual studies, and subgroup analyses were used to
30 analyse heterogeneities.
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36 **Setting, participants and measures** Observational studies providing PTSD prevalence
37 data in an adult HIV population were searched from January 2000 to November 2019.
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39 Measurements were not restricted, although the definition of PTSD had to align with the
40 Diagnostic and Statistical Manual of Mental Disorders (DSM) or the International
41 Classification of Diseases (ICD) diagnostic criteria.
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49 **Results** A total of 38 articles were included among 2406 records identified initially. The
50 estimated global prevalence of PTSD in PLWH was 28% (95% CI 24-33%). Significant
51 heterogeneity was detected in the proportion of PLWH who reported PTSD across
52 studies, which was partially explained by geographic area, population group,
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5 measurement and sampling method ($p<0.05$).
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7 **Conclusion** PTSD among PLWH is common worldwide. This review highlights that
8 PTSD should be routinely screened for and that more effective prevention strategies and
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10 PTSD should be routinely screened for and that more effective prevention strategies and
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12 treatment packages targeting PTSD are needed in PLWH.
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16 17 18 **Strengths and limitations of this study** 19

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

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5 and costly health problem in the general population is well recognized, and not only
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8 impairs a person's physical health, but also greatly influences social functioning.¹¹ The
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11 co-occurrence of PTSD and HIV-infection creates even more challenges regarding both
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13 the treatment of PTSD and the management of HIV. PTSD can negatively impact
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15 medication adherence and impair immune functioning,¹²⁻¹⁵ both of which are especially
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18 critical for PLWH. PLWH with PTSD have been found to be at increased risk of
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21 somatization and physical disorders.¹⁶ The illness experience of PTSD, such as
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24 persistent avoidance and re-experiencing the traumatic event, may also compromise
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27 quality of life and cause significant distress in PLWH.^{7 17} Subsequently, prolonged and
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30 untreated PTSD may lead to exacerbation of PTSD as well as HIV progression.¹⁸ There
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33 is also evidence suggesting that reductions in PTSD symptom severity are related to
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36 improved HIV-risk related outcomes.¹⁹ Given that PTSD elevates HIV-risk behaviors²⁰
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39 ²¹ and the possibility of HIV transmission also increases along with disease progression,
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42 PLWH suffering from PTSD are an important group to understand and with whom to
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45 intervene.

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

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5 prevalence of PTSD among women living with HIV in 2012.²³ But the lack of studies
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8 with other groups lowered the generalizability and global relevance of their findings.
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10 Moreover, the meta-analysis was conducted in 2012, and the increase of publications
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12 about PTSD among PLWH since then²⁴⁻²⁶ suggests that a timely update is urgently
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15 needed. Indeed, several reviews provide a useful overview of the possible prevalence of
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17 PTSD among PLWH;²²⁻²⁷ however, a number of gaps remain. First, to date, there has
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20 been no attempt to achieve a better understanding of the epidemiology of PTSD in
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23 PLWH and the reviews did not aim at an overall PTSD prevalence specifically. Second,
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25 economically and politically, while precise estimates of prevalence can support efficient
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27 allocation of resources, factors that might influence PTSD prevalence, such as
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30 population characteristics and socio-cultural context have been neglected.
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34 Therefore, to fill these knowledge gaps, we aimed to provide an estimate for the
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36 worldwide prevalence of PTSD in PLWH and to test whether PTSD prevalence in
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39 PLWH differs based between population groups, country income groups and study
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41 characteristics. This information can then be used to inform further practice and
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44 research for this highly co-morbid group.
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46 **METHODS**

47 **Search strategy**

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49 Systematic searches were conducted through 5 electronic English databases (Medline,
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52 Web of Science, CINAHL, EMBASE and Cochrane Library) and 3 Chinese databases
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55 (CNKI, Wanfang Database, Sinomed) to identify published studies on PTSD prevalence
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5 among PLWH from January 2000 to November 2019. The search terms were:
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7 posttrauma*, post trauma*, post-trauma*, stress disorder*, OR PTSD; AND HIV,
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9 acquired immunodeficiency syndrome, AIDS, OR PLWH\$; AND epidemiology,
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11 occurrence, incidence, OR prevalence (see online supplementary appendix 1 for the
12
13 precise search strategy). The reference lists of review articles and retrieved full-text
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15 articles were also examined for additional papers that were eligible for this review.
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20 21 **Eligibility criteria**

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23 Studies were included for this meta-analysis if they met the following predetermined
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25 selection criteria: (1) published in Chinese or English in a peer reviewed journal; (2)
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27 observational study where prevalence figures for PTSD were stated or can be calculated
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29 in an adult HIV population; and (3) underlined that PTSD cases were identified in
30
31 accordance with the Diagnostic and Statistical Manual of Mental Disorders (DSM) or
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33 the International Classification of Diseases (ICD) diagnostic criteria.^{28 29} Studies were
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35 excluded if (1) they only recruited those who had mental distress; (2) they specifically
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37 targeted only youth under 18 or children affected by HIV. No restriction was applied
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39 regarding gender, nationality, or sexual orientation. Additionally, articles were reviewed
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41 closely, and if repeated data were observed, only the earlier publication with one set of
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43 complete data was included.
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50 51 **Data extraction and analysis**

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53 Screening of papers was carried out by three of the authors (C.T., J.M. and X.X.)
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55 following PRISMA recommendations. C.T and X.X. searched the English papers and
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5 J.M. screened the Chinese language papers. After duplicates were deleted, each
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8 investigator read titles and abstracts closely to capture all potential studies. Full-text
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11 articles were obtained and reviewed for all criteria. Any discrepancies were resolved by
12
13 discussion with the research team. The PRISMA flow chart shows the results of the
14
15 systematic search (figure 1)
16

17 **Data extraction**

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19
20 Two authors (C.T. and X.X.) used a data extraction sheet to capture the following data
21
22
23 independently from included papers: first author, year of publication, country of study,
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25
26 sampling method, sample size, number of patients with PTSD, measurements and
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29 outcome data. The third investigator (H.W.) helped to verify all extracted data and
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31
32 resolve any uncertainties. To facilitate detection of sample/methodological
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35 heterogeneity, countries were categorized according to their income level, and
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38 measurements were classified into diagnostic questionnaire and clinical interview based
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41 on the approach to diagnosing PTSD. To minimize selection bias, we reviewed the
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44 articles included in the meta-analysis to ensure they met eligibility criteria. Gender and
45
46
47 sexual orientation were considered because of underlying differences in the epidemics
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50 of HIV and trauma.^{30–32} Specifically, populations were grouped as women and men, and
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53 samples of HIV-infected men were further classified into men who have sex with men
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56 (MSM) and non-MSM males.

54 **Assessment of methodological quality**

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57 We used the quality assessment forms for cross-sectional/prevalence studies
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5 recommended by the U.S. Agency for Healthcare Research and Quality (AHRQ)³³ to
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7 assess the reliability of the eligible studies. The checklist included 11 items. Each item
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9 was coded with a “Yes/No/Unclear”: “No” or “Unclear” was scored “0”, and “Yes” was
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11 scored “1”. Consistent with previous meta-analysis studies using the AHRQ
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13 assessments, a total score of 8-11, 4-7, and 0-3 indicated high, moderate and low
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15 quality, respectively.
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20 21 **Meta-analysis**

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23 In this study, all statistical analyses were performed using Stata 12.0 software (STATA
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25 Corporation, College Station, TX)³⁴. Heterogeneity was tested and quantified by the
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27 chi-square Q statistic and the I^2 statistic. The prevalence of PTSD among PLWH were
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29 combined and reported as proportions with corresponding 95% Confidence Intervals
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31 (CI). The pooled prevalence was estimated using a random-effects model when
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33 heterogeneity was statistically significant ($I^2 > 50\%$, $p \leq 0.10$). Otherwise, a fix-effects
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35 model was used.³⁵ As sources of heterogeneity may arise from socio-demographic and
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37 methodological factors, subgroup analyses were performed by (1) economic levels of
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39 the study country, (2) gender/sexual orientation, (3) sampling method and (4)
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41 assessment method for PTSD, when enough data was available. Chi-square (χ^2) tests
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43 were further used to investigate whether there were significant differences between
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45 groups. We only performed these subgroup analyses when data were extractable and
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47 sufficient. Separate sensitivity analyses were used for studies with low quality to
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49 examine the stability of the pooled prevalence. Publication bias was assessed using the
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5 Egger's and the Begg's tests.³⁶⁻³⁷ Significance level of p values < 0.05 were employed
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8 for all analyses.

9 10 **Patient and public involvement**

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12 Patients and the public were not involved in this study.

13 14 15 **Ethics approval**

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18 As this study is a systematic review based on published studies, ethical approval is not
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20
21 required.

22 23 **RESULTS**

24 25 **Search results**

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

59 60 **Study characteristics**

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5 Most of the papers (84.3%) scored 4 or more according to the AHRQ scale indicating a
6
7 generally moderate to high level of data quality (online supplementary appendix 2).
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10 Table 1 shows the characteristics of the included studies. These studies were published
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12 between 2002⁷² and 2019.³⁸ Geographically, over half (n=21, 55.3%) of the 38 included
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14 studies were conducted in the USA, followed by South Africa (n=6, 15.8%), China
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16 (n=3, 7.9%), the United Kingdom (n=2, 5.3%), Rwanda (n=1, 2.6%) and low-income
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18 countries including Gambia (n=1, 2.6%), Nigeria (n=1, 2.6%), Uganda (n=1, 2.6%),
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20 Haiti (n=1, 2.6%) and Zimbabwe (n=1, 2.6%). Twenty-five studies (65.8%) measured
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22 PTSD using diagnostic self-report questionnaires, while the other 13 studies (34.2%)
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24 conducted clinical interviews to diagnose PTSD. Though 8 studies (21.1%) did not
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26 report their sampling methods, convenience sampling methods were adopted in most
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28 studies (n=20, 52.6%), followed by consecutive sampling (n=7, 18.4%), and probability
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30 sampling (n=3, 7.9%). In all, 11743 PLWH were involved (sample size varied from 41
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32 to 1489), of which 2742 were identified with PTSD.
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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

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5	John ⁴⁵	2016	USA	consecutive sampling	359	44	Breslau	self-report questionnaire	moderate
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7									
8	Julnes ¹⁴	2016	USA	convenience sampling	114	39	CDQ	self-report questionnaire	moderate
9									
10									
11	Zhang ⁴⁶	2016	China	convenience sampling	243	106	PCL-C	self-report questionnaire	low
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13									
14									
15	Battaglia ⁴⁷	2015	USA	convenience sampling	200	72	PTSD checklist	self-report questionnaire	moderate
16									
17									
18	Hansrod ⁴⁸	2015	South Africa	convenience sampling	114	29	MINI	clinical interview	moderate
19									
20									
21	Brownley ⁴⁹	2015	USA	unclear	220	78	PSS	self-report questionnaire	moderate
22									
23									
24	Malee ⁵⁰	2014	USA	convenience sampling	1223	281	CDQ	self-report questionnaire	high
25									
26									
27	Glémaud ⁵¹	2014	USA	unclear	96	33	PRIME MD PHQ	clinical interview	low
28									
29									
30	Gore-Felton ⁵²	2013	USA	convenience sampling	94	28	PCL-C	self-report questionnaire	low
31									
32									
33									
34	Glover ⁵³	2013	USA	convenience sampling	99	24	PDS	self-report questionnaire	high
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36									
37	Déviex ⁵⁴	2013	Haiti	convenience sampling	104	52	PCL-C	self-report questionnaire	moderate
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5	Gard ⁵⁵	2013	Rwanda	unclear	705	380	HTS	self-report questionnaire	moderate
6									
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8	Peterson ⁵⁶	2012	Gambia	consecutive sampling	153	46	IES-R	self-report questionnaire	high
9									
10									
11	Kinyanda ⁵⁷	2011	Uganda	consecutive sampling	618	10	MINI	clinical interview	moderate
12									
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14									
15	Bogart ⁵⁸	2011	USA	convenience sampling	181	72	PDS	self-report questionnaire	moderate
16									
17									
18	Martin ⁵⁹	2011	UK	convenience sampling	85	46	CIDI	clinical interview	moderate
19									
20									
21	Reisner ⁶⁰	2011	USA	convenience sampling	63	16	AUDADIS-IV	clinical interview	moderate
22									
23									
24	Theuninck ⁶¹	2010	UK	convenience sampling	100	33	PCL-C	self-report questionnaire	low
25									
26									
27									
28	Joska ⁶²	2010	South Africa	unclear	536	164	HTS	self-report questionnaire	moderate
29									
30									
31	Adewuya ⁶³	2009	Nigeria	unclear	190	52	MINI	clinical interview	moderate
32									
33									
34	Spies ⁶⁴	2009	South Africa	unclear	429	92	MINI	clinical interview	moderate
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36									
37	Fincham ⁶⁵	2008	South Africa	consecutive sampling	456	23	MINI	clinical interview	moderate
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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

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

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 ($p \leq 0.001$, $I^2=98.1\%$) 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%

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5 (95%CI: 17% to 23%), respectively. Also, studies conducted with convenience
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8 sampling were more likely to have higher PTSD prevalence (pooled rate= 32%, 95%CI
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10 27% to 37%) than those using consecutive sampling (pooled rate= 17%, 95%CI 10% to
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13 24%).
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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%		

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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

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5 with HIV/AIDS. Therefore, the results of our study significantly underscore the
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7 importance of early assessment and trauma-directed psychological interventions for
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9 PLWH.
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13 Undoubtedly, heterogeneity between studies is expected in such a relatively large
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15 topic of review. In this review, the estimated PTSD prevalence in PLWH varied widely
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17 (1.6%-54.1%) across studies and countries, which is also a common problem in the
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19 epidemiology of psychological and mental health disorders.^{78 79} Consistent with the
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21 findings of previous research,⁵⁹ the majority of studies which have determined the
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23 incidence of HIV-related PTSD have been conducted in developed countries (n=23).
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25 Compared with lower-income countries, higher-income countries reported relatively
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27 higher prevalence of PTSD. This tendency and the varied prevalence of PTSD among
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29 PLWH may be explained by the cross-cultural differences in attitudes towards HIV
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31 infection. Turan et al.⁸⁰ found that the level of perceived HIV-related stigma in the
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33 community experienced by PLWH may cause adverse health and psychosocial
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35 outcomes. Social isolation and stigma might exacerbate symptoms of PTSD.⁸¹ In high-
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37 income countries, PLWH may experience “compound” or “layered” stigma, where
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39 stigmatizing beliefs are not only associated with HIV infection but also related to sexual
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41 orientation, commercial sexual behaviors, etc.⁸² Although, HIV-related stigma is highly
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43 burdensome in some mid-income countries, such as China,^{83 84} the reported prevalence
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45 of PLWH with PTSD was lower compared to higher-income countries. The differences
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47 between collectivism and individualism rooted in eastern and western culture may be an
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5 explanation.⁸⁵ It is worth noting that social context may not only influence the
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7
8 susceptibility of mental health disorders, but also constitutes an important factor in
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10 perceived stigma among individuals with mental illness. Compared to high-income
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12 countries, stigmatizing beliefs about the causes and presence of mental illness are still
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14 widespread in low- and middle-income countries,^{86 87} which may lead to less disease
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16 reporting. Caution must be applied, since there is a lack of studies investigating HIV-
17
18 related PTSD in lower- (n=5) and middle-income (n=10) countries. In particular,
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20
21 detection of prevalence is associated with the representativeness and size of sample. In
22
23 the context of low- and middle-income countries, it could be argued that lower HIV
24
25 testing rates may underestimate the PTSD prevalence and impact generalizability. Thus,
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27
28 more epidemiological studies are warranted to better understand and clarify the
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30
31 difference in PTSD prevalence among PLWH globally.
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36 Subgroup analyses indicated that the prevalence of PTSD differed significantly
37
38 when gender and sexual orientation were taken into consideration. Specifically, women
39
40 living with HIV exhibited a higher prevalence of PTSD (35%) in comparison with both
41
42 MSM (33%) and non-MSM male (20%) groups. This matches the pattern of prevalence
43
44 in PTSD, in which being female is a risk factor associated with PTSD development.¹⁶
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47 As suggested by the aforementioned findings, MSM living with HIV may experience
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49
50 higher levels of stigma and trauma related to their sexual orientation.^{30 88} Compared
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53 with heterosexual counterparts, MSM reported higher risk for suicidal ideation,⁸⁹ which
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56 also indicates greater psychological stress and mental health problems (i.e. PTSD and
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5 depression). The findings that MSM and female HIV-infected individuals are at higher
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7 risk of developing PTSD may indicate that related health promotion campaigns should
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9 be directed to these groups. Clinicians should also take into consideration the PTSD
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11 susceptibility in different groups of HIV-infected populations during diagnoses.
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15 Notably, most eligible studies did not provide separate the prevalence regarding the
16
17 gender of participants, and only 3 studies identified PTSD prevalence among MSM
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19 living with HIV. Given that these data are from a small number of studies and/or
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21 participants, this finding should be interpreted with caution. Nonetheless, given the high
22
23 prevalence of PTSD in this group, future efforts should be made to obtain more
24
25 prevalence data on PTSD among MSM living with HIV.
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31 In our study, we assessed methodological differences that may result in
32
33 heterogeneity. Factors including sampling strategies (convenience vs consecutive) and
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35 measurement (self-report vs clinical interview) were evaluated by subgroup analyses.
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37 Among 38 studies providing estimated prevalence of PTSD, 7 reported participants
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39 were consecutively enrolled via self-referral from flyers describing the study or
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41 advertisements from HIV health care providers, and generated a lower pooled rate
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43 (17%) compared with the other 20 studies using convenience sampling (32%), though
44
45 both sampling methods were non-probabilistic. An increase in reporting rate due to
46
47 convenience sampling has also been found in another meta-analysis synthesizing the
48
49 HCV seroconversion rates in MSM living with HIV.⁹⁰ Convenience samples may allow
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51 researchers to select participants who are more likely to have PTSD symptoms and lead
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5 to over-estimation, but given that only 4 studies were rated as high quality and limited
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7 description of study methods was detected in some studies, the reporting of
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9 epidemiology may not be sufficient to draw conclusions. Therefore, the appropriateness
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11 of calculating pooled prevalence estimates could be questioned, and the pooled
12
13 prevalence estimate regarding the varied recruitment approaches of the studies should
14
15 be interpreted with caution.
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21 In this review, a total of 14 different tools were used to assess PTSD symptoms
22
23 among PLWH across studies. Overall, the prevalence of PTSD screened by self-report
24
25 instruments (31%) was higher than that assessed by clinical interview (22%). Though
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27 both measurements were in accordance with the diagnostic criteria (i.e. DSM or ICD),
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29 clinical interviews most likely do a much better job of assessing symptoms carefully –
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31 for example, not counting symptoms that do not meet clinically meaningful thresholds,
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33 and self-report measures may inflate the prevalence estimates;⁹¹ alternatively, subjects
34
35 may be more comfortable reporting symptoms using self-report questionnaires
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37 (presumably paper or online surveys rather than face-to-face interviews). Screening or
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39 diagnosing with survey instruments is a common and practical method, especially in
40
41 resource-limited regions. We found that, though a number of measures have been used
42
43 to assess PTSD among PLWH, there is no tool designed for this population specifically.
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45 As the sensitivity and specificity of the measures may impact accurate PTSD detection,
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47 further research is required to identify a standardized measure accordingly to improve
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49 validity.
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5 Certain limitations should be acknowledged in this meta-analysis. First, though
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7 minimal potential for publication bias was presumed as all data drawn for this review
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9 were from studies reporting estimated point prevalence without intervention,
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11 publication bias cannot be ruled out for there are a number of studies published in
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13 languages other than English and Chinese that were not included in this review. Second,
14
15 the heterogeneity was high in the whole sample and most subgroups. Heterogeneity
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17 importantly influences the reliability and accuracy of a meta-analysis, and the only
18
19 reliable method for acquiring correct inferences is careful selection of appropriate
20
21 studies.⁹² Even though strict eligibility criteria were employed in addressing PTSD
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23 prevalence in this study, it should be noted that getting HIV is only one possible
24
25 traumatic event, and therefore it is possible that the PTSD experienced by participants
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27 in the selected studies was due to an event other than finding out they were HIV
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29 positive. Accordingly, we suggest that further studies assessing PTSD among PLWH
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31 include more detail on the specific traumas experienced by study participants. In
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33 addition, we have analysed the influences of region, population group, recruitment
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35 venue, and measurement method, which explained some of the heterogeneity. However,
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37 the results should be interpreted with caution. Third, though some studies have
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39 indicated that several sociodemographic factors such as age may be associated with
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41 PTSD incidence among PLWH, we were unable to conduct subgroup analyses stratified
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43 by age due to the lack of detailed information reported in the published studies. As the
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45 quality of reporting could increase the susceptibility to bias, it is imperative for
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5 researchers to report their findings of observational studies in accordance with the
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7 appropriate guidelines, such as the STROBE checklist.
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10 **CONCLUSIONS**

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12 This review contributes to evidence on the quantitatively pooled prevalence of PTSD
13 among PLWH. Stratified subgroups including geographic area, population group,
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15 sampling and measurement method were found to be significant factors accounting for
16
17 the varied prevalence of PTSD among PLWH. More effective intervention strategies
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19 targeting PTSD among PLWH are urgently needed. Future efforts should be made to
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21 obtain countries' own PTSD prevalence data among PLWH as well as specific
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23 vulnerable minorities, which will provide a basis for public health policy, health-care
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25 planning, and resource allocation for PTSD intervention initiatives. Our study also
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27 suggests that more research using robust and comprehensive methodology is needed to
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29 provide rigorous evidence for designing the targeted psychological interventions.
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41 **Figure 1** Flow chart of study inclusion

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43 **Figure 2** Forest plot presenting the prevalence of PTSD in PLWH

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45 **Contributors:** Conception of the work: HW and CT. Systematic review and article
46
47 evaluation: CT, JM, XX and LZ. Data analysis: CT and XX. Results interpretation: CT,
48
49 LAG, HW and ABW. Drafting the article: CT, LAG, HW and ABW. Critical revision
50
51 of the manuscript: LAG, HW and ABW. Final approval of the manuscript: all the
52
53 authors. All the authors fulfill the ICMJE criteria for authorship.
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21
22

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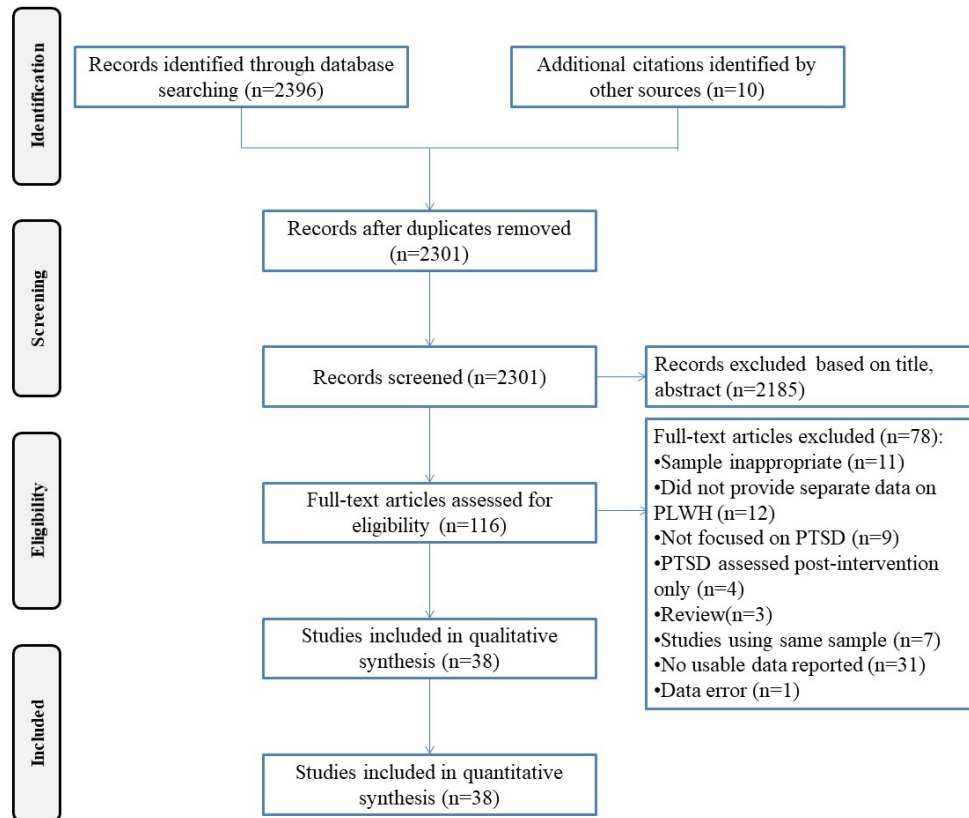


Figure 1 Flow chart of study inclusion

300x250mm (96 x 96 DPI)

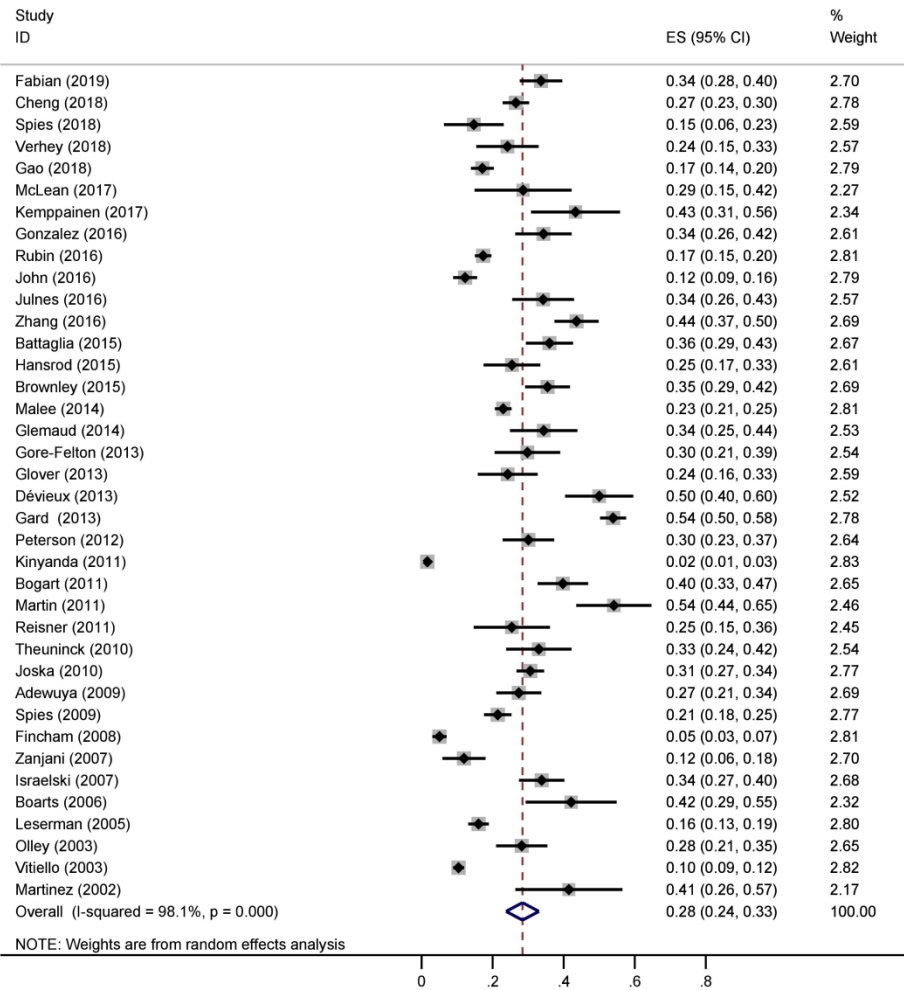


Figure 2 Forest plot presenting the prevalence of PTSD in PLWH

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 immunodeficiency 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 immunodeficiency syndrome" [tiab] OR "acquired immunodeficiency 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

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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	Dévioux 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	Theunink 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	