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Incidence and risk factors of suicidal ideation, attempts, and completion in persons with HIV: a protocol for a systematic review and meta-analysis

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Incidence and risk factors of suicidal ideation, attempts, and completion in persons with HIV: a protocol for a systematic review and meta-analysis

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Abstract

Aim To estimate the pooled incidence of suicide completion, and the incidence and prevalence of suicidal ideation and suicide attempts in people living with HIV/AIDS (PLWHA).

Method We will conduct a systematic review and meta-analysis of studies published between January 1, 1985 and January 1, 2020, reporting the prevalence and incidence of suicide risk in PLWHA. We will search the following databases: PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO. No age, geographical location, study-design or language limits will be applied. This protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols guidelines. Two reviewers will independently screen citations, abstracts and will identify full-text articles for inclusion, extract data and appraise the quality and bias of included studies. Discrepancies will be resolved by consensus or consultation with a third researcher. Risk of bias of included studies will be assessed by the appropriate Cochrane risk of bias tool. The primary outcomes will be the overall rate of suicide completion, suicide attempts, and suicide ideation in PLWHA. We will use the random-effects model with a logit transformation of proportions for the pooling of studies. We will assess the between-study heterogeneity using the I^2 statistic, and Cochrane's Q statistic (significance level < 0.05). We will perform subgroup meta-analyses to look at geographical differences in the suicide risk and conduct a meta-regression analysis, using study level median age, and study level gender proportions, the proportion of study population with AIDS, HAART proportions, mean/median CD4 counts and percentage of the study population with a diagnosis of depression. We will report absolute differences (per 1000) in the overall probability of suicide. The Egger's test and funnel plots will be used to assess publication bias.

Ethics and dissemination No ethics clearance is required as no primary data will be collected. The results of this systematic review and meta-analysis will be presented at scientific conferences and published in a peer-review journal. The results may inform clinical management of PLWHA and may guide future population-specific interventions.

PROSPERO registration number pending: CRDXXXXXXXXXXX

Strengths and limitation of this study

- This will be the first comprehensive systematic review and meta-analysis to synthesize the current literature on the prevalence and incidence of suicide in PLWHA.
- We adhered to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines to ensure transparency and reproducibility of the study.
- The review and meta-analysis may have implications for the management of PLWHA.
- Heterogeneity in the tools used to assess suicidal ideations, and suicide attempts may be a limitation.
- Heterogeneity in the cohort selection within each body of work; some studies may limit their work to perinatally infected individuals, pregnant women and/or IV drug users.
- To overcome these limitations, we will use meta-regression to statistically explore the sources of heterogeneity in the outcome of interest.

Background

Since its discovery in the 1980s, Human Immunodeficiency Virus (HIV) continues to carry a significant global burden of disease. While the disease remains incurable, anti-retroviral therapy (HAART) has been effective in controlling disease progression, improving quality of life, and prolonging longevity[1]. In 2018, the World Health Organization and the United Nations Program on HIV/AIDS (UNAIDS) approximated that globally, approximately 40 million people are living with HIV/AIDS (PLWHA)[2]. HIV caused approximately 1 million deaths worldwide and was responsible for the annual 48 DALYs per 100,000 population [3 4]. While UNAIDS and the WHO provide an effective framework in controlling HIV infection, the current strategies fail to adequately address interventions for the psychosocial burden experienced by PLWHA.

Despite the improved prognosis of HIV, studies continue to find an association between HIV and suicide. Marzuk and colleagues found that nearly 9% of suicide victims had HIV[5]. Likewise, a cross-sectional study found that 77% of minority PLWHA had suicidal thoughts within the past week, and 26% had attempted suicide since diagnosis[6]. Data thus far has shown that patient suicide rates within the first year of HIV diagnosis exceed that of the general population [7-9]. While the factors leading to suicide may mirror those seen in depression, identifying the risks correlated to suicidal behavior in HIV patients will inform effective preventative measures against suicide. Furthermore, as discussed above identification of risk factors of suicidal behavior can improve HIV management in at-risk populations.

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, morbidity and mortality rates have declined in PLWHA[10], although the relationship between HAART and suicide risk remains unclear. A longitudinal study followed 163 PLWHA for two years and found that HAART increased CD4 counts and decreased depressive symptoms with a temporal relationship[11]. However, other studies have suggested that HAART with clarithromycin or efavirenz can induce a neuropsychiatric reaction, potentially increasing depressive symptoms and suicide risk [12-14].

To our knowledge, there is no systematic review and meta-analysis of the pooled incidences of suicide in PLWHA and examine associated risk factors.

OBJECTIVES

The objective of this study is to present a protocol for review and meta-analysis to ascertain the incidence of suicide ideation, attempt, and completion in PLWHA and to delineate the associated risk factors. Specific aims are:

(i) To examine the global incidence of suicide completion in PLWHA

(ii) To examine the global prevalence of suicide ideation, attempt, and completion in PLWHA

(iii) To delineate risk factors associated with suicide ideation, attempt and completion in PLWHA

Review question

What is the incidence/prevalence of suicidal ideation, attempt, and completions in PLWHA is as reported in studies between January 1, 1985, and January 1, 2020?

METHOD

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) 2015 statement and guidelines to inform the development of this protocol.[15 16] See online supplementary appendix 1 for the checklist.

Patient and public involvement statement

Patients were not involved in the development of this protocol.

Study design

We will incorporate the following inclusion criteria:

Studies that:

- Reported suicide rates in PLWHA
- Published between January 1, 1985, to November 20, 2019
- Published in any language

We will exclude:

- Studies not conducted in humans
- Case reports and studies that did not report the incidence of suicide, suicide attempts, or suicide ideations were excluded
- Meeting abstracts, review papers, and commentaries

Domain

We will include studies if they are related to HIV/AIDS and suicide

Population

We will include studies that report data generated from HIV-infected participants, regardless of age, gender and sex.

Outcomes

The primary outcomes will be the overall rate of suicide completion, suicide attempts, and suicide ideation in PLWHA

Search Strategy

Geographical context

We will include studies from all over the globe. We will, however, estimate regional differences through subgroup analysis.

Database searches

The following databases will be searched: PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO. We will use a snowballing method to include to search the citation lists of included papers. This will be accomplished by using the 'cited by' tool in Google Scholar. Efforts will be made to contact authors of ongoing studies and in-press literature for information regarding additional studies or missing data.

Search Terms

Our keyword search will be based on Medical Subject Headings (MeSH) with various combinations of "Suicide", OR "Depression", OR "Suicide attempt", OR "Suicidal Ideation*", OR "Suicide Completion*" OR "Mental Illness*" OR "Anxiety*", AND "HIV*" OR "Human immunodeficiency syndrome" OR "AIDS" OR "Acquired Immunodeficiency Syndrome". This search strategy will be further adapted and tailored for use with each database, using Boolean operators, truncations, proximity operators and Medical Subject Heading, as appropriate for each database. For a complete list of search terms see online supplementary appendix 2.

Study selection and data extraction

Title and abstract screening

The citations will be downloaded into the Endnote software and will exclude duplicate articles. Two review team members will independently screen studies in two stages. In the first stage, the two reviewers will independently screen titles and abstracts. They will document, with reasons, the studies excluded from the review.

Full-text screening and data extraction

In the second stage, full-text versions of selected abstracts will be downloaded/retrieved and assessed independently by the two reviewers. They will extract data from eligible papers identified during the abstract screening step. In the event of disagreement, the two authors will confer and discuss with each other and, if necessary, a third review author (PS) to reach consensus. When abstracts and subsequently included papers are not available in English, translators will be sought. Using the format of the standard data extraction form that has been validated and used somewhere,[17] we will extract the following information: first author, country in which the study was conducted, year of publication, study period, research methodology, total sample size, number of patients with suicidal ideation, number of patients with suicidal attempt, number of patients with suicidal completion, percent

of study sample that was male, mean age, percent of population with HAART, average CD4 count, mean viral load, percent with reported depression and percent of individuals with AIDS and study limitations. Data will be extracted independently by two authors. In case of missing data, one attempt will be made to contact the corresponding authors of studies by email. If the author fails to provide additional information, a decision will be made as to whether to include the study in the final review.

Assessment of Methodological Quality of the Papers

Two authors will independently assess the quality of the papers included in the review. We anticipate finding only observational studies. Therefore, assessment of methodological quality will be conducted using the Newcastle-Ottawa Quality Assessment Scale, which is a validated tool for assessing quantitative cross-sectional, case-control and cohort studies.[18] Scores between 7 and the maximum score of 9 will be defined as high quality; scores between 4 and 6 will be defined as intermediate quality and scores between 1 and 3 will be defined as low quality. Discrepancies in scoring will be resolved by discussion with a third author. Studies will be included regardless of the risk of bias and quality scores, but sensitivity analysis will be conducted to ascertain the impact of their inclusion.

Data synthesis and analysis

We will use the metaprop function of the *meta*-package in R Statistical Software for analysis.[19] The primary outcomes will be the overall rate of suicide completion, suicide attempts, and suicide ideation in PLWHA. We will use the random-effects model with a logit transformation of proportions for the pooling of studies. The confidence intervals will be calculated using the exact binomial (Clopper-Pearson) interval method.[19] We will assess the between-study heterogeneity using the I^2 statistic, expressed as %, low (25%), moderate (50%), and high (75%), and Cochrane's Q statistic (significance level < 0.05). We will perform subgroup meta-analyses to look at geographical differences in the suicide risk and conducted a meta-regression analysis, using study level median age, and study level gender proportions, year of study, the proportion of study population with AIDS, HAART proportions, mean/median CD4 counts and percentage of the study population with depression diagnosis. We will report absolute differences (per 1000) in the overall probability of suicide. The Egger's test and funnel plots will be used to assess publication bias.

Risk of bias assessment for retained studies

We will perform sensitivity analysis by the use of subgroup meta-analyses to look at geographical differences in the suicide risk and conduct a meta-regression analysis,[20] using study level median age, and study level gender proportions, year of study, the proportion of study population with AIDS, HAART proportions, mean/median CD4 counts and percentage of the study population with depression diagnosis. We will report absolute differences (per 1000) in the overall probability of suicide. The Egger's test and funnel plots will be used to assess publication bias.

Presentation of results and reporting

The PRISMA guidelines will be used and the checklist will accompany the publication. Quantitative data will be summarized and presented in tables, forest plots and maps. The prevalence and incidence of suicide in PLWHA will be presented by continents, by study design. Meta-regression analysis will be reported as absolute differences (per 1000) in the overall probability of suicide.

Potential amendments

The review of the protocol commenced in 2020 and the study is expected to be completed by 2021. We do not foresee amendments to this protocol. However, in case a need for amendment should arise, it will be registered and reported.

Patient and public involvement

Patients were not involved in the development of this systematic review protocol.

Conclusion

This first systematic review and meta-analysis to address an existing knowledge gap in the risk of suicide in people living with HIV/AIDS. This review may improve suicide risk assessments and help to prioritize them in PLWHA, especially those in subgroups that could be at heightened risk.

Dissemination

The results of this systematic review and meta-analysis will be presented at conferences and published in a peer-review journal. The results will guide future population-specific interventions.

Contributors PS conceived this study. AS and PS drafted the manuscript. HW, MP, MC, NL, MM, VMC critically reviewed the manuscript and provided comments. All authors approved the final manuscript.

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Competing interests None declared.

Patient consent for publication Not required.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	**Incidence and risk factors of suicidal ideation, attempts, and completion in persons with HIV: a protocol for a systematic review and meta-analysis** (page 1)
Update	1b	NA
Registration	2	PROSPERO submission under review (Page 2)
Authors:		
Contact	3a	All names, institutional affiliations, e-mail address of all protocol authors are provided as well as physical mailing address of corresponding author (Page 1)
Contributions	3b	The contributions of protocol authors are listed and the guarantor of the review is identified (Page 7).
Amendments	4	Amendments are not expected but all deviations will be documented and discussed (Page 5).
Support:		
Sources	5a	No specific funding or sponsorship has been provided for this review (Page 6)
Sponsor	5b	No specific funding or sponsorship has been provided for this review (Page 6)
Role of sponsor or funder	5c	No specific funding or sponsorship has been provided for this review (Page 6)
INTRODUCTION		
Rationale	6	The rationale for the review is described in contrast to what is already known and the gaps in literature (page 3).
Objectives	7	We provided our explicit objectives (Page 3) and the participants, interventions, comparators, and outcomes (PICO) on (page 4)
METHODS		
Eligibility criteria	8	We explicitly described our inclusion and exclusion criteria (Page 4).
Information sources	9	We described our search strategy, databases that will be used and data sources (Page 4)
Search strategy	10	We described our search strategies and databases that will be systematically explored. We also described how we will extract the data (Page 4).
Study records:		
Data management	11a	We described the mechanism that will be used to manage records and data throughout the review (Pages 4-5)
Selection process	11b	We clearly state the process that will be used for selecting studies (Page 4)
Data collection process	11c	We described the plan of extracting data from reports (Page 4)
Data items	12	We listed and defined all variables for which data will be sought Page 4)
Outcomes and prioritization	13	We listed and defined all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (Page 4)

Risk of bias in individual studies	14	We described anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level (Page 5)
Data synthesis	15a	We described criteria under which study data will be quantitatively synthesised (Page 5)
	15b	We described our plan to assess heterogeneity (Page 5)
	15c	We describe our additional analyses (including sensitivity, subgroup analyses, and meta-regression) (Page 5)
	15d	If quantitative synthesis is not appropriate, narrative synthesis will be used (Page 5)
Meta-bias(es)	16	We described the meta- bias
Confidence in cumulative evidence	17	We will use a quality score as described. (Page 5)

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

PubMed (MEDLINE) search terms

1. (("HIV"[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh]))
2. (("Suicide"[Mesh] OR "Suicide, Attempted"[Mesh] OR "Suicide, Completed"[Mesh] OR "Suicidal, Ideation"[Mesh)
3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr]))
4. 1 AND 2
5. 1 AND 3

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Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Mental health, Global health
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Suicide & self-harm < PSYCHIATRY, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES

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Abstract

Introduction The prevalence of HIV/AIDS is high and is associated with psychiatric morbidity and suicide risk. The objective of this study will be to assess the incidence of suicidal ideation, suicide attempts, and suicide deaths in people living with HIV/AIDS (PLWHA).

Methods and Analysis We designed and registered a study protocol for a systematic review and meta-analysis of studies reporting the suicidality outcome (suicidal ideation, suicide attempts, and suicide deaths) in PLWHA. We will search PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO from their inception until January 1, 2020. No age, geographical location, or language limits will be applied. The primary outcome will be the incidence of suicidality outcomes. Secondary outcomes will be risk factors of suicide risk. Four reviewers will independently screen all citations, full-text articles, and abstract data. Potential conflicts will be resolved through discussion. The study methodological quality (or bias) will be appraised using an appropriate tool. If feasible, we will conduct random-effects meta-analysis with a logit transformation of proportions. We will report the probability of suicide risk as a measure of incidence rate, relative risk ratios (with 95% confidence intervals) to report the effects of the risk factors. Additional analyses will be conducted to explore the potential sources of heterogeneity (e.g. age, gender, geographical location, publication year). The Egger's test and funnel plots will be used to assess small study effects (publication bias).

Ethics and Dissemination No ethics clearance is required as no primary data will be collected. The results of this systematic review and meta-analysis will be presented at scientific conferences and published in a peer-review journal. The results may inform clinical management of PLWHA and may guide future population-specific interventions.

PROSPERO registration number: CRD42020161501

Strengths and limitation of this study

- This will be the first comprehensive systematic review and meta-analysis to synthesize the current literature on the epidemiology of suicidality outcome in PLWHA.
- We adhered to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines to ensure transparency and reproducibility of the study.
- Heterogeneity in the tools used to assess suicidality outcome may be a limitation.
- Heterogeneity in the cohort selection within each body of work; some studies may limit their work to perinatally infected individuals, pregnant women and/or IV drug users.
- To overcome these limitations, we will use meta-regression to statistically explore the sources of heterogeneity in the outcome of interest.

Background

Since its discovery in the 1980s, Human Immunodeficiency Virus (HIV) continues to carry a significant global burden of disease. While the disease remains incurable, anti-retroviral therapy (HAART) has been effective in controlling disease progression, improving quality of life, and prolonging longevity[1]. In 2018, the World Health Organization (WHO) and the United Nations Program on HIV/AIDS (UNAIDS) approximated that 40 million people globally are living with HIV/AIDS (PLWHA)[2]. HIV caused an estimated 1 million deaths worldwide and was responsible for the annual 48 disability-adjusted life years (DALYs) per 100,000 population [3 4]. While UNAIDS and the WHO provide an effective framework in controlling HIV infection, the current strategies fail to adequately address interventions for the psychosocial burden experienced by PLWHA.

Despite the improved prognosis of HIV, studies continue to find an association between HIV and suicide. Carrieri and colleagues reported in 2017 that 6.3% of PLWHA are at risk for suicide[5]. Likewise, a cross-sectional study found that 77% of minority PLWHA had suicidal thoughts within the past week, and 26% had attempted suicide since diagnosis[5]. Data thus far has shown that patient suicide rates within the first year of HIV diagnosis exceed that of the general population [6-8]. Furthermore, societal factors such as stigma, discrimination and lack of social support have been implicated[9 10]. Because the risk factors implicated in suicidality in PLWHA are multifactorial, identifying the risks correlated to suicidal behavior in HIV patients may inform effective preventative measures against suicide. Furthermore, as discussed above identification of risk factors of suicidal behavior can improve HIV management in at-risk populations.

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, morbidity and mortality rates have declined in PLWHA[11], although the relationship between HAART and suicide risk remains unclear. A longitudinal study followed 163 PLWHA for two years and found that HAART increased CD4 counts and decreased depressive symptoms with a temporal relationship[12]. However, other studies have suggested that HAART with clarithromycin or efavirenz can induce a neuropsychiatric reaction, potentially increasing depressive symptoms and suicide risk [13-15]. To our knowledge, there is no systematic review and meta-analysis of the pooled incidences of suicide in PLWHA and examine associated risk factors.

Objectives

The objective of this study will be to assess the incidence and risk factors of suicidal ideation, suicide attempt, and suicide deaths in PLWHA. The specific review questions will be:

(i) What is the global incidence of suicide deaths in PLWHA?

(ii) What is the global prevalence of suicidal ideation and suicide attempt in PLWHA?

(iii) What are the risk factors associated with suicidality outcome in PLWHA?

Methods

The present protocol has been registered with PROSPERO (registration ID: **CRD42020161501).** The present study protocol is being reported in accordance with the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement protocol.[16 17] (see PRISMA-P checklist in Additional file 1).

Eligibility criteria

Studies will be selected according to the following criteria: participants, condition or outcome(s) of interest, study design and context.

* **Participants (population):** We will include studies involving children, adolescents and adult patients living with HIV (regardless of age or sex). Studies not conducted in humans will be excluded.

* **Condition or outcome(s) of interest:** The primary outcome will be the incidence of suicidality outcome, indicating the rate of new (or newly diagnosed) cases of suicidal ideations, suicide attempts or suicide deaths in people living with HIV. It is generally reported as the number of new

cases occurring within a period of time (e.g., per month, per year) or as a fraction of the population at risk of developing the outcome (e.g. new cases per 1,000 or 10,000) We will use author-reported definitions (according to accepted diagnostic criteria). Secondary outcomes will be the risk factors associated with suicidality outcome (for example, HIV viral lead, CD4 T cell count, age, gender and race, major depression, alcohol or drug abuse and dependence, panic disorder, social phobia, and schizophrenia)

* **Study design and context:** Eligible studies will be randomized trials, observational cohort (prospective or retrospective) and cross-sectional studies reporting outcome data and conducted in a wide range of people living with HIV. We will exclude case series and case reports. No limitations will be imposed on study conduct period, and language of publication. Reviews, commentaries, and conference/meeting abstracts will be excluded.

Information sources and search strategy

The primary source of literature will be a structured search of electronic databases: PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO from their inception until January 1, 2020. The secondary source of potentially relevant material will be a search of the grey or difficult to locate literature, including Google Scholar. We will perform hand-searching of the reference lists of included studies, relevant reviews or other relevant documents. Efforts will be made to contact authors of ongoing studies and in-press literature for information regarding additional studies or missing data. The search will be based on Medical Subject Headings (MeSH), a broad range of terms and keywords related to: "suicide" and " human immunodeficiency syndrome / acquired immunodeficiency syndrome ". A draft search strategy for MEDLINE is provided in Additional file 2.

Study selection and data extraction

All articles identified from the literature search will be screened by four reviewers (HW, NL, MC and MP) independently.

Title and abstract screening

In the first stage, four reviewers will independently screen titles and abstracts of articles returned from initial searches will based on the eligibility criteria outlined above. They will document, with reasons, the studies excluded from the review. In the case of potential disagreement, the four reviewers will consult a senior reviewer (PS) to reach consensus. The citations will be downloaded into the Endnote software and will exclude duplicate articles.

Full-text screening and data extraction

In the second stage, full-text versions of selected abstracts will be downloaded/retrieved and assessed independently by the four reviewers. They will extract data from eligible papers identified during the abstract screening step. In the event of disagreement, the authors will confer and discuss with each other and, if necessary, a senior reviewer (PS) to reach consensus. When abstracts and subsequently included papers are not available in English, translators will be sought. Using the format of the standard data extraction form that has been validated and used somewhere,[18] we will extract the following information: first author, country in which the study was conducted, year of publication, study period, research methodology, total sample size, number of patients with suicidal ideation, number of patients with suicidal attempt, number of patients with suicidal completion, percent of study sample that was male, mean age, employment, homelessness, partner presence, percent of population with HAART, regimen of antiretroviral therapy, mean CD4 T cell count, median viral load, proportion with major depression, anxiety and other psychiatric illness, proportion with AIDS and **AIDS associated central nervous system conditions**. In case of missing data, one attempt will be made to contact the corresponding authors of studies by email. If the author fails to provide additional information, a decision will be made as to whether to include the study in the final review. A flow chart showing details of studies included and excluded at each stage of the study selection process will be provided.

Assessment of Methodological Quality of the Papers

Four authors will independently assess the quality of the papers included in the review. We anticipate finding only observational studies. Therefore, assessment of methodological quality will be conducted using the Newcastle-Ottawa Quality Assessment Scale, which is a validated tool for assessing

quantitative cross-sectional, case-control and cohort studies.[19] Scores of 8 to the maximum score of 9 will be defined as high quality; scores of 5 to 7 will be defined as intermediate quality, and scores of 1 to 4 will be defined as low quality. Discrepancies in scoring will be resolved by discussion with a third author. Studies will be included regardless of the risk of bias and quality scores, but sensitivity analysis will be conducted to ascertain the impact of their inclusion.

Data synthesis

The data from each paper (e.g. study characteristics, participants, outcomes and findings) will be used to build evidence tables of an overall description of included studies. Incidence and prevalence estimate of suicidality outcome will be presented as cases per 1,000 along with 95% confidence intervals. Relative risk ratios (RR) or odds ratios (OR) with 95% confidence intervals will be used to report the association of suicidality outcome with the risk factors. If feasible and appropriate, data points from primary studies will be used to perform random effects meta-analyses. Since heterogeneity is expected a priori, we will estimate the pooled incidence and its 95% confidence interval using the random effects model with logit transformation and back transformation. We will use the metaprop function of the *meta*-package in R Statistical Software for analysis.[20] The confidence intervals will be calculated using the exact binomial (Clopper-Pearson) interval method.[20] The random effects model assumes the study estimates follow a normal distribution, considering both within-study and between-study variation. Forest plots will be used to visualize the extent of heterogeneity among studies. We will quantify statistical heterogeneity by estimating the variance between studies using I^2 statistic. The I^2 is the proportion of variation in prevalence estimates that is due to genuine variation in prevalence rather than sampling (random) error. I^2 ranges between 0% and 100% (with values of 0-25% and 75-100% taken to indicate low and considerable heterogeneity, respectively). We will also report Tau^2 and Cochran Q test with a P value of < 0.05 considered statistically significant (heterogeneity).

Additional analyses

If sufficient studies are identified and data points are available, potential sources of heterogeneity will be investigated further by subgroup or meta-regression analyses according to baseline characteristics and methodological covariates. We plan to conduct analyses by geographical location (e.g. region and/or country), age (median), gender (e.g. proportion), year of study conduct, comorbidities (e.g. proportion of major depressive disorder, mean body mass index), CD4 T cell counts (median), HAART (proportion), AIDS (proportion) and quality score of each included study (high versus low/medium score).

Small study effects (publication bias) will be assessed by inspection of the funnel plots for asymmetry and with Egger's test, with the results considered to indicate potential small study effects when P values < 0.10.

Software considerations

All analyses will be conducted in meta-package in R Statistical Software for analysis.

Presentation of results and reporting

The PRISMA guidelines will be used and the checklist will accompany the publication. Quantitative data will be summarized and presented in tables, forest plots, and maps. The prevalence and incidence of suicide in PLWHA will be presented by continents, by study design. We define the prevalence of suicide as the number of existing cases within the described time period, and we define the incidence of suicide as the rate of new cases that occur amongst cohorts during the described time period. Meta-regression analysis will be reported as absolute differences (per 1000) in the overall probability of suicide. Strength of evidence will be assessed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) framework using four levels of quality of evidence: very low, low, moderate, and high. We use the following domains GRADE: risk of bias, imprecision, inconsistency, indirectness, and publication bias.[21] We will report the overall strength of evidence of the outcome of interest.

Patient and public involvement

Patients were not involved in the development of this systematic review protocol.

Discussion

The systematic review and meta-analysis of studies presented in this protocol will identify, collect, and evaluate the existing knowledge underlying the incidence, prevalence and risk factors of suicidality associated with HIV infection. To our knowledge, there is no other systematic review and meta-analysis addressing this specific issue. The proposed systematic review and meta-analysis will be reported in accordance with the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement[22] and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting guideline.[23] Any amendments made to this protocol when conducting the study will be outlined and reported in the final manuscript. Results will be disseminated through conference presentations and publication in a peer-reviewed journal. Major limitation is the inconsistence in the reporting of suicidality outcome at the study level. Such inconsistences may lead to lower or higher pooled prevalence of suicidality outcome. We will first conduct qualitative synthesis before carrying out meta-analysis. If we find a very high degree clinical, and methodological heterogeneity, we will not pool the results but will instead summarize the results qualitatively by using tables and figures. If we end up conducting a meta-analysis, will however mitigate the heterogeneity by conducting subgroup analysis and meta-regression. The results of this systematic review and meta-analysis will be presented at conferences and published in a peer-review journal. The results will guide future population-specific interventions and may improve mental health and survival in people living with HIV, especially those in subgroups that could be at heightened risk.

Contributorship Statement PS conceived this study. AS and PS drafted the manuscript. HW, MP, MC, NL, MM, VMC critically reviewed the manuscript and provided comments. All authors approved the final manuscript.

Guarantor of the review: PS

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Competing interests None declared.

Patient consent for publication Not required.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	**Incidence and risk factors of suicidal ideation, suicide attempts, and suicide deaths in persons with HIV: a protocol for a systematic review and meta-analysis** (page 1)
Update	1b	NA
Registration	2	PROSPERO submission under review (Page 2)
Authors:		
Contact	3a	All names, institutional affiliations, e-mail address of all protocol authors are provided as well as physical mailing address of corresponding author (Page 1)
Contributions	3b	The contributions of protocol authors are listed and the guarantor of the review is identified (Page 7).
Amendments	4	Amendments are not expected but all deviations will be documented and discussed (Page 6).
Support:		
Sources	5a	No specific funding or sponsorship has been provided for this review (Page 7)
Sponsor	5b	No specific funding or sponsorship has been provided for this review (Page 7)
Role of sponsor or funder	5c	No specific funding or sponsorship has been provided for this review (Page 7)
INTRODUCTION		
Rationale	6	The rationale for the review is described in contrast to what is already known and the gaps in literature (page 3).
Objectives	7	We provided our explicit objectives (Page 3) and the participants, interventions, comparators, and outcomes (PICO) on (page 4)
METHODS		
Eligibility criteria	8	We explicitly described our inclusion and exclusion criteria (Page 3, 4).
Information sources	9	We described our search strategy, databases that will be used and data sources (Page 4)
Search strategy	10	We described our search strategies and databases that will be systematically explored. We also described how we will extract the data (Page 4).
Study records:		
Data management	11a	We described the mechanism that will be used to manage records and data throughout the review (Pages 4-5)
Selection process	11b	We clearly state the process that will be used for selecting studies (Page 4)
Data collection process	11c	We described the plan of extracting data from reports (Page 4)
Data items	12	We listed and defined all variables for which data will be sought Page 4)

Outcomes and prioritization	13	We listed and defined all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (Page 4)
Risk of bias in individual studies	14	We described anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level (Page 4,5)
Data synthesis	15a	We described criteria under which study data will be quantitatively synthesised (Page 5)
	15b	We described our plan to assess heterogeneity (Page 5)
	15c	We describe our additional analyses (including sensitivity, subgroup analyses, and meta-regression) (Page 5)
	15d	If quantitative synthesis is not appropriate, narrative synthesis will be used (Page 5)
Meta-bias(es)	16	We described the meta- bias (5)
Confidence in cumulative evidence	17	We will use a quality score as described. (Page 5)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

PubMed (MEDLINE) search terms

1. (("HIV"[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh]))
2. (("Suicide"[Mesh] OR "Suicide, Attempted"[Mesh] OR "Suicide, Completed"[Mesh] OR "Suicidal, Ideation"[Mesh])
3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr]))
4. 1 AND 2
5. 1 AND 3

BMJ Open

Incidence and risk factors of suicidal ideation, suicide attempts, and suicide deaths in persons with HIV: a protocol for a systematic review and meta-analysis

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Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Mental health, Global health
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Suicide & self-harm < PSYCHIATRY, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES

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Incidence and risk factors of suicidal ideation, suicide attempts, and suicide deaths in persons with HIV: a protocol for a systematic review and meta-analysis

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Abstract

Introduction The prevalence of HIV/AIDS is high and is associated with psychiatric morbidity and suicide risk. The objective of this study will be to assess the incidence of suicidal ideation, suicide attempts, and suicide deaths in people living with HIV/AIDS (PLWHA).

Methods and Analysis We present a study protocol for a systematic review and meta-analysis of studies reporting the suicidality outcome (suicidal ideation, suicide attempts, and suicide deaths) in PLWHA. PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO databases will be searched from their inception until January 1, 2020. The primary outcome of interest will be the incidence of suicidality outcomes and associated . Secondary outcomes will be risk factors. Citations, full-text articles, and abstract will be screened by four reviewers independently. Disagrrements will be resolved through discussion. The study methodological quality (or bias) will be appraised using an appropriate tool. Random-effects meta-analysis will be conducted if we find that the studies are very heterogenous. For the suicidality outcome, probability of suicide risk will be reported. Relative risk ratios (with 95% confidence intervals) will be reported for the effects of the risk factors. Potential publication bias will be by conducting Egger's test and creating funnel plots. We will conduct additional analyses to explore the potential sources of heterogeneity (e for example age, sex and geographical location).

Ethics and Dissemination No ethics clearance is required as no primary data will be collected. The results of this systematic review and meta-analysis will be presented at scientific conferences and published in a peer-review journal. The results may inform clinical management of PLWHA and may guide future population-specific interventions.

We will search PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO from their inception until January 1, 2020.

PROSPERO registration number: CRD42020161501

Strengths and limitation of this study

- This will be the first comprehensive systematic review and meta-analysis to synthesize the current literature on the epidemiology of suicidality outcome in PLWHA.
- We adhered to Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols guidelines to ensure transparency and reproducibility of the study.
- Heterogeneity in the tools used to assess suicidality outcome may be a limitation.
- Heterogeneity in the cohort selection within each body of work; some studies may limit their work to perinatally infected individuals, pregnant women and/or IV drug users.
- To overcome these limitations, we will use meta-regression to statistically explore the sources of heterogeneity in the outcome of interest.

Background

Since its discovery in the 1980s, Human Immunodeficiency Virus (HIV) continues to carry a significant global burden of disease. While the disease remains incurable, anti-retroviral therapy (HAART) has been effective in controlling disease progression, improving quality of life, and prolonging longevity[1]. In 2018, the World Health Organization (WHO) and the United Nations Program on HIV/AIDS (UNAIDS) approximated that 40 million people globally are living with HIV/AIDS (PLWHA)[2]. HIV caused an estimated 1 million deaths worldwide and was responsible for the annual 48 disability-adjusted life years (DALYs) per 100,000 population [3 4]. While UNAIDS and the WHO provide an effective framework in controlling HIV infection, the current strategies fail to adequately address interventions for the psychosocial burden experienced by PLWHA.

Despite the improved prognosis of HIV, studies continue to find an association between HIV and suicide. Carrieri and colleagues reported in 2017 that 6.3% of PLWHA are at risk for suicide[5]. Likewise, a cross-sectional study found that 77% of minority PLWHA had suicidal thoughts within the past week, and 26% had attempted suicide since diagnosis[5]. Data thus far has shown that patient suicide rates within the first year of HIV diagnosis exceed that of the general population [6-8]. Furthermore, societal factors such as stigma, discrimination and lack of social support have been implicated[9 10]. Because the risk factors implicated in suicidality in PLWHA are multifactorial,[11] identifying the risks correlated to suicidal behavior in HIV patients may inform effective preventative measures against suicide. Furthermore, as discussed above identification of risk factors of suicidal behavior can improve HIV management in at-risk populations.

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, morbidity and mortality rates have declined in PLWHA[12], although the relationship between HAART and suicide risk remains unclear. A longitudinal study followed 163 PLWHA for two years and found that HAART increased CD4 counts and decreased depressive symptoms with a temporal relationship[13]. However, other studies have suggested that HAART with clarithromycin or efavirenz can induce a neuropsychiatric reaction, potentially increasing depressive symptoms and suicide risk [14-16]. To our knowledge, there is no systematic review and meta-analysis of the pooled incidences of suicide in PLWHA and examine associated risk factors.

Objectives

The objective of this study will be to assess the incidence and risk factors of suicidal ideation, suicide attempt, and suicide deaths in PLWHA. The specific review questions will be:

(i) What is the global incidence of suicide deaths in PLWHA?

(ii) What is the global prevalence of suicidal ideation and suicide attempt in PLWHA?

(iii) What are the risk factors associated with suicidality outcome in PLWHA?

Methods

The methods of this protocol is similar to those reported elsewhere.[17] This protocol has been registered with PROSPERO (registration ID: **CRD42020161501)** and is being reported in accordance with the reporting guidance provided in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement protocol.[18 19] (see PRISMA-P checklist in Additional file 1).

Eligibility criteria

* **Participants (population):** Children, adolescents and adult patients living with HIV. No age and sex constraint.

* **Outcome(s) of interest:** The primary outcome will be the incidence of suicidality outcome. New cases of suicidal ideations, suicide attempts or suicide deaths in people living with HIV. Risk factors associated with suicidality outcome (for example, HIV viral lead, CD4 T cell count, age, gender and race, major depression, alcohol or drug abuse and dependence, panic disorder, social phobia, and schizophrenia) are the secondary outcomes.

* **Study design:** Randomized control trials, observational cohort (prospective or retrospective) and cross-sectional studies reporting suicidality in people living with HIV. Case reports, case series, meta-analysis and reviews will be excluded.

Information sources and search strategy

PubMed (MEDLINE), Scopus, EMBASE, Cochrane Library, OVID (HEALTH STAR), OVID (MEDLINE), Joana Briggs Institute EBF Database, Web of Science and PsychINFO databases will be searched from their inception until January 1, 2020. In addition, grey literature will be searched. We will perform hand-searching of the reference lists of included studies, relevant reviews or other relevant documents. The search will be based on Medical Subject Headings (MeSH), a broad range of terms and keywords related to: "suicide" and " human immunodeficiency syndrome / acquired immunodeficiency syndrome ". A draft search strategy for MEDLINE is provided in **Additional file2.**

Study selection and data extraction

All articles identified from the literature search will be screened by four reviewers (HW, NL, MC and MP) independently.

Title and abstract screening

In the first stage, four reviewers will independently screen titles and abstracts of articles returned from initial searches will based on the eligibility criteria outlined above. They will document, with reasons, the studies excluded from the review. In the case of potential disagreement, the four reviewers will consult a senior reviewer (PS) to reach consensus. The citations will be downloaded into the Endnote software and will exclude duplicate articles.

Full-text screening and data extraction

In the second stage, full-text versions of selected abstracts will be downloaded/retrieved and assessed independently by the four reviewers. They will extract data from eligible papers identified during the abstract screening step. Disagreements will be resolved through discussion until a consesus is reached. When abstracts and subsequently included papers are not available in English, translators will be sought. The following information will be extracted: first author, country in which the study was conducted, year of publication, study period, research methodology, total sample size, number of patients with suicidal ideation, number of patients with suicidal attempt, number of patients with suicidal completion, percent of study sample that was male, mean age, employment, homelessness, partner presence, percent of population with HAART, regimen of antiretroviral therapy, mean CD4 T cell count, median viral load, proportion with major depression, anxiety and other psychiatric illness, proportion with AIDS and AIDS associated central nervous system conditions. A PRISMA flow chart detailing the study selection process will be provided.

Assessment of Methodological Quality of the Papers

Methodological quality of studies will be conducted using the Newcastle-Ottawa Quality Assessment Scale, which is a validated tool for assessing quantitative cross-sectional, case-control and cohort studies.[20] Scores of 8 to the maximum score of 9 will be defined as high quality; scores of 5 to 7 will be defined as intermediate quality, and scores of 1 to 4 will be defined as low quality. Any discrepancy or disagreements in scoring will be resolved by discussion. Further, sensitivity analysis will be carried out using study quality score.

Data synthesis

The data from each paper (e.g. study characteristics, participants, outcomes and findings) will be used to build evidence tables of an overall description of included studies. Incidence and prevalence estimate of suicidality outcome will be presented as cases per 1,000 along with 95% confidence intervals. Relative risk ratios (RR) or odds ratios (OR) with 95% confidence intervals will be used to report the association of suicidality outcome with the risk factors. If feasible and appropriate, data points from primary studies will be used to perform random effects meta-analyses. Since heterogeneity is expected a priori, we will estimate the pooled incidence and its 95% confidence interval using the random effects model with

logit transformation and back transformation. We will use the metaprop and metagen functions of the *meta*-package in R Statistical Software for analysis.[21] The confidence intervals will be calculated using the exact binomial (Clopper-Pearson) interval method.[21] The random effects model assumes the study estimates follow a normal distribution, considering both within-study and between-study variation. Forest plots will be used to visualize the extent of heterogeneity among studies. Quantification of statistical heterogeneity will be accomplished by estimating the variance between studies using *I2* statistic, which is the proportion of variation in prevalence estimates that is due to true variation in prevalence rather than sampling (random) error. I^2 ranges between 0% and 100% (with values of 0-25% and 75-100% indicating low and considerable heterogeneity, respectively). In addition, We will report Tau^2 and Cochran Q test with a p value of < 0.05 considered statistically significant (heterogeneity). Potential publication bias will be explored using Egger's test and funnel plots.

Additional analyses

Potential sources of heterogeneity will be explored further by subgroup or meta-regression analyses by using baseline characteristics and methodological covariates. In addition, we plan to conduct analyses by geographical location, age (median), sex (e.g. proportion), comorbidities (e.g. proportion of major depressive disorder, mean body mass index), CD4 T cell counts (median), HAART (proportion), AIDS (proportion) and quality score of each included study (high versus low/medium score). We will assess publication bias by inspectiing the funnel plots for asymmetry and with Egger's test, with the results considered to indicate potential small study effects when p values < 0.10.

Software considerations

All analyses will be conducted in meta-package in R Statistical Software for analysis.

Presentation of results and reporting

The PRISMA guidelines will be used and the checklist will accompany the publication. Quantitative data will be summarized and presented in tables, forest plots, and maps. The prevalence and incidence of suicide in PLWHA will be presented by continents, by study design. We define the prevalence of suicide as the number of existing cases within the described time period, and we define the incidence of suicide as the rate of new cases that occur amongst cohorts during the described time period. Meta-regression analysis will be reported as absolute differences (per 1000) in the overall probability of suicide. Strength of evidence will be assessed using the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) framework using four levels of quality of evidence: very low, low, moderate, and high. We use the following domains GRADE: risk of bias, imprecision, inconsistency, indirectness, and publication bias.[22] We will report the overall strength of evidence of the outcome of interest.

Patient and public involvement

Patients were not involved in the development of this systematic review protocol.

Discussion

The systematic review and meta-analysis of studies presented in this protocol will identify, collect, and evaluate the existing knowledge underlying the incidence, prevalence and risk factors of suicidality associated with HIV infection. We will report the findings of the systematic review and meta-analysis in accordance with the reporting guidance in the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement[23] and the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) reporting guideline.[24] The results of the proposed systematic review and meta-analysis will be presented at conferences and published in a peer-review journal. The hope and believe the findings of the proposed review will guide interventions to improve the mental health of people living with HIV with the potential of improving their quality of care and overall and survival

Contributorship Statement PS conceived this study. AS and PS drafted the manuscript. HW, MP, MC, NL, MM, VMC critically reviewed the manuscript and provided comments. All authors approved the final manuscript.

Guarantor of the review: PS

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Competing interests None declared.

Patient consent for publication Not required.

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PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	**Incidence and risk factors of suicidal ideation, suicide attempts, and suicide deaths in persons with HIV: a protocol for a systematic review and meta-analysis** (page 1)
Update	1b	NA
Registration	2	PROSPERO submission under review (Page 2)
Authors:		
Contact	3a	All names, institutional affiliations, e-mail address of all protocol authors are provided as well as physical mailing address of corresponding author (Page 1)
Contributions	3b	The contributions of protocol authors are listed and the guarantor of the review is identified (Page 7).
Amendments	4	Amendments are not expected but all deviations will be documented and discussed (Page 6).
Support:		
Sources	5a	No specific funding or sponsorship has been provided for this review (Page 7)
Sponsor	5b	No specific funding or sponsorship has been provided for this review (Page 7)
Role of sponsor or funder	5c	No specific funding or sponsorship has been provided for this review (Page 7)
INTRODUCTION		
Rationale	6	The rationale for the review is described in contrast to what is already known and the gaps in literature (page 3).
Objectives	7	We provided our explicit objectives (Page 3) and the participants, interventions, comparators, and outcomes (PICO) on (page 4)
METHODS		
Eligibility criteria	8	We explicitly described our inclusion and exclusion criteria (Page 3, 4).
Information sources	9	We described our search strategy, databases that will be used and data sources (Page 4)
Search strategy	10	We described our search strategies and databases that will be systematically explored. We also described how we will extract the data (Page 4).
Study records:		
Data management	11a	We described the mechanism that will be used to manage records and data throughout the review (Pages 4-5)
Selection process	11b	We clearly state the process that will be used for selecting studies (Page 4)
Data collection process	11c	We described the plan of extracting data from reports (Page 4)
Data items	12	We listed and defined all variables for which data will be sought Page 4)

Outcomes and prioritization	13	We listed and defined all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale (Page 4)
Risk of bias in individual studies	14	We described anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level (Page 4,5)
Data synthesis	15a	We described criteria under which study data will be quantitatively synthesised (Page 5)
	15b	We described our plan to assess heterogeneity (Page 5)
	15c	We describe our additional analyses (including sensitivity, subgroup analyses, and meta-regression) (Page 5)
	15d	If quantitative synthesis is not appropriate, narrative synthesis will be used (Page 5)
Meta-bias(es)	16	We described the meta- bias (5)
Confidence in cumulative evidence	17	We will use a quality score as described. (Page 5)

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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PubMed (MEDLINE) search terms

1. (("HIV"[Mesh] OR "Acquired Immunodeficiency Syndrome"[Mesh]))
2. (("Suicide"[Mesh] OR "Suicide, Attempted"[Mesh] OR "Suicide, Completed"[Mesh] OR "Suicidal, Ideation"[Mesh])
3. (("Mental Disorder "[Majr] OR "Depressive Disorders"[Majr]))
4. 1 AND 2
5. 1 AND 3