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Review protocol for a systematic review and meta-analysis on HIV inequities in transgender and non-binary populations

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ABSTRACT

Introduction Global disparities in HIV prevalence among transgender women are well documented. However, current epidemiological literature on HIV disparities demonstrates gaps in research that include the diversity within transgender populations—for example, transgender men and non-binary trans people across global regions. This systematic review and meta-analysis protocol aims to summarise global HIV inequities among all transgender and non-binary (trans) populations. The objectives of this review are to estimate pooled HIV prevalence and prevention outcomes (pre-exposure prophylaxis and antiretroviral therapy) and differences by gender identity, global regions and self-report versus lab-confirmed findings among trans adults worldwide.

Methods and analysis We will conduct a systematic review of all studies on HIV outcomes among trans youth and adults (aged 15+ years) published between 2000 and 2024, following the Preferred Reporting Items for Systematic Review and Meta-Analysis Prereporting guidelines. We will use Covidence software for the title and abstract screening, full-text review and data abstraction processes. We will summarise the study's descriptive statistics and conduct meta-analyses of extracted data points to calculate and synthesise pooled findings and effect size. Specifically, we will use the Mantel–Haenszel method with random effects to model our meta-analyses and the DerSimonian and Laird Q test for heterogeneity testing. We will conduct a narrative synthesis on the areas of research that have been conducted to improve HIV prevention and treatment among trans populations and summarise their findings. Subgroup analyses by gender identity, global regions and self-report versus lab-confirmed findings will be conducted.

Ethics and dissemination Ethics approval is not applicable for this review since we will not be collecting primary data. The results will be disseminated through peer-reviewed publications and conference presentations.

PROSPERO registration number The protocol is registered in the International Prospective Register of Systematic Reviews database (PROSPERO ID: CRD42022357285).

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Our systematic review and meta-analysis will fill existing gaps in the literature by including a more expansive definition of gender identity, incorporating a decade-worth of updated findings, expanding to a global context, and providing a framework for ethical and trans-centred HIV research practice.
⇒ We will use a gender-inclusive and gender-specific approach, when necessary, to elucidate shared versus unique contexts and recommendations for addressing HIV inequities across and within each gender group to help inform programme design and policy.
⇒ Our methodology will include a Cochrane risk-of-bias assessment and be in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Prereporting guidelines.
⇒ Definitions of gender identity may differ, and we may be limited in how gender identity is reported between studies.
⇒ Capturing HIV diagnoses may vary by geographic region.

BACKGROUND

While advancements in HIV treatment, prevention, and policy have moved us closer to the Joint United Nations Programme on HIV and AIDS' (UNAIDS) goals of eliminating the AIDS epidemic as a public health threat by 2023,[1] transgender and non-binary (trans) populations still experience a high burden of HIV. Furthermore, these communities have been historically excluded, erased, or aggregated from HIV research and surveillance.[2–4]

Previous studies have shown HIV disparities among trans populations. A 2013 meta-analysis using laboratory-confirmed HIV prevalence rates showed that transfeminine adults of reproductive age are 49 times more likely to be living with HIV across 15 countries, with a pooled HIV prevalence of 19.1% among 11 066 trans women included in the analysis.[5] While this systematic review assessed the HIV burden among trans women worldwide, the study did not characterise HIV disparities among transmasculine and non-binary communities—a major gap that

this study aims to fill. Another recent meta-analysis from the Centre for Disease Control and Prevention showed laboratory-confirmed HIV prevalence of 9.2% among trans adults in the US, with 14.2% among transfeminine adults and 3.2% among transmasculine adults.[6] Moreover, inequities in HIV prevention outcomes were also observed, with about 27% of participants reporting no history of HIV testing and only 48.6% reporting awareness of pre-exposure prophylaxis (PrEP). These disparities are even more apparent among communities of colour, specifically among Black and Latine trans women. The former study found that among transfeminine individuals, Black adults had the highest prevalence estimates (44.2%), followed by Latine adults (25.8%), unlisted adults of other races and ethnicities (9.8%) and White adults (6.7%). Too few studies were included to examine HIV prevalence by race and ethnicity for transmasculine adults, noting a significant gap in this literature base.

In studies that collected data on transmasculine populations, estimates range from 0% to 4.3% for laboratory-confirmed HIV status and from 0% to 10% for self-reported HIV, suggesting that trans masculine individuals may also be more vulnerable to HIV compared with cisgender men.[7 8] To our team's knowledge, the literature that examines HIV prevalence from an intersectional lens or acknowledges the convergence of trans identities is scant—a point for further research—both in the US and globally. One study using observational data from a global survey sampling trans and non-binary people found that among the 120 people who reported living with HIV, 73% identified as non-binary, suggesting the need for HIV research to further characterise this group's vulnerabilities to HIV.[9]

The HIV care continuum includes HIV prevention (eg, PrEP) and linkage to care (eg, initiating and maintaining antiretroviral therapy (ART)). PrEP is a daily oral HIV prevention method that has demonstrated efficacy in reducing HIV acquisition by as much as 96%.[10–14] The inclusion of trans populations in HIV prevention trials, including PrEP studies, has been limited.[15] A systematic review of randomised controlled trials (RCTs) on PrEP effectiveness and safety, which included 15 RCTs, found that PrEP was effective among cis men who have sex with men, serodiscordant couples and people who inject drugs; however, this review did not include data for trans populations.[16] The practice of initiating PrEP has been shown to be low (<10%) among transfeminine individuals.[17] The PrEP initiative, the only placebo-controlled RCT that included trans women to date, found low adherence to PrEP.[18 19] A recent study on HIV testing and PrEP prescriptions among commercially insured trans women and trans men in the US found that in 2021, among trans women and trans men who received a test or diagnosis of a sexually transmitted infection (STI) in the previous 12 months, 20.2% and 10.2% were prescribed PrEP, respectively, and there was an overall increase in PrEP prescriptions between 2014 and 2021.[20] Concerns about drug interactions with gender-affirming hormone therapy (GAHT) have been cited as a barrier to taking PrEP as well as ART adherence.[21 22] Studies have found that transfeminine individuals are less likely to adhere to ART compared with cisgender individuals.[10 23 24] Barriers to PrEP and ART use include concerns regarding interactions between GAHT and PrEP/ART, lack of trust in medical institutions/providers, limited access to and avoidance of healthcare due to stigma and previous experiences of discrimination.[10 25 26] Taken together, previous findings suggest that trans individuals are disproportionately impacted by HIV, particularly transfeminine individuals, and data on HIV among transmasculine and non-binary individuals are still very limited.[27] Few recent systematic reviews and meta-analyses have comprehensively updated this previous systematic review of HIV among transgender women.[5] Moreover, in existing research, there are concerns about sampling bias as previous studies have relied on convenience samples of trans women engaging in sex work, thus potentially inflating HIV prevalence rates.[28 29] Additionally, there have been significant developments in HIV prevention in recent years, such as the emergence of PrEP.[29] An updated systematic review and meta-analysis based on the previous study was conducted to examine the worldwide prevalence and the burden of HIV among transfeminine and transmasculine individuals among literature published between 2000 and 2019.[27 29] However, this study only focused on laboratory-confirmed cases and did not explore the HIV prevalence among non-binary individuals.

Our systematic review and meta-analysis will build on existing research and expand this work to all transgender and non-binary populations to better understand global and intersectional (eg, gender-specific and gender-inclusive) impacts of HIV, as well as bring in a decade-worth of updated findings from included peer-reviewed literature to further guide decisions around HIV prevention and implementation strategies for these communities.

For our systematic review and meta-analysis protocol, we aim to review global HIV inequities among transgender and non-binary populations. Our main review questions include: (1) What are the pooled HIV, PrEP and ART estimates (eg, testing, incidence, prevalence, uptake and adherence) among trans and non-binary adults worldwide? (2) How do these estimates differ by gender identities (eg, transfeminine, transmasculine and non-binary) and global regions? and (3) How do these estimates differ by outcome report (ie, self-report vs lab-confirmed)?

METHODS

This protocol follows the Preferred Reporting Items for Systematic Review and Meta-Analysis Prereporting guidelines.[30] The guidelines and search strategy can be found in the online supplemental appendix. The protocol is registered in the International Prospective Register of Systematic Reviews database (PROSPERO ID: CRD42022357285; 11 September 2022). Future

modifications of the systematic review or meta-analysis will be reflected on PROSPERO.

Patient and public involvement

None. Neither patients nor the public were involved in this manuscript, as it is a systematic review of prior literature.

Study population, intervention(s), exposure(s), outcome(s)

We will conduct a systematic review of all studies that reported HIV outcomes with trans youth and adults of reproductive age (15+years) published between 2000 and 2024. All known epidemiologic exposures of HIV will be accounted for, including but not limited to condomless sex, needlestick injury, blood transfusion, breastfeeding, etc. The primary outcomes of interest are the prevalence or incidence of HIV diagnosis (both self-report and confirmed lab testing diagnoses), with secondary outcomes including HIV prevention methods such as PrEP and ART use. When possible, findings will be disaggregated by self-report versus confirmed lab testing diagnoses.

Search strategy

We will use online databases of PubMed, Ovid MEDLINE, Embase, PsycINFO, Global Health, Scopus, Sociological Abstracts, Web of Science, Global Medicus Indicus, Cumulative Index to Nursing and Allied Health Literature, POPLine and LexisNexis for peer-reviewed studies published in English, dated from 1 January 2000 to 1 February 2024. Search terms and strategies for all the databases are listed in the online supplemental appendix. Our initial search began in 2022. Our anticipated end date for this review is December 2026. We will search for Medical Subject Headings (MeSH) terms related to (a) HIV and AIDS outcomes (mainly prevalence and incidence), (b) PrEP (eg, willingness and uptake), (c) ART (eg, uptake and adherence) and (d) transgender and non-binary populations. Conference abstracts will be found by searching online archives of relevant conferences, such as the International AIDS Conference and the Conference on Retroviruses and Opportunistic Infections. Using relevant HIV review articles, we will search reference lists manually to include studies that may have been missed.

Inclusion/exclusion criteria

We will include all studies in the review that meet the following criteria:

1. Report data on HIV outcomes (table 1) among transgender participants aged 15 years or older, including those who are in the spectrum of transfeminine, transmasculine and non-binary gender identities, either by self-report or clinician diagnosis of gender dysphoria.
2. Original peer-reviewed research of any design that includes quantified HIV measures.
3. Report disaggregated data on transgender adults. We will include relevant data reporting transgender identities in the context of other cultures.
4. Report data on HIV point estimates (eg, prevalence and incidence).
5. Published between 1 January 2000 and 1 February 2024.

Table 1 HIV outcome data collected

HIV	PrEP	ART
► Prevalence point estimate ► Incidence point estimate	► Awareness and knowledge ► Willingness and acceptability ► Initiation, utilisation and uptake ► Adherence	► Initiation, utilisation and uptake ► Adherence (viral load and CD4 count) ► Retention

ART, antiretroviral therapy; PrEP, pre-exposure prophylaxis.

Studies with the following characteristics will be excluded from this review:

1. Studies that did not report disaggregated data on transgender individuals, such as participants who are cisgender, children/non-adults (aged <15 years) and intersex individuals who are not trans, or those that combined transgender participants with other non-trans groups.
2. Non-peer-reviewed articles.
3. If HIV point estimates (eg, prevalence and incidence) are presented in another included study, remove duplicates.
4. Studies with sample sizes under 50.
5. Studies not in English.

Screening and selection

We will use Covidence software for title and abstract screening, full-text review and data abstraction processes. We will also consider using an AI-supported data extraction tool called Elicit to explore new methods for this review. A data extraction form will be created to systematically record data. Reasons for exclusion will be documented. Two reviewers will independently perform title and abstract screening of potentially eligible studies until they establish consensus. Articles selected for inclusion by both reviewers will proceed to full-text review. Additionally, two independent reviewers will review full texts. Disagreements will be discussed until a consensus is reached, and a senior author will resolve any disagreements in both screening stages.

Data abstraction

We will extract study-level and participant-level data. Study-level data will include study characteristics, such as year of publication, setting/region, study type, study design, sample size and exposures/outcomes; and study methodologies, such as participant recruitment and engagement approaches and methods of collecting participant demographic, exposure and outcome data. Participant-level data will include frequency (count and percentage) of age, gender identity, race and ethnicity,

and other demographic data (eg, socioeconomic status), as well as HIV diagnosis (self-report vs confirmed lab testing diagnoses), PrEP and ART outcomes. Data abstraction and quality checking will be completed by at least two independent reviewers, and discrepancies will be resolved by a senior author.

Data synthesis and analysis

We will summarise the study's descriptive statistics and conduct meta-analyses of the data points we extract to calculate and synthesise pooled findings and effect size. Specifically, we will use the Mantel–Haenszel method with random effects to model our meta-analyses and the DerSimonian and Laird Q test for heterogeneity testing. Forest plots will be created to display findings. Analyses will be conducted in Stata.

To assess the risk of bias, we plan to use the Cochrane Risk of Bias 2.0 tool for RCTs, the ROBINS-I for non-randomised studies of interventions, the ROBINS-E for non-randomised studies of exposures and the Joanna Briggs Institute Prevalence Critical Appraisal Tool for assessing prevalence and incidence data. Two independent reviewers will assess each article for risk of bias at 20% until they establish consensus, and a senior author will resolve any disagreements. Differences will be resolved through discussion between reviewers and the senior author. Thereafter, all included studies will be assessed for risk of bias by one reviewer.

Finally, we will conduct a narrative synthesis when meta-analyses cannot be performed, focusing on the areas of research that have been conducted to improve HIV prevention and treatment among trans populations and summarising their findings. Subgroup analyses by gender identity and global region[31] will be conducted. Additionally, we will aggregate PrEP use and ART use across studies and run a moderator analysis with the proportion of trans individuals on GAHT as a moderator.

DISCUSSION

Our systematic review and meta-analysis aim to summarise the pooled HIV, PrEP and ART estimates among trans and non-binary adults worldwide, stratify these estimates by gender identity and by global regions, and assess differences by self-report versus lab-confirmed findings. While a considerable amount of HIV research and surveillance focuses on trans populations, there are concerns about research practices alienating, exploiting or re-traumatising the communities that are intended to benefit from this work.[32 33] Our systematic review and meta-analysis seek to critique these methodological and ethical concerns, fill existing gaps in the literature by including a more expansive definition of gender identity and incorporating a decade-worth of updated findings and provide a framework for ethical and trans-centred HIV research practice.[32] The results of this review will be published in a peer-reviewed journal and will further guide decisions around HIV prevention and implementation strategies for trans communities. We will summarise our findings by using a gender-inclusive and gender-specific approach when necessary to elucidate shared versus unique contexts and recommendations for addressing HIV inequities across and within each gender group to help inform programme design and policy. These findings will be disseminated via academic publications and conferences in addition to non-academic settings, such as community-based organisations and community-related events in HIV advocacy.

ETHICS STATEMENTS

Ethics approval is not applicable for this review since we will not be collecting original data. The results will be disseminated through peer-reviewed publication and conference presentations. This review will further guide decisions around HIV prevention and implementation strategies for trans communities.

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Contributors AR, RM and DO conceptualised the protocol. All authors made substantial contributions to the conception and design of the study. RL led the writing of this protocol. All authors were major contributors to the writing of this protocol. HR led the search strategy. All authors read and approved the final manuscript. AR is responsible for the overall content as guarantor.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

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