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Protocol for a systematic review of substance use and misuse prevalence and associated factors among transgender and non-binary youth living in the USA

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ABSTRACT

Background Transgender and gender non-binary (TNB) youth living in the USA report elevated levels of substance use compared with their cisgender counterparts, with previous literature pointing to minority stressors as some of the factors that could facilitate such elevated levels. Yet, substance use and misuse prevalence and associated modifiable factors among TNB youth are not fully known. The current paper details the protocol for a systematic review aimed at (1) identifying substance use and misuse prevalence among TNB youth (ages <25) and related demographic disparities (based on racial, ethnic and gender identity, and sexual orientation), (2) examining factors associated with substance use and misuse among TNB youth and (3) examining protective factors against substance use and misuse among TNB youth.

Methods and analysis Systematic searches will be conducted across four databases: PubMed, LGBTQ+ Source, CINAHL and PsycInfo to identify quantitative, qualitative and mixed-methods peer-reviewed research publications. An exhaustive list of keywords and corresponding MeSH (Medical Subject Headings) terms representing the concepts of ‘TNB’ (the population of interest) and ‘substance use and misuse’ (outcome) will be employed. Identified records will be initially screened via a review of titles and abstracts. Full text of the remaining records will be reviewed corresponding to the inclusion and exclusion criteria. Extracted data will be synthesised in table and narrative format. A meta-analysis will be considered contingent on the existence of sufficient data. Methodological quality and risk of bias of studies will be assessed.

Ethics and dissemination This review does not require approval from the Institutional Review Board as it involves no interactions with human subjects. We will disseminate our findings via peer-reviewed manuscripts and academic conference presentations.

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Transgender and gender non-binary (TNB) persons in the USA experience poorer substance use outcomes, patterns and prevalence in comparison with their cisgender counterparts. Specifically, TNB persons, in comparison to cisgender persons, have reportedly higher prevalence of nicotine, alcohol and illicit drug use and related disorders. A study of college students identified higher frequency and quantity of alcohol use in addition to higher number of alcohol-related social, academic and health repercussions among transgender students relative to cisgender college students. Similar findings have been demonstrated among school-aged youth as well. For instance, in a comparison study of transgender and cisgender youth in the state of California, findings illustrated that transgender youth used alcohol, cigarettes, cannabis, and other illicit substances at higher rates than cisgender youth.

The gender minority stress model theorises that the disparities in substance use outcomes of TNB persons could be explained through exposure to minority stressors. In other words, the model posits that in addition to general stressors in the lives of all persons, gender minorities are subjected to minority stressors. Three types of minority stressors are introduced as part of this model: distal stressors (eg, discrimination, violence, gender non-affirmation), anticipation and expectation stressors (ie, expectancy of distal...
stressors, resulting in fear and rejection expectation) and proximal stressors (ie, internalisation of distal stressors, internalised transphobia). Accordingly, the model posits that more experiences with minority stressors would lead to poorer mental health and increased substance use. Conversely, the model also introduces stress-ameliorating factors (eg, social support) that could moderate this relationship.

TNB persons, including youth, living in the USA report experiencing minority stressors at alarming high rates in many facets of their lives. As an example, a national survey of students identified that transgender youth report high levels of discrimination and bullying at their schools, with around 80% of transgender students across the nation reporting feeling unsafe and experiencing harassment or assault at school due to their transgender identity. In addition, this survey highlighted that transgender youth experience higher levels of physical and verbal assault compared with cisgender youth at their schools. Recently, increasing number of US states have also enacted policies and laws aimed at limiting the civil rights of transgender youth and young adults. Much of transphobic legislative efforts in many US states focus on prohibiting TNB youth from playing in sports or using restrooms that align with their gender identity, limiting the discussion of sexual and gender identity in schools in addition to criminalising the use of potentially life-saving gender affirming care such as hormone blocker treatment used by transgender youth.

Supporting the primary tenets of the gender minority stress model, previous literature has identified a link between victimising experiences and increased substance use among transgender youth. Preliminary evidence also points to an increased use of substances as a coping mechanism employed to deal with experiences of transphobic violence. Recent systematic reviews and meta-analyses focusing on transgender adults have also identified similar substance use disparities. Yet, to the best of our knowledge, no systematic reviews have focused on the factors associated with substance use and misuse or related protective factors among TNB youth to date. Systematic reviews and meta-analysis inclusive of TNB youth to date have reviewed studies that assess mental health outcomes and healthcare access. Considering the increased identification with non-cisgender identity among youth in addition to increased exposure to minority stress factors among TNB youth, it is critical to understand the prevalence of and factors associated with substance use and misuse among this population. Of equal importance is to be explicit about the fact that TNB youths’ experiences with minority stressors or substance use behaviours are not monolithic. Growing literature points to disparities in this community, with evidence suggesting sexual, racial and ethnic minority TNB youth as well as young transgender women and girls facing disproportionately higher minority stressors. Recognising the diverse experiences of TNB youth in the USA that transcend their gender identity, examining within group demographic disparities is necessary to gain a complete understanding of the complex substance use related burdens that TNB youth living in the USA face.

**OBJECTIVE**

The current paper details the protocol for a systematic review aimed at (1) identifying substance use and misuse prevalence among TNB youth (ages <25) and related demographic disparities (based on racial, ethnic and gender identity, and sexual orientation), (2) examining modifiable factors associated with substance use and misuse among TNB youth and (3) examining modifiable protective factors against substance use and misuse among TNB youth. The proposed systematic review will synthesise evidence with the goal of informing best practices for providing substance use services to TNB youth. The proposed systematic review will answer the following research questions:

1. What is the prevalence of substance use and misuse among TNB (ages <25) living in the USA?
2. How does substance use and misuse prevalence vary among TNB youth (ages <25) living in the USA, based on race, ethnicity, gender, and sexual orientation?
3. What are the modifiable factors associated with substance use and misuse among TNB youth (ages <25) living in the USA?
4. What are the modifiable protective factors against substance use and misuse among TNB youth (ages <25) living in the USA?

**METHODS AND ANALYSIS**

**Protocol reporting guidelines and registration**

We report this protocol using the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) checklist (online supplemental appendix 1). This systematic review protocol has been registered on PROSPERO.

**Patients and public involvement**

There will be no direct involvement with TNB youth as part of this systematic review.

**Ethics and dissemination**

This systematic review does not require approval from the Institutional Review Board as it involves no interactions with human subjects and is focused solely on analysis of published data. The dissemination of findings of the current systematic review will be in the form of peer-reviewed manuscripts and academic conference presentations.

**Criteria for including studies**

**Types of studies**

The types of studies examined as part of this systematic review will include longitudinal and cross-sectional quantitative (experimental, quasi-experimental), qualitative and mixed-methods studies. Published work consisting of synthesis of
evidence such as meta-analyses, and systematic, mini, and scoping reviews will not be examined as part of this review.

Inclusion and exclusion criteria
The current review will only include peer-reviewed work published in English based on a sample of TNB youth (<25) living in the USA. Center for Disease Control and Prevention definition of youth is followed.35 Partly informed by the systematic review conducted by Cotaina and colleagues, studies will only be included if the study outcomes pertain to substance use, misuse, abuse, consumption, dependence, addiction or substance use disorders.3 Further, studies that include participants above the age of 25 will only be included if they disaggregate findings for those below the age of 25. Similarly, research focused on sexual and gender minorities will only be included if it disaggregates findings by gender identity. Studies published prior to 2006 will be excluded given the unavailability of surveys inquiring about gender identity related to transgender populations prior to this year.36 Articles published based on samples of youth residing outside of the USA will also be excluded, as the experiences of TNB persons related to their race, ethnicity, gender identity and other characteristics may be specific to social, cultural and legislative context of the country of residence. No constraints will be placed based on sample size or methodology employed in any of the studies.

Outcomes
The current systematic review will have the following main outcomes:

- We will examine the prevalence of substance use and misuse among TNB youth living in the USA as well as related demographic disparities based on racial, ethnic and gender identity, and sexual orientation.

Substances of interest include but are not limited to alcohol, nicotine (including e-cigarettes, vapes), cannabis, sedatives (e.g., opioids, benzodiazepines), stimulants (amphetamine, methamphetamine, crack, cocaine) and club drugs (e.g., MDMA/ecstasy, GHB, poppers). Behavioural patterns of interest related to substance use, misuse, abuse, consumption, dependence, addiction or substance use disorders will be examined.

- We will investigate modifiable facilitators of substance use and misuse and modifiable factors considered protective against substance use and misuse among TNB youth.

Search strategy
Literature search will be conducted by a research librarian at the University of Maryland Baltimore Health Sciences and Human Services Library (HSHSL) using search terms developed through the HSHSL database. Systematic searches will be conducted using four databases: PubMed, LGBTQ+ Source, CINAHL and PsycInfo. Table 1 presents the search terms that will be used in PubMed as an example (see online supplemental appendix 2 for the list of search terms on all four databases).

Search terms represent two main concepts: TNB identity (the population of interest) and substance use and misuse (outcome of interest). Considering the diversity of terms used in relation to the members of the TNB community, numerous variations of the terms describing TNB persons were deemed necessary. Considering the population of interest included TNB youth under the age of 18 and adults under the age of 25, terms such as ‘youth’ and ‘children’ were not included as keywords. The search terms around the concept of substance use and misuse were chosen to be as extensive as possible without placing any restrictions based on substances. To the best of authors’ knowledge, the search terms used around the concepts of TNB identity and substance use are consistent if not more encompassing than previous systematic reviews and meta-analysis on the health of transgender community members to date.23 26 28 39

Reference lists
This systematic review will also involve a search of the reference lists of all included studies for additional articles that may meet the eligibility criteria.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Search terms on PubMed</th>
</tr>
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<tbody>
<tr>
<td>Terms for gender</td>
<td>Terms for substance use</td>
</tr>
<tr>
<td>Transgender(title/abstract); Transfeminine; Transmasculine; Transsexual; Gender variant; Gender non-conforming; Gender diverse; Genderqueer; Gender non-binary; Gender minority; Gender identity disorder; Transwoman; Transman; Non-binary; Gender fluid; Gender dysphoria; Gender identity; Gender expansive; Two-spirit; MeSH: Sexual and gender minorities; Transgender persons</td>
<td>Substance; Substance induced disorder; Substance related disorder; Drug use disorder; Drug substance disorder; Alcohol; Addict; Oral substance abuse; Intravenous substance abuse; Intravenous substance use; Risky use of alcohol; Excessive drinking; Alcohol induced disorder; Alcohol related disorder; Binge drinking; Smoking; tobacco; Cigarette; Nicotine; Vape; Vaping; Cocaine; Cocaine related disorder; Heroin; Opioid; Opioid related disorder; Amphetamine related disorder; Marijuana; Cannabis; Opiate use; Prescription drug abuse; Prescription drug misuse; Illegal substance; Illicit drug; Narcotic related disorder; Harmful substance use; Inhalant abuse; MSMA; Methamphetamine; Amphetamine; Overdose; Chemical dependent; Substance addiction; Heavy drinking; Heavy episodic drinking; Drug dependence*; E-cigarette; ‘opiate’; MeSH: Substance-related disorders</td>
</tr>
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MeSH, Medical Subject Headings.
Grey literature

Grey literature, including dissertations, theses, behavioural and public health conference proceedings as well as published reports by nonpartisan organisations will not be considered as part of this review.

Screening

As a mechanism for ensuring that screening and selections avoid repetition, the authors will be importing citations into Covidence software to remove duplicates. Pilot testing will include the use of a screening form used by three teams of two individuals to independently review a sample of titles and abstracts. A Cohen’s kappa statistic set at 95% will be used for measurement of interrater reliability. Only articles that meet this threshold will be included in the full review.

Prior to data extraction, all potentially relevant articles will be retrieved and screened in full detail by the three independent teams of two. If any disagreement occurs throughout this process, consensus will be the method employed to reach a resolution. Should consensus not be reached, the principal investigator will mediate the disagreement.

Data extraction, analyses and reporting

Procedures outlined by the PRISMA will be followed for reporting of the findings. Three authors, TM, DLW and LJ M will engage in data extraction using Covidence. Table 2 details the data that will be extracted from each study. Tables and narratives will be used to summarise findings. Quantitative data will be synthesised via meta-analysis conducted on Stata V.17 SE, if sufficient data exists. Assuming heterogeneous true effects, a random-effects modelling will be used. Following recommendations provided by the Cochrane Handbook for Systematic Reviews of Interventions, we will examine heterogeneity via $I^2$ statistics and a forest plot to discern sources of heterogeneity. Subgroup analyses will be conducted quantitatively (contingent on the existence of sufficient data) or narratively based on gender, race and sexual orientation. Substance use and misuse prevalence will be grouped corresponding to demographic characteristics (ie, racial and ethnic identity, gender identity and sexual orientation). Further, data will be grouped based on type of factors. These groupings will include facilitators of substance use and misuse and protective factors against substance use and misuse. If possible, these factors will be grouped according to the constructs outlined by the gender minority stress model (ie, distal stressors, proximal stressors, stress-ameliorating factors). Meta-synthesis approach will guide the synthesis of qualitative literature. Using an inductive approach, findings will be re-interpreted and organised to develop more generalised themes and narratives.

The number of studies, research design and type, methodological quality, as well as relevant findings will be presented in a table format. Data synthesis, identification of prevalent themes, methodological quality and gaps in knowledge will be in the narrative format. Quality appraisal of quantitative literature will be conducted using the Strengthening the Reporting of Observational Studies in Epidemiology Statement Checklist whereas risk of bias (RoB) will be assessed via the Hoy and colleagues RoB checklist. Consolidated Criteria for Reporting Qualitative Research and Enhancing Transparency in Reporting the Synthesis of Qualitative Research will be used in quality appraisal of qualitative literature. For evaluation of mixed methods literature, Mixed Methods Appraisal Tool will be employed.

Strengths and limitations

The proposed systematic review comes at a time when TNB youth face increasingly hostile minority stressors and reduced access to moderating resources, underscoring the necessity of the review. Another strength of
the proposed review is its employment of a deliberately expansive inclusion criteria, allowing for all pertinent and available literature to be included. The proposed review is not without limitations, as the scope of the review is limited to TNB youth living in the USA. Although this limitation is purposeful considering the importance of geographical context, it, nevertheless, excludes growing literature focused on the experiences of TNB youth living outside the USA. In the same vein, literature published in languages other than English will be excluded, marking another limitation. Thus, the generalisability of the review will be limited.

**DISCUSSION**

Due to transphobia, TNB youth are more likely to be exposed to harassment, discrimination and victimisation compared with cisgender youth. A recent study found TNB youth are six times more likely to report gender-based bullying in schools. Furthermore, transgender youth are also more likely to report cyber bullying with 30% of transgender youth reporting cyberbullying in one study. In addition to bullying, TNB youth are more likely to report being involved in physical fights, property damage and physical injury compared with cisgender youth.72

Exposure to harassment and victimisation has been linked to poor mental health outcomes among TNB youth. A recent study found that TNB youth who experienced bullying were at greater risk for depression and suicidality.50 The relationship between exposure to harassment and victimisation and poor mental health outcomes among TNB youth can be understood through the gender minority stress model. Gender minority stress model suggests TNB individuals experience stressors related to their gender identity and may lead to poor mental health. Previous research suggests substance use among TNB youth may be associated with experiences of transphobia.22 The proposed systematic review seeks to examine the prevalence of substance use and related demographic disparities among TNB youth in the USA. At present, there are over 300 pieces of legislation seeking to further marginalise and oppress TNB youth across the country. As previously suggested, increased experiences of oppression may have debilitating effects on the mental health of TNB youth. This systematic review has significant potential public health impact, given the current national climate related to TNB youth rights.

**Contributors** TM is the principal investigator and conceptualised the study. GB developed the search strategy in collaboration with TM and with input from DLW. DLW drafted the ‘Discussion’ section and supervised the manuscript preparation process. L-JMM drafted the ‘Screening’ section. All authors contributed substantively to manuscript writing and reviewed the finalised manuscript prior to submission.

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**Competing interests** None declared.

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

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data sharing not applicable as no data sets generated and/or analysed for this study.

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