The mental health of trans and gender diverse populations: an umbrella review of systematic review with or without meta-analysis

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Abstract

Aims: This umbrella review aimed to comprehensively assess the prevalence of mental disorders, suicidal behaviors, substance use, and other mental health conditions among trans and gender-diverse (TGD) populations. It sought to provide a synthesized overview of existing systematic reviews and meta-analyses, shedding light on the mental health challenges faced by TGD individuals.

Methods: A systematic literature search was conducted in PubMed, Embase, PsycInfo, CINAHL, Web of Science, Scopus, LILACS, and Cochrane Library. The search covered studies from database inception to search date (January 27, 2023). The inclusion criteria required that systematic reviews and meta-analyses had reported prevalence rates of mental disorders, suicidal behaviors, substance use, and related conditions among TGD populations. The selection process, quality assessment using AMSTAR-2, and data extraction were performed by two independent assessors.

Results: The review identified 21 systematic reviews and 2 meta-analyses that met the inclusion criteria. Only two SRs used structured clinical interviews to establish diagnoses of mood disorders, substance use (disorders), and other mental health conditions, whereas the other SR/MAs used mixed assessment methods (diagnostic interviews and self-report measures), or self-report measures only.

Findings revealed high prevalence rates of mood disorders, anxiety disorders, and suicidal ideation and attempts among TGD populations. Substance use, particularly tobacco and illicit drug use, was also prevalent. Additionally, other mental health conditions, such as post-traumatic stress disorder (PTSD) and eating disorders, were observed. The included reviews exhibited varying quality levels.

Conclusion: The umbrella review revealed a high burden of mental health challenges among TGD populations, with high prevalence rates of mood disorders, anxiety disorders, substance use, and suicide-related behaviors. Findings of this review should be taken with caution considering the large variability in the quality of the studies, use of self-report instruments instead of structured clinical interviews, different assessment measures, outcomes, and subgroups of TGD individuals, and lack of relevant comparison groups or randomly selected samples. Nevertheless, this umbrella review underscores the need to address the mental health disparities experienced by TGD individuals. The prevalence of mental disorders, suicidal behaviors, and substance use among this population emphasizes the importance of developing and implementing inclusive and affirming care approaches

to mitigate the mental health challenges faced by TGD individuals due to societal struggles such as discrimination and violence. Additionally, it highlights the necessity for further high-quality research to better understand and address the complexities of mental health within the TGD community.

Key words: transgender, gender-diverse, mental health, prevalence, systematic review, meta-analysis.

1. Introduction

An estimated 0.3-0.5% of adults identify themselves as transgender (TG) and 0.5-4.5% as gender-diverse (Zhang et al., 2020). Transgender people are people whose gender identities and/or gender expressions are not what is typically expected for the sex to which they were assigned at birth, whereas gender-diverse people have gender identities and/or expressions that are different from social and cultural expectations attributed to their sex assigned at birth (Coleman et al., 2022). Transgender people may self-identify as TG, female, male, trans women or trans man, transsexual, nonbinary or one of many other gender-diverse identities. Genders may be expressed in a variety of masculine, feminine, and/or androgynous ways among trans and gender diverse (TGD) populations (Coleman et al., 2022). Conversely, the term "cisgender" describes individuals whose gender identity and expression align with their assigned sex at birth (Reisner et al., 2016). Additionally, the term "non-binary" is used to describe individuals whose gender identity, role, or expression does not fit into the traditional binary gender categories of male or female and may include those who identify as both or neither gender (e.g., bigender and pangender) (American Psychological Association [APA], 2015; Coleman et al., 2012; Nakamura et al., 2022).

The terminology used to describe individuals who are TG or gender diverse (GD) has undergone significant changes over the years and continues to evolve rapidly (Chang et al., 2018; Coleman et al., 2012). Historically, terms that were once used in medical and psychological fields are now considered pathologizing or reductionist and have been replaced (e.g., transsexual by TG, and gender identity disorder by gender dysphoria; (APA, 2013)). In the most recent version of the International Classification of Diseases (ICD-11, World Health Organization), gender incongruence was moved from the mental health chapter to a chapter for sexual and gender health.

TGD individuals have been found to be at increased risk for adverse mental health outcomes, such as depression (Scheim et al., 2020), posttraumatic stress disorder (PTSD; (Marchi et al., 2023)) suicidal behaviors (James, 2016; Rimes et al., 2019; Yıldız, 2018) and substance use (Cotaina et al., 2022). The high incidence of mental disorders found among TGD people has been explained by the minority stress model (Hendricks & Testa, 2012; Meyer, 2003), suggesting that being a member of a stigmatized minority, increases exposure to social stress, which in its turn increases the risk for mental

health problems, substance use, and suicidal behaviors; see Hendricks and Testa (2012) for an overview. Testa et al. (2015) introduced the term “nonaffirmation” which is when TGD individuals' internal gender identities are not acknowledged or affirmed by others. This lack of affirmation can be particularly pronounced for those who identify as genderqueer and may vary based on how their gender expression is perceived in different social contexts, which feeds into gender minority stress. Indeed, studies have shown that TGD people may be confronted with profound social exclusion, encompassing rejection by family, discrimination in various spheres of life, and bullying in educational and workplace settings. Familial rejection is particularly debilitating as it often results in the loss of a foundational support system, further exacerbating feelings of isolation and vulnerability (Bockting et al., 2013). Discrimination in areas such as education, employment, housing, and public accommodations is pervasive, and it not only limits the opportunities available to TGD people but also amplifies their exposure to socioeconomic stressors and other proximal stressors (Lefevor et al., 2019). The phenomenon of social exclusion is not merely an ancillary factor; it is postulated to play a pivotal role in the mental health disparities observed among the TGD population (Lefevor et al., 2019; Tan & Saw, 2022). This reinforces the importance of creating supportive and inclusive environments for people experiencing discrimination to buffer against these detrimental outcomes. In addition, for people who are experiencing adverse mental health impacts as a result of discrimination, access to effective support for their health should be in place.

However, there are still many uncertainties regarding the prevalence rates of mental disorders, suicidal behavior and ideation, and substance abuse among TGD populations. First, reported prevalence rates have been found to vary greatly between studies. This may be explained by variability between studies, for example in the types of samples studied (e.g., trans women only vs. a more heterogeneous sample of GD people, and people seeking gender affirmative care vs. a random population sample), the type of instruments used (e.g., diagnostic interviews vs. self-report instruments), of which accuracy may also differ across populations and cultures. Second, there are indications that specific mental disorders may be more prevalent among TGD populations (Lefevor et al., 2019), whereas others such as substance use disorders (SUDs) may not (Cotaina et al., 2022). Improving clarity about the prevalence and burden of mental disorders among TGD populations will

outline the need for targeted services for the TGD population to address mental health, the need to support health workers in improving competency to support the mental health of TGD populations and to consider mental health and substance use in gender affirmative care.

This umbrella review examined the burden by compiling the available published data on prevalence rates found across systematic reviews and meta-analyses (SR/MAs) of (1) (symptoms of) mental disorders, (2) suicidal behaviors and suicidal ideation, and (3) substance use, and substance use disorder among trans and gender-diverse populations.

2. Methods

This umbrella review comprises a narrative summary based on data extracted from SRs/MAs for three outcomes and is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (www.prisma-statement.org). The study was pre-registered at the Open Science Framework OSF (https://osf.io/ykp2t), ↗,) and was a collaborative effort between Vrije Universiteit Amsterdam (VU), Amsterdam UMC Medical Psychology, and the WHO Department of Mental Health and Substance Abuse.

2.1 Search strategy

A literature search (in PubMed, Embase, PsycInfo, CINAHL, Web of Science, Scopus, and Cochrane Library) was performed on January 27, 2023 from inception up to January 27, 2023 and LILACS on and up to April 17, 2023, in with a medical information specialist at Vrije Universiteit Amsterdam. The following terms were used (including synonyms and closely related words) as index terms or free-text words: "Transgender", "Suicide", "Substance-related disorders", "Mental disorders", "Systematic reviews", "Meta-analysis".

The references of the identified articles were searched for relevant publications. All languages were accepted. Duplicate articles were excluded by a medical information specialist using Endnote X20.0.1 (Clarivate^{tm}), following the Amsterdam Efficient Deduplication (AED)-method (Otten et al.,

2019) and the Bramer-method (Bramer et al., 2016). The full search strategies for all databases can be found in Appendix A / Supplementary material.

2.2 Eligibility criteria

SRs/MAs of cross-sectional or longitudinal studies were considered eligible for inclusion in the review if they met the following criteria: 1) selection criteria had been reported; 2) at least one bibliographical database had been searched systematically; 3) a list and synthesis of included studies had been provided; and 4) prevalence rates or mean symptom scores of any mental disorder based on a validated diagnostic interview or proportion of participants above a cut-off on an established and/ or validated mental health symptom questionnaire on a single time-point were reported and possible to be extracted for TGD populations separately; 4) the participants/populations in eligible studies were: a) trans and gender-diverse people, as defined[1] by WHO as "those whose gender identity, roles or expression does not conform to the norms and expectations traditionally associated with the sex assigned to them at birth; it includes people who are transsexual, transgender, or otherwise gender diversity or gender incongruent". TG people may self-identify as transgender, female, male, trans women, or trans man, transsexual, or one of many other gender-nonconforming identities. They may express their genders in a variety of masculine, feminine, and/or androgynous ways[1]; and b) at least 50% of the study population in the included primary studies were adults (>16). Further, 5) eligible SR/MAs should report on the following outcomes: a) Prevalence or mean symptom scores of any mental disorder based on a validated diagnostic interview or proportion of participants above a cut-off on an established and/ or validated mental health symptom questionnaire on a single time-point. Prevalence rates or mean symptom scores at pre-intervention were reported for SRs/MAs that were a treatment outcome study (e.g., of gender affirmative care); b) Incidence/prevalence of suicide and/ or suicidal behavior (dichotomous scores of suicide deaths or attempted suicides, self-harm or suicidal behavior), or proportion of participants above a cut-off or mean symptom scores on a validated suicidal behavior, suicidal thoughts, suicidal ideation or self-harm questionnaire; c) Prevalence of any

[1]WHO Guidelines on the health of trans and gender diverse people; Guideline Planning Proposal (2022); pending approval.

substance-use related or addiction-related disorders based on a validated diagnostic interview or proportion of participants above a cut-off or mean symptom scores on a validated mental health symptom questionnaire on a single time-point. Prevalence rates or mean symptom scores at baseline in treatment outcome studies (e.g., gender affirmative care) were reported for SRs/MAs that included studies of a longitudinal design. However, pre- and post-changes after gender affirmative care were not reported.

All eligible reviews published since database inception from any geographical area worldwide were included without language restrictions. The non-English language titles, abstracts, and full text for eligible articles were assessed by team members native in the respective languages. Only peer-reviewed articles were included, and pre-prints were not considered. Studies that did not have a systematic search were also excluded.

2.3 Selection process

The selection of eligible systematic reviews was performed using Rayyan (https://rayyan.ai). Before the selection process was initiated, the eligibility criteria and the procedure for including and excluding articles were discussed with the research team and the medical information specialist. All titles and abstracts were screened independently by two reviewers (M.E. and Z.Z.), and any citations deemed potentially eligible by either reviewer were later reviewed in full text. Later, the two reviewers conducted the full-text review separately for each research question. All disagreements were resolved via consensus and discussion between the two reviewers and the project supervisor.

2.4 Data extraction and synthesis

After the inclusion/exclusion process of eligible articles was completed, data extraction for each full SR/MA was conducted independently by the two reviewers (M.E. and Z.Z.). The following general characteristics were extracted for the included studies: title/authors, year of publication, study designs of included primary studies, number and main characteristics (inclusion criteria) of included participants/population, the language of included primary studies, inclusion and exclusion criteria of included primary studies, country of included primary studies, quality assessment and publication bias

of included primary studies, heterogeneity, type of assessment used in the included primary studies, type of analysis (SR/MA), and the summary of results (pooled mean change/ summary estimate/ prevalence). The two reviewers completed the data extraction independently and then compared the results for discrepancies. All discrepancies were resolved via consensus and discussion between the two reviewers and the last author (M.S.). In reporting and synthesizing the data, we prioritized the SR/MAs with stronger methodologies over those with weaker methodologies, that is SR/MAs that included only studies with prevalence rates based on clinical diagnostic instruments (e.g., Structured Clinical Interview for DSM-5 Disorders–Clinician Version; (SCID), Mini-International Neuropsychiatric Interview (M.I.N.I.) Composite International Diagnostic Interview (CIDI), or disorder-specific interviews) instead of self-report instruments, studies on TGD populations that included a comparison group (e.g., cisgender people) or used a probability sampling approach.

2.5 Quality Assessment

The quality of the included studies was assessed using an adapted version of the AMSTAR-2 tool (Shea et al., 2017). Two reviewers (M.E & Z.Z) independently evaluated sixteen core features of methodological quality. The AMSTAR-2 tool was originally adapted for umbrella reviews by Witteveen et al. (2023) and was further adapted for the current umbrella review. This adaptation was necessary due to the predominant inclusion of systematic reviews without meta-analysis (n=21). To address this, we introduced the option "no meta-analysis conducted" into item 9, which pertains to the assessment of risk of bias (RoB) in individual studies included, and item 14, which deals with explaining and discussing observed heterogeneity in the review results. Notably, items 9, 11, 12, 13, 14, and 15 were exclusively scored for inclusions that performed a meta-analysis (n=2). While the original AMSTAR-2 tool prioritizes a critical score (Shea et al., 2017), it is important to note that there has been much debate regarding this approach. Therefore, for each included review, we also calculated the total score, as shown in Table 1. In keeping with the AMSTAR-2 scoring protocol, seven specific items were considered critical: item 2 (prior establishment of review protocol), item 4 (comprehensiveness of search strategy), item 7 (list of excluded studies with justification), item 9 (assessment of Risk of Bias (RoB) using satisfactory techniques), item 11 (appropriateness of meta-

analysis methods), item 13 (discussion of RoB in interpretation of findings), and item 15 (investigation and discussion of publication bias).

The quality of the SR/MA was classified as having a critical flaw when not meeting any of the seven critical AMSTAR-2 items, whereas not fulfilling the remaining AMSTAR-2 items was classified as a 'non-critical weakness'. Reviews received a "high" quality rating when having no or one non-critical weakness, a "moderate" quality rating when having more than one non-critical weakness, "low" quality when having one critical flaw with or without non-critical weaknesses, and "critically low" when having more than one critical flaw with or without non-critical weaknesses. Discrepancies were resolved by consensus and after discussion with another review team. An overview table of (quality) characteristics of selected SRs/MAs for each key question was developed.

3. Results

3.1 Search Results

The literature search generated a total of 3323 references: 438 in PubMed, 1043 in Embase.com, 514 in APA PsycInfo, 322 in CINAHL, 482 in Web of Science, 466 in Scopus, 5 in Cochrane Library and 53 in LILACS. After removing duplicates of references that were selected from more than one database, 1923 references remained, of which 1787 were excluded at title and abstract screening. The remaining 136 full texts were assessed by two independent researchers (M.E & Z.Z). Common reasons for exclusion were articles that did not report prevalence rates of mental health conditions, articles conflating TGD data with LGBTQIA+ data (i.e. data for TGD could not be extracted separately), or articles that reported on TGD youth only (<16). Finally, 23 articles met the inclusion criteria for the umbrella review. The flow chart of the search and selection process, including reasons for exclusion at the full-text level, is presented in Figure 1.

3.2 Characteristics of Included Studies

Characteristics of the 23 included reviews are provided in Table 1. Of the included studies, two performed meta-analyses (refs), one examined the prevalence rates of non-suicidal self-injury (NSSI; (Liu et al., 2019)) and one examined substance abuse and SUDs (Cotaina et al., 2022) and the

rest (n=21) were narrative systematic reviews. The majority of the reviews targeted the TGD population specifically (n=16), however, for studies including data on LGBTQ, LGBT or both sexual and gender minorities in one group (SGM) (n=7) data was extracted only for TGD populations. The included studies were conducted in the following WHO regions (Table 1): European region, Region of the Americas, Western pacific region, South-East Asia Region, Eastern Mediterranean region, and African region. Most studies (n=20) had no language restrictions (although none searched non-English databases); one required English, one required, English or Chinese, and one required English, Turkish, Spanish, or German.

3.3 Quality assessments

Based on the 7 critical domains of AMSTAR-2 that rate the quality assessment by outcome across all eligible systematic reviews and meta-analyses, we found that 3 out of the 23 included reviews established a priori protocol, only 1 conducted a comprehensive literature search, none of the systematic reviews with meta-analyses provided a list of excluded studies with justification. All of the included reviews with meta-analysis (n=2) used satisfactory techniques for assessment of the risk of bias in individual studies, appropriate methods for meta-analysis, discussed the risk of bias in the interpretation of findings and examined and discussed publication bias. These numbers are demonstrated in Figure 2. The total AMSTAR 2 score and sub-scores of critical items are presented in Table 1. Total scores on AMSTAR 2 ranged from 2 to 13 with a mean total score of 5.4. None of the included reviews fulfilled all the critical AMSTAR 2 ratings. AMSTAR-2 ratings for each SR/MA can be found in Appendix B/Supplementary material.

3.4 Prevalence of Mood Disorders

Nine SR were included on prevalences of mood disorders, and no MAs. No SRs were included that were strictly based on studies comparing TGD with the general population, or with random probability samples. One SR, however, reported based on one primary cross-sectional study among TG, non-binary and cisgender individuals that TG women (34.6%) and non-binary individuals (36.8% AFAB, 33.7% assigned male at birth; AMAB) exceeded the clinical cutoff score for

depression on the PHQ-9 assessment, in contrast to TG men (27.5%), cisgender females (16.1%), and cisgender males (14.1%).

Only one SR exclusively used clinical diagnostic interviews (de Freitas et al., 2020). The only SR including exclusively diagnostic interviews was that of de Freitas et al. (2020), which included studies reporting that based on a sample of 577 individuals with the then used diagnoses for ICD or DSM transsexualism/ gender identity disorder/ gender incongruence, mood disorders were 42.1% prevalent. When examining specific disorders in a sample of 228 individuals with GD, major depressive disorder, was 10% prevalent, dysthymia was 4.8%, and bipolar disorder was 1.7% (de Freitas et al., 2020).

The other 8 SRs presented prevalence rates based on a mixture of clinical diagnoses and self-report instruments. Dhejne et al. (2016) found a lifetime prevalence of mood and adjustment disorders of 56% for TG women and 70.4% for TG men as per the M.I.N.I. However, this is based on only one of their total included studies (total n = 38) with a sample of 157 trans women and 71 trans men. Regarding prevalence rates based on self-report measures, in their SR Baker et al. (2021) reported a proportion of 42.0% in a sample of 107 TGD individuals exhibited symptoms of depression when measured using the Beck Depression Inventory (BDI-II). Pinna et al. (2022) reported a lifetime prevalence of depression of 44.1%-78% among a sample of TG individuals, 13.5%-68.6% for trans women, and 9.8%-15.6% among trans men. They also found a 12-month prevalence rate of 84.4% and a 6-month prevalence rate of 73.6% among TG individuals. Regarding a current diagnosis of depression, the prevalence was 22.3% - 82% for a mixed trans group, 45.4%-80.5% for trans women, and 48.3%-87.5% for trans men (Pinna et al., 2022). Other included SRs have indicated prevalence rates of 44.1% for symptoms of depression among a mixed TG population (Drabish & Theeke, 2022) using an unspecified online survey. An SR among TGD people in South-East Asia found ranges of 19.1% - 56.0% for depression among their TG sample (Tan & Saw, 2022). Lin et al. (2021) found symptoms of depression to be 32.0% - 54.5% prevalent among of TGD people in Mainland China. Finally, in their SR Mark et al. (2019) reported that 50% of the TG military serving and ex-serving personnel in the USA, Canada, and Switzerland were suffering from depression, not specifying whether it was lifetime or a current diagnosis.

3.5 Prevalence of Anxiety Disorders

Nine of the included reviews reported prevalence rates for anxiety symptoms and disorders, but no MAs. We did not include SR/MAs with the general population or cisgender comparison groups or with random probability samples.

Prevalence rates of anxiety disorders based only on diagnostic interviews (SCID-I, MINI-Plus) were reported in a SR that included a sample of 228 individuals with GD as 26.8% for an anxiety disorder (specific phobia, adjustment disorder, generalized anxiety disorder, panic disorder, social phobia, obsessive–compulsive disorder, and agoraphobia), 10% for specific phobias, 5.7% for adjustment disorder, 5.7% for generalized anxiety disorder, and 4.8% for panic disorder (de Freitas et al., 2020).

In the SR of Dhejne et al. (2016), primary studies using a mixture of diagnostic interviews and self-report measures were reported. One of the included primary studies reported that 17%-28% of their TG population received an anxiety disorder diagnosis as per the M.I.N.I. Prevalence rates reported for specific anxiety disorders among TG individuals included 8.8% and 5.6% for generalized anxiety disorder (GAD) among trans women and trans men respectively, and 8.2% and 11.3% for social phobia among trans women and trans men individuals respectively (Dhejne et al., 2016). Seven SRs only included primary studies using self-report instruments. Baker et al. (2021) reported on one of their included prospective studies (total n=20) which examined 52 TGM and reported that 12% of trans men experienced symptoms of anxiety as per the Hospital Anxiety and Depression Scale (HADS) anxiety scores pre-gender affirming care. Other SRs have indicated prevalence rates for anxiety ranging from 17% to 68% for TG people (Millet et al., 2016), 33.2% (Drabish & Theeke, 2022). Moreover, Lin et al. (2021) reported the prevalence of any anxiety disorder among their sample of TGNC people as 28.5%-51%. Another SR reported prevalence rates of anxiety symptoms among TGW at 34.5%-40.4% and among TGM at 47.5%. In their SR examining mental health in TG individuals, Pinna et al. (2022) reported different prevalence rates for the various anxiety disorders in various TGD subgroups ranging from 7.5% to 98% %.

3.6 Prevalence of Substance Use and Substance Use Disorders

Nine studies investigated substance use and SUDs among TGD individuals. No SRs/MAs with the general population or cisgender comparison groups or random samples were found.

The only included meta-analysis based on primary studies that used self-report instruments for substance use or SUDs reported that TG people were more likely to use tobacco products (odds ratio (OR) = 1.65; 95% CI [1.37, 1.98]), have used substances throughout their lives (OR = 1.48; 95% CI [1.30, 1.68]), and have present current use of specific substances (OR = 1.79; 95% CI [1.54, 2.07]) (Cotaina et al., 2022) however, they also report that apart from the previously mentioned, there was no difference in the presence of SUDs between TG people and cis-gender people. Dhejne et al. (2016) also reported a prevalence of 30.2% of non-alcohol substance abuse/dependence among TGW using a clinical interview (MINI-2).

Three SRs included primary studies that reported prevalence rates of tobacco use, e-cigarette use (Blackwell & López Castillo, 2020), illicit drug use, heavy episodic drinking (HED) (Connolly & Gilchrist, 2020), and probability of binge drinking (Pinna et al., 2022) (see Table 2 for details). Blackwell and López Castillo (2020) reported prevalence rates of lifetime tobacco use at 53.6%, past 30-day use at 1-.2%-39.7%, regular use at 32.6%, and current use at 21.0%. They also reported on e-cigarettes lifetime use ranging from 16.0% to 53.6%, past 30-day use at 17.4%-21.3%, regular use at 12.4%, and current use at 27.8% (Blackwell & López Castillo, 2020). Connolly & Gilchrist (2020) found that 32% of TG participants reported heavy episodic (binge) drinking at least monthly in the previous year and that illicit drug use was found to be 59.4% among TG people, 6.8% reported past year cocaine use and 1.6% reported past year amphetamine use. Moreover, a prevalence rate of 64% was found for tobacco use (Cotaina et al., 2022), 24% for misuse of prescribed medications such as analgesics, anxiolytics, stimulants, and sedatives (Cotaina et al., 2022). Gilbert et al. (2018) reported prevalence rates ranging from 7% to 61% for binge drinking and from 47% to 48% for hazardous drinking as per the Alcohol Use Disorders Identification Test (AUDIT) scores. Drug use was found to be 20.9% prevalent among a sample of TGNC people in China (Lin et al., 2021). Finally, among a sample primarily comprised of US participants (80%), Gilbert et al. (2018) reported that across two of

their total 44 included primary studies, the rate of alcohol use based on the AUDIT scores indicative of hazardous drinking was 47%-48%.

3.7 Prevalence of Other Disorders

Other mental health disorders included PTSD (n=5) eating disorders (n=3), somatization (n=3), dissociative disorders (n=2), and psychosis (n=1). One of the included SRs was based on diagnostic interviews (de Freitas et al., 2020), one reported on a mixture of diagnostic interviews and self-report measures (Dhejne et al., 2016), and six were based only on self-report measures (Drabish & Theeke, 2022; Hayek et al., 2022; Jones et al., 2016; Lin et al., 2021; Mark et al., 2019; Pinna et al., 2022).

The reported prevalence rates of PTSD based on a diagnostic interview; SCID-I, MINI-Plus among a sample of 577 individuals diagnosed with GD were 0.8% (de Freitas et al., 2020). Based on a self-report measure, symptoms of PTSD were reported at 41.0% among a sample of serving or ex-military serving TGD people in the USA and Canada (Mark et al., 2019), 8.6%-45.3% (current PTSD) (Pinna et al., 2022), 24.0% based on one primary study with TGW in China (Lin et al. 2021), and 63% to 66% among TGD individuals of Arab descent despite their place of residence (Hayek et al. 2022).

Moreover, eating disorders were investigated by three included studies. Based on a diagnostic interview Anorexia Nervosa was found to be 0.4% among a sample of individuals with a diagnosis of gender dysmorphia (de Freitas et al., 2020). Additionally, Pinna et al. (2022) reported that 23% of MtF (n=152) and 22% of their FtM (n=288) participants endorsed clinically significant levels on the Eating Attitudes Test & Eating Disorder Testing (EAT-26). Another SR reported a prevalence of 0.7% for eating disorders in a sample of TG individuals (Jones et al., 2016). and 10.6% for a sample of TG individuals (Pinna et al., 2022). A past diagnosis of Bulimia Nervosa, and binge eating, was 4.2% and 1.6% respectively in a sample of TG individuals (Pinna et al., 2022). Finally, Drabish & Theeke (2022) reported that 27.5% of their participants had somatization, and a prevalence rate of 29.6% dissociative disorders were reported in a sample of 38 TG individuals when screened for by the MINI and SCID-II (Dhejne et al., 2016).

3.8 Prevalence of Suicide and Suicide-related Behaviors

Suicide and suicide-related behaviors were examined by 12 of this review's included studies.

None of the included SRs/MAs directly compared TGD to the general population or a cis-gender group, however, three SRs include one primary study each which did, using self-report measures. In their SR, Jackman et al., 2016 provided a prevalence rate of NSSI of 36.8%-41.9% in a TG group and 4% for a cis-gender group. Marshall et al. (2016) reported a lifetime history of suicidal ideation of 37%-81% in a TG group and 13%-24.2% in a cis-gender group. They also reported lifetime history of suicide attempts of 20% (TGW) and 41% (TGM) against 11% (cis women) and 5% (cis men) (Marshall et al., 2016). Finally, in their SR Pinna et al. (2022) reported that 11-13% of cis men and 14-27% cis women self-reported having engaged or had thoughts of "self-harm", whereas the prevalence was 36.8% - 67.72% for a TG group.

The only included MA of Liu et al. (2019), reported a pooled prevalence of 21.6%–22.7% for "self-harm attempts", 32.3%–44.7% for NSSI ideation, 11.1%–25.7% for suicide attempts, and 12.7%–50.0% for suicidal ideation. NSSI ideation or thoughts were reported by one SR at 32.3% - 44.7% (Lin et al., 2021). NSSI attempts were reported at 21.6% - 22.7% (Lin et al., 2021), and 36.8% - 41.9% (Jackman et al., 2016).

Prevalence rates of suicidal ideation were examined using self-report instruments and varied among reviews and among specific trans populations. Pinna et al. (2022) reported lifetime suicidal ideation of 46.3% - 58.3% and a past 12-month prevalence of 39.7% among TGW and 50.6% among TGM. In a recent study by Hayek et al. (2022), the prevalence of suicidal ideations without a plan was reported to be 15%. Similarly, Lin et al. (2021) and Liu et al. (2019) found prevalence rates for ideation in the range of 12.7% to 50.0%. Adams and Vincent (2019) reported an average prevalence rate of 46.55% for suicidal ideation. McNeil et al. (2017) reported a range from 37% to 83%. Adams et al. (2017) reported a prevalence rate of 55% for lifetime ideation and 51% for past-year ideation. Lastly, Marshall et al. (2016) observed lifetime ideation rates between 37% and 81%, with past-year ideation rates ranging from 10% to 19% for a mixed TG group.

Regarding suicide attempts, none of the included SRs/MAs directly compared TGD populations to other groups. Pinna et al. (2022) reported a wide prevalence range of 22.5% to 73%. In

their study focusing on TGD individuals of Arab descent, Hayek et al. (2022) reported a lifetime suicide attempt rate of 46% among TGW (TG women). Drabish and Theeke (2022) focused on the impact of stigma and discrimination against TGD people, included 15 primary studies and found a prevalence rate of 32% for suicide attempts among their participants. Lin et al. (2021) reported prevalence rates for suicide attempts in the range of 21% to 22.7% among their sample of TGNC people in China. Adams and Vincent (2019) reported an average prevalence rate of 27.19% for suicide attempts across their 64 primary studies among TGD adults between 1997 and 2017. McNeil et al. (2017) observed substantial variability in suicide attempt rates, ranging from 9.8% to 44%, with a specific focus on a 43% rate among TG women. Adams et al. (2017) reported a prevalence rate of 29% for lifetime suicide attempts and 11% for past-year suicide attempts in their study. Lastly, Marshall et al. (2016) reported rates between 10% and 41% for lifetime attempts, with distinct rates of 41% for TGM (TG men) and 20% for TG women.

Death by suicide was examined by one of the included SRs. Baker et al. (2021) reported on one of their total included primary studies (n=20) conducted in the Netherlands, stating that there were 17 deaths by suicide among TG women (n = 966) and 1 among TG men (n = 365) between 1975 and 2007. They further stated that the authors of this primary study estimated the number of deaths by suicide for the age-matched general population of Dutch males over this period as 0.208 but did not report on females (Baker et al., 2021).

4. Discussion

To our knowledge, this is the first umbrella review to narratively summarize outcomes on the prevalence rates of mental disorders, substance use and SUDs, suicide, and suicide-related behaviors among TGD people. This review included 23 systematic reviews, only two of which were meta-analyses. We examined ten reviews for the prevalence rate of mood disorders and symptoms, nine reviews for the prevalence rates of anxiety symptoms and disorders, twelve reviews for the prevalence rates of suicide and suicidal behaviors, nine reviews for the prevalence rate of substance-related behaviors and substance use disorders among trans and gender-diverse populations, and finally eight

reviews for other outcomes including PTSD, somatization, eating disorders, and dissociative disorders.

A wide range of prevalence rates for various mental health conditions among TG and gender-diverse (TGD) populations were revealed. Only two SRs reported on studies that established clinical diagnoses with structured clinical interviews, and these reported prevalence rates of 42.1% to 70.4% for mood disorders, 5.6% to 26.8% for anxiety disorders, 14.7% to 30.2% for SUDs, 0.8% for PTSD, 1.0% for eating disorders, 0.1% to 29.6% for dissociative disorders, and 0.5% for somatoform disorder. The SR/MAs that were based on self-report or a mixture of self-report and diagnostic interviews, showed markedly higher rates (9.8%- 56% for symptoms of depression, 7.5%-68% for anxiety, 8%-58.3% for NSSI and 36.8%-57.7% for NSSI ideation, 13.5% to 83% for suicidal ideation. Also, percentages ranging fr0m 9.8%-73% for suicide attempts were found. Moreover, rates of substance use and its related behaviors also varied among the SRs based on self-report measures; 7% to 61% for problematic alcohol use/binge drinking/drinking to intoxication, 12.4% to 40.2% for e-cigarette use, 10.2% to 53.6% for use of tobacco products, 1.6% to 59.4% for illicit drug use, and 32% to53% for sexualized drug use. This discrepancy may be explained by the common finding that self-report instruments tend to overestimate prevalence estimates of common mental disorders by a factor of 1,5 to 2 (Charlson et al., 2019).

This umbrella review has provided valuable insights into the mental health challenges faced by TGD populations, and -despite the enormous heterogeneity in prevalence rates found across studies, suggests that the burden of mental disorders is higher than those typically seen in the general population. For reference, general population rates are approximately 3.8% for depression, 4% for anxiety, 5.5% for substance abuse, 5.1% for alcohol abuse, 9.2% for suicidal ideation, and 2.7% for attempted suicide (Nock et al., 2008). Note, however, that no SRs or MAs could be included that compared TGD individuals to relevant reference groups such as a general population or cisgender samples or were based on random population sample studies only. It is also of note that despite the observed high co-occurrence between TGD identities and Autism Spectrum disorder (ASD) (Murphy et al., 2020), this review did not include ASD as an outcome as it was not regarded as a result of the burden of gender minority stress of other challenges TGD populations experience.

It is important to acknowledge the limitations of this umbrella review. Firstly, our search indicated that the overall quality of the systematic reviews and meta-analyses included in this umbrella review varied, with some exhibiting methodological shortcomings and potential biases. Only two meta-analyses were included, presenting pooled prevalence rates, whereas the majority were narrative SRs, that reported wide ranges of prevalence rates of primary studies. Furthermore, the challenges associated with distinguishing between various TGD subpopulations (e.g., TGM, TGW, GD, GNC, etc...) within the umbrella term can lead to heterogeneity in the data, making it difficult to draw precise conclusions about the mental health experiences of specific TGD groups. Despite these limitations, this umbrella review's strengths lie in its synthesis of existing evidence, providing a comprehensive overview of the prevalence of mental health disorders among TGD individuals.

As we chart the path forward, efforts should be geared toward the development and evaluation of prevention and care strategies that are both culturally sensitive and inclusive of TGD communities. Finally, a critical area that demands immediate attention is the knowledge transfer and training of healthcare providers on TG and gender-diverse identities. This education should extend beyond gender-affirming care and encompass general practitioners, mental health care providers, and hospital staff. Cultivating a healthcare workforce that is sensitive, informed, and competent in providing care to TGD individuals is pivotal to addressing the mental health disparities identified in this study and ensuring equitable healthcare access for all.

Several key directions for future research in the field of mental health among TGD populations emerge. It is advised that forthcoming research employs clinical diagnostic interviews for establishing prevalence rates of mental health conditions among TGD individuals, thereby ensuring the highest methodological rigor in capturing the true extent of these disparities. Relying on self-report instruments, while informative, can be complemented by clinical diagnostic interviews to provide more precise estimations of the prevalence and nature of mental health challenges within this demographic. Researchers should also consider the incorporation of comparison groups or the utilization of random sampling methods. By doing so, future studies can enhance the validity of their findings, permitting more accurate comparisons between TGD individuals and cisgender counterparts or the general population. Moreover, the multifaceted aspects of minority stress, “nonaffirmation”,

social exclusion, and discrimination should be further explored, seeking to unravel the intricate mechanisms through which these stressors exert their influence on mental well-being. Uncovering these nuances can guide the development of targeted prevention efforts and support systems tailored to mitigate the adverse effects of such social determinants.

In conclusion, the evidence presented in this review underscores the prevalence of mental health challenges among TGD populations. These challenges are particularly pronounced in the context of societal factors, discrimination, and stigma. The implications of these findings extend to the critical need for research and interventions that prioritize the mental well-being of TGD individuals. Timely and evidence-based policies must be enacted to address these disparities, emphasizing accessible and culturally competent psychological interventions. As the global landscape continues to evolve, it remains imperative to advocate for equitable mental healthcare and support systems to mitigate the enduring impact of societal and systemic challenges on the mental health of TGD populations.

Conflict of interest

None declared.

Acknowledgments

[To be added]

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Figure 1. Flowchart of the search and selection procedure of studies.

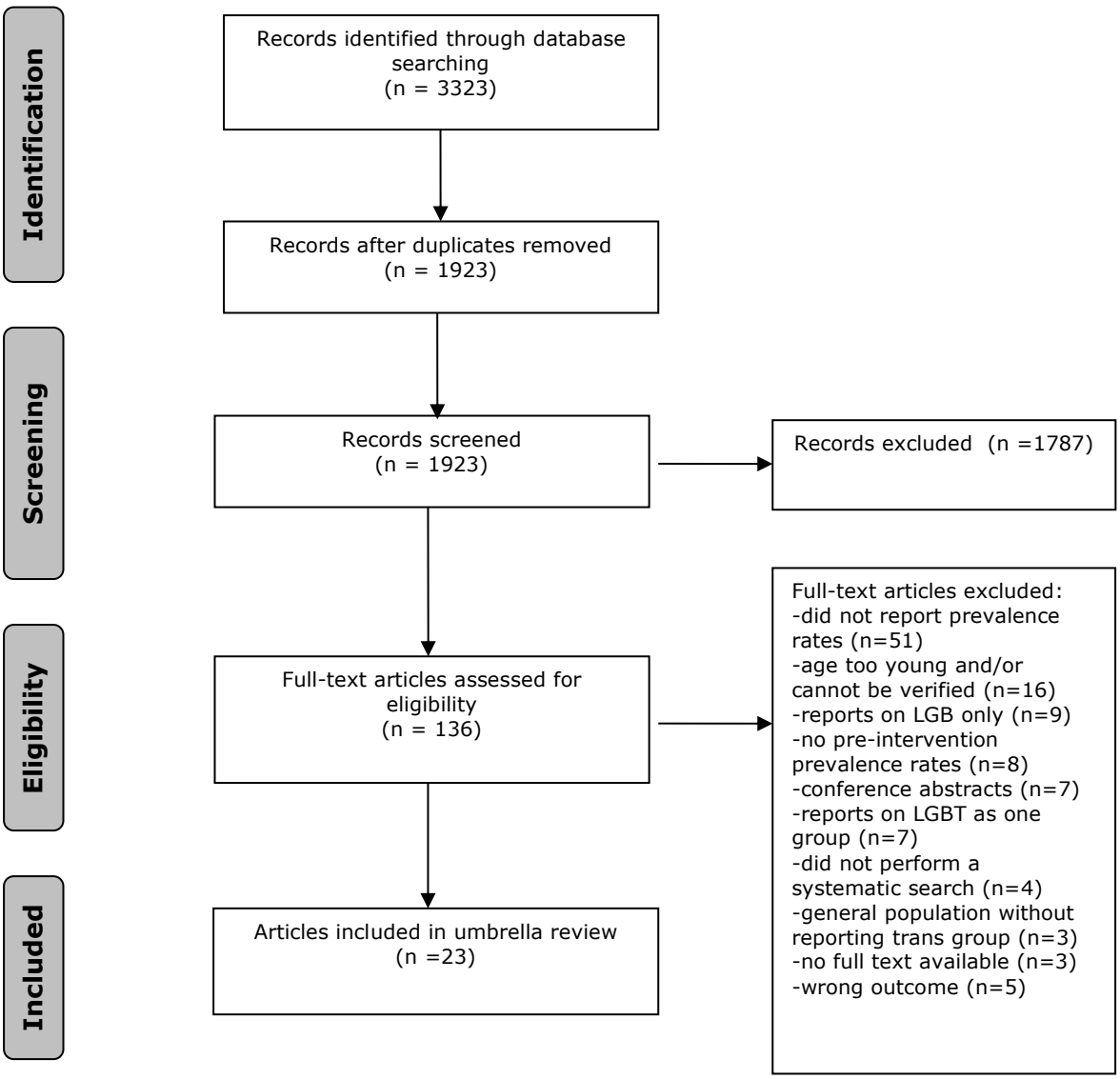

Figure 2. AMSTAR-2 quality assessment results

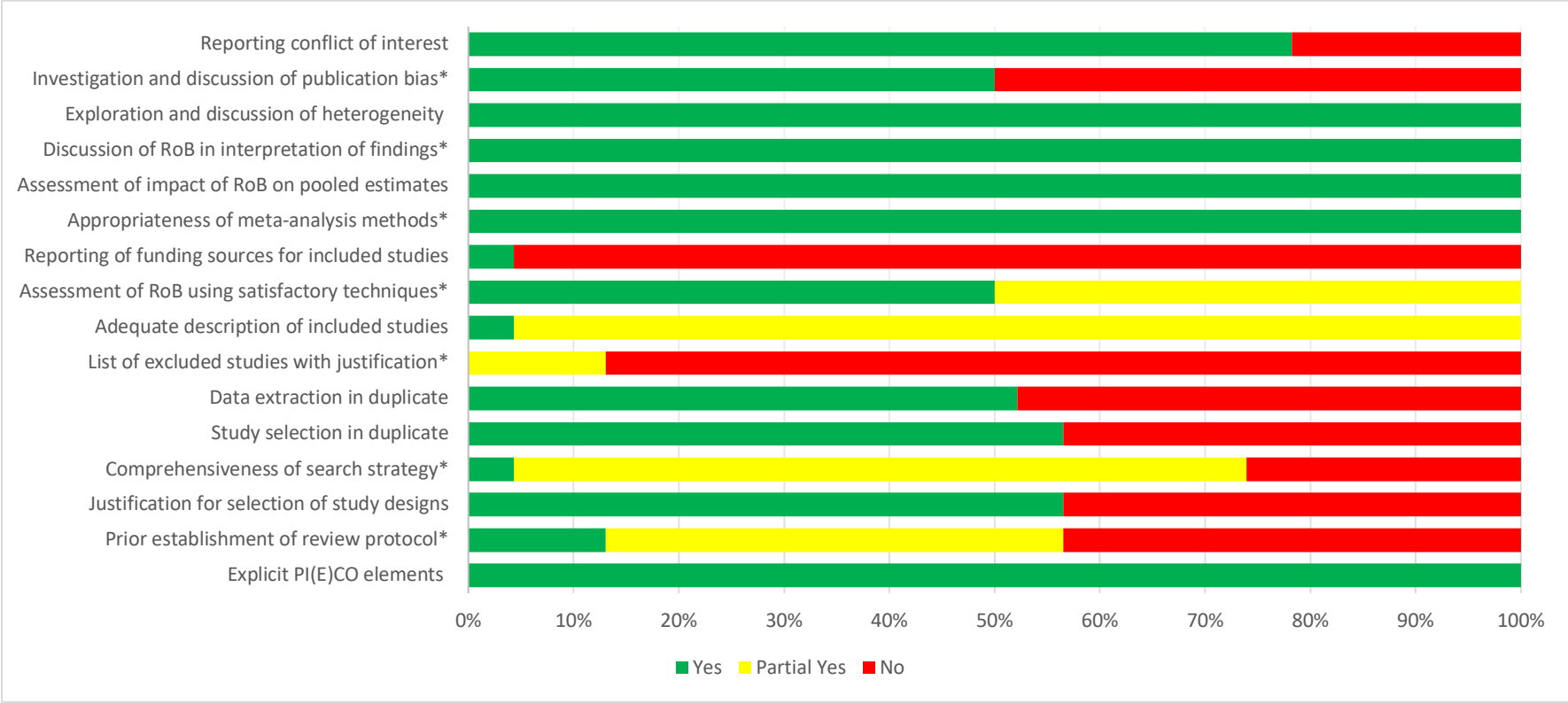

Table 1. characteristics of included studies

Study	End date search	Studies (n)	Study type	Outcome(s)	Study populations	Countries/regions/ continents/ nationalities	AMSTAR-2 scores	
							Critical	Total
Adams and Vincent (2019)	Dec/17	64 studies (reported in 108 articles)	SR	Suicidal ideation, suicidal attempts	TG	USA, Canada	1	4
Adams et al. (2017)	Feb/16	42 studies	SR	Suicidality (ideation, attempts)	TG	North American (Canada and the United States)	0	2,5
Baker et al. (2021)	Jun/20	20 studies reported in 22 publications	SR	Depression, anxiety, death by suicide	TG	Italy, Belgium, Netherlands, USA, Spain, UK, Turkey, France, Switzerland, Germany, Norway.	1,5	5,5
Blackwell and López Castillo (2020)	Aug/19	77 papers	SR	Use of electronic nicotine delivery systems (ENDS)	LGBTQ persons who smoke	USA	0,5	2
Connolly and Gilchrist (2020)	May/19	41 studies	SR	Substance use (Alcohol, Illicit drugs, Meth/injection drugs, Cocaine, Amphetamines)	TG	North America (USA n = 27, Canada n = 2). Spain (n = 2), India (n = 2),Brazil (n = 2), Cambodia (n = 2) and one study from each of Malaysia, Mexico, Pakistan, and the Dominican Republic.	0,5	4
Cotaina et al. (2022)	July/21	21 studies	MA	current tobacco use, current tobacco use disorder, current alcohol use, current alcohol use disorder, lifetime substance (all) use, current substance use (excluding tobacco and alcohol), current use of specific substances (excluding tobacco and alcohol and including cocaine, amphetamines,	TG	Spain, USA, Canada, Australia	5,5	13

				methamphetamines, ecstasy, stimulants, heroin, opiates, cannabis, marijuana, LSD, hallucinogens, steroids, inhalants, sedatives, Ritalin or Adderall, diet pills, cold medicine, prescription medications, polysubstance, other club drugs, and other illegal drugs), and current substance use disorder (excluding tobacco and alcohol).				
de Freitas et al. (2020)		5 articles	SR	Depression, Specific phobia, Adjustment disorder, GAD, Dysthymia, Panic disorder, Social phobia, OCD, Bipolar, DID	Individuals diagnosed with GD	four in Europe (n=4), Iran (n=1)	0,5	5
Dhejne et al. (2016)	Apr/15	38 studies	SR	Symptoms and diagnosis of Axis 1 disorders, substance use	TG	Norway, Australia, Germany, Switzerland, South Korea, Spain, Italy, Belgium, Japan, Sweden, Hungary, France, UK, Serbia, Ireland, Netherlands, Iran, and Finland.	0	1,5
Drabish and Theeke (2022)	Not mentioned	15 studies	SR	clinical depression, anxiety, somatization, attempts.	TG	USA (Puerto Rico, Guam, Virgin Islands), Argentina, UK	0	2,5
Francisco et al. (2020)	not mentioned	13 studies	SR	Anxiety symptoms, anxiety disorders	SGM	USA, China, Sweden, Taiwan	1	3,5
Gilbert et al. (2018)	Apr/17	44 studies	SR	Substance use (alcohol)	TG	United States, Brazil, Canada, El Salvador, Peru, Portugal, and South Africa	1,5	5,5

Hayek et al. (2022)	Jun/20	7 studies	SR	Depression, Suicidality (ideations, attempts), PTSD	LGBTQ Individuals Who are Arab or of an Arab Descent	Lebanon (n = 5), Austria and the Netherlands (n = 1), Iraq (n = 1)	2	7,5
Jackman et al. (2016)	Apr/15	26 Articles	SR	NSSI	LGBT	USA	1	4
Jones et al. (2016)	Apr/15	26 studies	SR	Symptoms of disordered eating	TG	USA, UK, Finland, Italy, Germany, Turkey, Netherlands, Switzerland, China, Austria.	1,5	6,5
Lin et al. (2021)	Aug/21	30 articles	SR	Depression and depressive symptoms, Anxiety disorders, PTSD, Sexualized Drug Use, Suicidality (attempts, ideation, Self-harm ideation, Self-harm attempt)	TGNC	Mainland China	3	8,5
Liu et al. (2019)	Jul/19	51 aritcles, 54 studies	MA	NSSI	LGBT	Not mentioned	4,5	12
Mark et al. (2019)	Jul/18	30 articles	SR	Suicide and suicidal ideation	LGBTQ military serving and ex-serving personnel	USA, Canada, Switzerland	1	4
Marshall et al. (2016)	Apr/15	31 papers	SR	Suicidality (ideation, attempts), NSSI	TG	UK (n=5), USA (n=12), Netherlands (n=2), Australia (n=2).	1,5	6,5
McNeil et al. (2017)	Nov/16	30 articles	SR	Suicidality (ideation, attempts)	TG	USA (n= 21), Japan (n=2), South America (n=2), Argentina (n=1), Brazil (n=1), Canada (n=1), UK (n=1), Belgium (n=1); Italy (n=1); Netherlands, Belgium, Germany, and Norway (n=1).	1,5	3,5
Millet et al. (2017)	Apr/15	25 studies	SR	Anxiety symptoms, anxiety disorders	TG	Switzerland, Spain, Japan, Italy, Iran	1,5	6,5

Pinna et al. (2022)	Feb/22	165 articles	SR	1) mood and anxiety disorders, eating disorders, suicidality (ideation, NSSI), trauma and stress-related disorders, personality disorders, substance use disorders, co-morbid disorders.	TG	America, Australia, Sweden, Dominican Republic, China, Portugal, Brazil, Italy, Poland, South Korea, Cambodia, Argentina, Peru, Canada, Turkey, Norway, India, France, Japan, Guatemala, Spain.	0,5	5,5
Rowniak et al. (2019)	Sep/17	7 studies (552 participants)	SR	Depression symptoms, Anxiety symptoms	TG, those who did not identify with the gender binary and were using cross-sex hormones.	France, Belgium, Italy, Spain, Japan.	2,5	6,5
Tan and Saw (2022)	Aug/21	25 studies	SR	Depression, anxiety, non-suicidal self-injury, and suicidality	LGBTQ people in Southeast Asia	Thailand (40%), the Philippines (20%), and Singapore (16%). Remaining: Cambodia, Vietnam, and Malaysia.	0,5	2

SR: Systematic Review; LGBTQ: Lesbian, Gay, Bisexual, Transgender, Queer; TG: Transgender; MA: Meta-analysis; IDU: Injecting drug use; 2SLGBTQ+: Two-spirit, Lesbian, Gay, Bisexual, Transgender, Queer, plus; TGNC: Trans/gender non-conforming; GD: Gender Dysphoria; SGM: Sexual and Gender Minorities; LGBT: Lesbian, Gay, Bisexual, Transgender.

Table 2. Outcomes of included studies

Study	Study populations	Studies (n)	Specific outcome	Designs of included studies	Assessment measure	Prevalence rates/ranges	Comparator
Mood disorders							
Baker et. al., 2021	TG	20 (22 articles)	Depression symptoms	1 before-after trial 9 prospective cohorts 2 cross-sectional	BDI-II, HADS (depression subscale), Ad hoc questionnaire, SCL-90-R (depression subscale), Zung SDS, MMPI, BDI, CESD-R, PHQ-9	42% (Zung SDS, SCL-90-R depression subscale)	None
de Freitas et al. (2020)	GD diagnosis	5 studies (577 subjects)	Mood disorders (Major depressive disorder, Dysthymia, Bipolar disorder)	cross-sectional, prospective, and retrospective, structured clinical interview	SCID-I MINI-Plus	42.1% (243 individuals) (These are all people with gender dysphoria.)	None
(Dhejne et al., 2016)	TG	38 (1 for mood disorders)	Mood and adjustment disorders diagnosis (lifetime)	Single center (gender clinic) cross-sectional	MINI	56% (MtF) 70.4% (FtM)	None
Drabish and Theeke (2022)	TG	15 (1093 trans people)	Depression	cross-sectional	Unspecified online self-report	44.1%	None
Lin et al. (2021)	TGNC	30 (data based on 4 studies)	Depression	cross-sectional	Center for Epidemiological Studies Depression (CESD)-9 items, Depression-Patient Health Questionnaire-9 items, Zung Self-Rating Depression Scale, and CESD-20 items.	32.0% - 54.5%	None

(Mark et al., 2019)	TG	30 (298 participants)	Depression	Quantitative	N/A	50% of transgender participants screened positive for depression	None
Pinna et al. (2022)	TG	165	Depression	cross-sectional	CES-D, BAI, CES-D 20 (cut-off > 16), SCID-I, CESD-R, HADS, PROMIS Depression-Short Form 8A instrument, Life Chart Interview, DASS-21, PHQ-9, C-SSRS, ZRS	Lifetime: All 44.1% - 78% MtF 13.5% - 68.6% FtM 9.8% - 15.6% 12-months: 84.4% Last 6 months: All 73.6% Past week: MtF 42.9% Current: All 22.3% - 82% MtF 45.35%- 80.5% FtM 48.3% - 87.5%	Based on one included study of: 29,988 patients: 17,521 cis-men, 9,288 cis-women, 987 TGM, 1,002 TGW, 762 Non-binary AMAB More transgender women (34.6%) and non- binary patients (36.8% AFAB, 33.7% AMAB) met the clinical cut-off score of PHQ-9 for depression, compared to transgender men (27.5%), cisgender women (16.1%), and cisgender men (14.1%).
Rowniak et al. (2019)	TG, non-binary	7 (5 papers for depression with 408 participants)	Depression symptoms	Prospective, cross-sectional, observational	BDI, SDS, SCL-90, SCL-90-R, MMPI, MMPI-2	Zung Depression Scale (39.98 ± 10.79, P<0.001) TG SCL-90-R (0.51 ± 0.49, P<0.001) TG SCL-90 (34.7 ± 14.3, P<0.001) TG MMPI-2 (52.6 ± 9.6, P = 0.001) MtF (52.3 ± 11.6, P = .421) FtM	None

						The Beck Depression Inventory (5.00 5.85, P = 0.044) TG	
Tan and Saw (2022)	LGBTQ (data extracted for TG)	25	Depression	cross-sectional	Depression in the past week on the Center for Epidemiological Studies-Depression (CES- D) scale.	56.0%	None
Anxiety disorders							
Baker et al. (2021)	TG	20 (22 articles)	Anxiety symptoms	7 prospective cohorts 1 cross-sectional	Ad hoc questionnaire (DSM criteria), HADS (anxiety subscale), DSM, SCL-90-R (anxiety subscale), Zung SAS, SADS, STAI (trait subscale)	12% (DSM criteria) 50% (Zung SAS)	TG receiving gender affirmative care (hormones)
de Freitas et al. (2020)	GD diagnosis	5 studies (577 subjects)	Anxiety disorders (specific phobia, adjustment disorder, generalized anxiety disorder, panic disorder, social phobia, obsessive–compulsive disorder, agoraphobia)	cross-sectional, prospective, and retrospective, structured clinical interview	SCID-I, MINI-Plus	26.8% (155 individuals) (These are all people with gender dysphoria.)	None
Dhejne et. Al., 2016	TG	38	Anxiety disorders	Cross-sectional, longitudinal	MINI, SCID-II	17% - 28%	None
			Generalized anxiety disorder	Cross-sectional, longitudinal	MINI	8.8% (MtF) and 5.6% (FtM)	None
			Social phobia (current)	Cross-sectional, longitudinal	MINI	8.2% (MtF) 11.3% (FtM)	None
Drabish and Theeke (2022)	TG	15 (1093 trans people)	Anxiety symptoms	Cross-sectional	Online self-report sampling	33.2%	None

(Francisco et al., 2020)	LGBT (data extracted for TG)	13	Anxiety symptoms	Quantitative, transversal	CES-D, BAI, SAS	MtF 34.5% - 40.4% FtM 47.5%	None
Lin et al. (2021)	TGNC	30 (data based on three studies)	Anxiety symptoms	Cross-sectional	Generalized Anxiety Disorder-7 items, and Zung Self-Rating Anxiety Scale.	28.5–51.0%	None
Millet et al. (2017)	TG	25	Anxiety disorders (Separation Anxiety Disorder, Selective Mutism, Specific Phobia, Social Anxiety Disorder (Social Phobia), Panic Disorder, Panic Attack (Specifier), Agoraphobia, Generalized Anxiety Disorder, Substance/Medication-Induced Anxiety Disorder, Anxiety Disorder Due to Another Medical Condition)	cross-sectional (n = 17) and longitudinal (n = 8)	SCL-90-R, STAI, the Brief Symptom Inventory (BSI)-18, a shortened version of the SCL-90-R), HADS.	17% - 68%	None
(Pinna et al., 2022)	TG	165	Anxiety symptoms	Cross-sectional	CES-D, BAI, CES-D 20 (cut-off > 16), SCID-I, CESD-R, HADS, PROMIS Depression-Short Form 8A instrument, Life Chart Interview, DASS-21, C-SSRS, GAD-7	Lifetime All 78% MtF 66.9% FtM 7.5% Past diagnosis MtF 25% FtM 29.8% Current All 31.1% - 98% MtF 34.5% - 70.3% FtM 47.5% - 66.3%	None
Rowniak et al. (2019)	TG, non-binary, using	7 (2 studies for anxiety	Anxiety symptoms	Prospective, cross-sectional	SAS, SCL-90. SCL-90-R	Zung Anxiety Scale (37.908.97 versus 44.919.59, P<0.001)	TG receiving gender affirmative care (hormones)

	cross-sex hormones.	with 164 participants)				and the anxiety scale of the SCL-90-R (0.54 0.56 versus 1.05 0.94, P < 0.001).	
					SCL-90	Scores statistically worse (higher) than the general population (17.06.4 versus 12.84.4, P < 0.001)	General population
Suicide and suicidal behaviours							
(Adams & Vincent, 2019)	TG	64 research projects (108 articles)	Ideation Attempts	Longitudinal	Clinical interviews, questionnaires	46.55% (suicide ideation average) 27.19% (suicide attempts average)	The majority of participants were Caucasian, whereas the highest rate of suicide attempts (55.3%) was among First Nations, and Caucasians had the lowest attempt rate (36.80%).
Adams et. Al., 2017	TG	42	Ideation Attempts	Cross-sectional, cohort study, longitudinal	self-administered questionnaires, administered questionnaires, face-to-face interviews, and chart reviews	55% (lifetime ideation) 29% (lifetime attempts) 51% (past year ideation) 11% (past year attempt)	Suicidal ideation was higher among individuals of a male-to-female (MTF) than female-to- male (FTM) alignment, and lowest among those who were gender non-conforming (GNC). Conversely, attempts occurred most often among FTM individuals, then

							decreased for MTF individuals, followed by GNC individuals.
Baker et. al., 2021	TG	22 (20 studies)	Death by suicide	Retrospective cohort (n=1)	Death by suicide (confirmed by autopsy report; medical report or physician information)	1-1.8% TG women 0.3% TG men 17 deaths by suicide among transgender women (n = 966) and 1 among transgender men (n = 365) between 1975 and 2007	Age matched general population: The authors calculated the number of suicide deaths expected in an age-matched stratum of the general male Dutch population over this period to be 0.208. No data were reported for transgender men (n = 122).
Drabish and Theeke (2022)	TG	15 (1093 trans people)	Suicide attempts	Cross-sectional	Online self-report sampling	32%	None
Hayek et al. (2022)	LGBTQ (data extracted for trans, gender queer, gender non-conforming)	7 (only 1 is eligible and only includes trans women) This study has 54 participants.	Ideation, attempts	Cross-sectional, longitudinal	Nothing mentioned for suicide	46% MtF (lifetime suicide attempt)	None
Jackman et. Al., 2016	LGBT (data extracted for transgender)	26	NSSI	longitudinal	One item assessing past 12 months (dichotomous), one item on methods of NSSI, one screening item listing 16 behaviours, one item assessing nonsuicidal intention, Nonsuicidal Self-Injury Assessment Tool, 1 question assessing lifetime history (dichotomous),	36.8% - 41.9%	Prevalence of NSSI: Cisgender: 4% (chart review)

					Self-Injurious Thoughts and Behaviours Interview, How I Deal with Stress Questionnaire, One item assessing frequency of cutting in past six months, one item about motivations (five response options), Two items on cutting: frequency in past 12 months, what helped refrain from cutting, Interview, Self-Injury Questionnaire (assesses cutting only), ISAS (primary outcome is dichotomised lifetime history), Data abstraction from physician clinical visit narratives, extracted from patient files and clinician reports, and chart review.		
Lin et al. (2021)	TGNC	30	Attempts, ideation, NSSI attempts, NSSI ideation	Cross-sectional	Unspecified self-report measures	11.1% - 25.7% (attempts) 12.7% - 50.0% (ideation) 32.3% - 44.7% (NSSI ideation) 21.6% - 22.7% (NSSI attempt)	None
Liu et. al., 2019	LGBT	51 (54 studies)	NSSI, Ideation, attempts	Cross-sectional	SIQ, SSM, ISAS, SITBI, and DSHI	NSSI: Lifetime prevalence: 46.65% (39.35%-54.10%)	None

						Last-year prevalence: 46.61% (35.45%-58.12%)	
(Mark et al., 2019)	LGBTQ (data extracted for TG)	30 (5117 participants)	Death by suicide	Quantitative	N/A	The crude suicide rate among veterans with transgender-related ICD-9 diagnoses was approximately 82/100,000 person/year	None
Marshall et. Al., 2016	TG	31	NSSI Ideation Attempt	Cross-sectional and longitudinal	Self-report, survey	NSSI: 24% - 57.7% (lifetime) 57.7% (FtM Lifetime) 26.2% (MtF Lifetime) Ideation: 37% - 81% (lifetime) 10% - 19% (in the past year) Attempts: 10% - 41% (lifetime) 41% (FtM lifetime) 20% (MtF lifetime)	Prevalence for a lifetime history of suicide ideation: Cisgender women: 24.2% Cisgender men: 13% Prevalence for suicide attempt: Cisgender women: 11.4% Cisgender men: 5%
McNeil et. Al., 2017	TG	30	Ideation Attempts	Cross-sectional	interviewer-delivered surveys, computer-based delivery, and clinical diagnostic assessments	suicidal ideation: 37% - 83%. Suicide attempt: 9.8% - 44% 43% (MtF) Suicide range reported in gender	Trans people and cis women had higher rates of lifetime suicide attempt than did cis men and suggested that because most of their trans sample were women (82.3%), findings may reflect an effect of

						clinics: 9.8% to 21.2%. Other places: 11.2% to 44%.	being female over being male. Suicidal ideation in trans people (although again greater than for cis people) was not different from that for psychosocially matched cis women or cis lesbians.
(Pinna et al., 2022)	TG	165	NSSI ideation, NSSI, Suicidal ideation, suicidal attempt	Cross-sectional, prospective	Self-report, DSM, ICD-10	NSSI ideation: Lifetime All 36.8% - 67.72% Past 12 months MtF 41.3% FtM 49.1% Past week All 67.2% Current All 56% MtF 26.2% FtM 57.7% NSSI: Lifetime All 46.3% (DSM) - 58.3% Past 12-months months All 31.3% MtF 19% (ICD-10) FtM 23.7% Current	The prevalence of lifetime self-harm and self-harm thoughts: Cisgender males: 11-13% Cisgender females: 24-27% Currently engaging in NSSI: Control group: 4%

						All 19% - 28.73% MtF 8% FtM 35% Suicidal ideation: Lifetime MtF 46.4% FtM 47% - 47.4% Past 12-months MtF 39.7% FtM 50.6% Current All 48.3% MtF 13.5% FtM 35.7% Suicide attempts: All 22.5% - 73%	
Substance use							
Blackwell et. al., 2020	LGBTQ	77	Tobacco, eCigs	N/A	Interview survey	Tobacco products: 53.6% (lifetime use), 10.2% - 39.7% (past 30-day use), 32.6% (regular use), 21.0% (current use). eCigs: 16.0% - 40.2% (lifetime use), 17.4% - 21.3% (past 30-day use), 12.4% (regular use), 27.8% (current use)	Cigarette smoking: cisgender: 20.7% Past 30-day use of any tobacco product: cisgender: 25.1% Past 30-day use of eCigs: cisgender: 5.0% Current cigarette smoker: cis: 14.8% Lifetime eCigs use: cis: 18.8% Current eCigs use: cis: 19.8%

							Lifetime tobacco use: cis: 31.5% past 30-day tobacco use: cis: 3.5% Lifetime eCigs use: cis: 23.0% Past 30-day eCigs use: cis: 5.6% Regular use of any tobacco product: cis: 23.6% Regular use of eCigs: cis: 6.5%
Connolly et. al., 2020	TG	41	Alcohol Illicit drugs Cocaine Amphetamines	Cross-sectional, retrospective database study, and prospective study	fear of negative evaluation scale, social avoidance and distress scale	32% (heavy episodic (binge) drinking at least monthly in the previous year) 13.5% (hazardous or harmful drinking) 59.4% (illicit drug use) 6.8% (past year cocaine use) 1.6% (past year amphetamine use)	Illicit drugs: cisgender: 9.4% Monthly HED: cisgender: 21.9% substance use: cisgender: 9.4%
Cotaina et. al., 2022	TG	20 studies/ 2,376,951 participants (18,329 of whom were transgender)	current tobacco use, current tobacco use disorder, current alcohol use, current alcohol use disorder, lifetime substance (all) use, current substance use (excluding tobacco and	N/A	N/A	Transgender people were more likely to use tobacco (odds ratio (OR) = 1.65; 95% CI [1.37, 1.98]), have used substances throughout their lives (OR = 1.48; 95% CI	Transgender people do not differ from cisgender people in terms of alcohol use or in the presentation of substance use disorders.

			alcohol), current use of specific substances (excluding tobacco and alcohol and including cocaine, amphetamines, methamphetamines, ecstasy, stimulants, heroin, opiates, cannabis, marijuana, LSD, hallucinogens, steroids, inhalants, sedatives, Ritalin or Adderall, diet pills, cold medicine, prescription medications, polysubstance, other club drugs, and other illegal drugs), and current substance use disorder (excluding tobacco and alcohol).			[1.30, 1.68]), and present current use of specific substances (OR = 1.79; 95% CI [1.54, 2.07]).	
de Freitas et al. (2020)	GD diagnosis	5 papers (577 subjects)	Substance use/abuse disorders	cross-sectional, prospective, and retrospective, structured clinical interview	SCID-I MINI-Plus	Substance related disorders: 14.7% (85 individuals)	None
(Dhejne et al., 2016)	TG	38	Non-alcohol substance abuse/ dependence	Single center (gender clinic) cross-sectional	MINI	30.2% (MtF)	None
Gilbert et. al., 2018	TG	44	Alcohol	cross-sectional	Ad hoc questionnaires, Three multi-item scales: Daily Drinking Questionnaire; Rutgers Alcohol Problem Index; modified Drinking Motives Questionnaire,	Binge drinking: 7%-61% Drinking to intoxication: 25%-58%	Transgender populations may also experience greater secondary harms related to alcohol use than cisgender peers.

					Past-year alcohol use & past-year sex while using alcohol via CDC HIV Risk Assessment, Hazardous drinking via Alcohol Use Disorders Identification Test, Drinking Motives Questionnaire-Revised	Sexual risk behaviours while intoxicated: 32%-53% Alcohol use disorder: 47%-48% (as per Alcohol Use Disorders Identification Test AUDIT) 26% (Lifetime) 11% (past year)	
Lin et al. (2021)	TGNC	30	Sexualized drug use	Cross-sectional	N/A	20.9%	None
(Mark et al., 2019)	TG	30 (298 participants)	Alcohol misuse	Quantitative	Not reported	13% screened positive for alcohol misuse.	None
(Pinna et al., 2022)	TG	165	Alcohol misuse, substance use, tobacco use, drug use, cigarette use	Cross-sectional, retrospective, prospective	Alcohol misuse: HED, BRFSS-surveys, AUDIT-10, AUDIT-3, clinical interview, online survey, questionnaire, USTS, interview, DAST-10, AUDIT-10, AUDUT-C, structured questionnaire in face-to-face interviews Substance use: Questionnaire, DAST-10, AUDIT-10, interview Tobacco use: Clinical interview	Alcohol misuse: Transwomen: 61.3% (HED), 86.9% for binge drinking and 72.3% are hazardous drinkers with 44.9% alcohol use (AUDIT-10), alcohol use: 21.5% (clinical interview), excessive use: 21.5% (online survey), 3 months ago for alcohol: 57.8% (questionnaire), alcohol dependence diagnosis: 10.0%, past 30 days consume alcohol: TGW: 57.6%	The MtF subcategory was more likely to binge drink (aOR 1⁄4 1.88) compared to cisgender females. The FtM subcategory had lower odds of binge drinking (aOR 1⁄4 0.49) compared to cisgender males (BRFSS-surveys). Cisgender past 30-day use of any cigarette: 25.1%, higher current use of cigarettes: 20.7%, cigars: 9.3%, e-cigarettes: 5.0% Transgender respondents, compared

					Drug use: Survey, THINS, clinical interview, online survey, clinical evaluation, ICD-10, questionnaire, interview, AUDIT, CUDIT-R, DAST-10, Trans PULSE survey, AUDIT-C, structured questionnaire in face-to-face interviews Cigarette use: Self-reported structured questionnaires, retrospective study, clinical interview, AUDIT, CUDIT-R, interview	and TGM: 63%, binge drink in the past 30 days: TGW: 21.5% and TGM: 26.8%, frequent binge drinking within the past month: TGW: 7.2% and TGM: 8.1% (USTS), excessive drinking: 21% (questionnaire), binge drinking episode in the past 7 days for transgender women: 40.2% (interview), hazardous alcohol use: 46.3%, recent alcohol: 57.7% (questionnaire), alcohol use disorder: 54% (AUDIT-10, DAST-10), transwomen used alcohol: 58% (questionnaire), any alcohol use: 52.8%, unhealthy alcohol use: 6.6%, high-risk alcohol use: 2.8%, heavy episodic drinking: 10.4%, alcohol use disorder: 8.6%, alcohol-specific conditions: 1.3% (AUDIT-C), alcohol intoxication in the past month: 25.1%, binge	with cisgender, had significantly higher odds of past 30–day tobacco product use for and cigarette/cigar/e-cigarette product (OR 1⁄4 1.97), e-cigarettes (OR 1⁄4 5.15), cigars (OR 1⁄4 3.56), and cigarettes (OR 1⁄4 2.10). Among cisgender adults, cannabis and opioid SUDDs were equally prevalent. The age-adjusted prevalence of alcohol use is 48.6% of Transmasculine vs 59.2% of U.S. Males, 43.4% of U.S. Females and 51% of Total U.S. Population; cigarette smoking (current and former respectively) is 14.2% and 33.8% of Transmasculine vs 21.5% and 25.3% of U.S. Males, 17.3% and 18% of U.S. Females and 19.3% and 21.6% of Total U.S. population. US general prevalence of lifetime nonmedical

						drinking: 43.3% (structured questionnaire in face-to-face interviews) Substance use: In the past 3 months: 59.5% (questionnaire), substance-related problems in TGW: 39% (DAST-10, AUDIT-10), previous substance abuse: 28.8% (interview), transwomen used substances: 43.3% (questionnaire) Tobacco use: Trans women problematic use: 56.6% (clinical review) Drug use: Transwomen: 28.0%, lifetime: 24%-26.5%, analgesics: 21.2%-23.9%, anxiolytics: 14.4%-17.4%, stimulants: 12.5%-13.5%, sedatives: 8.4%-8.7%, non-medical use of hormones: 30.3%, past 6-month: 26.1% (THINS), cannabis: 28.9 (clinical	prescription opioid use: 12.5% Alcohol use disorder: cismen: 11.0%, ciswomen: 8.8% Substance use disorder: 6.2% among cismen and 1.9% among ciswomen.

						interview), 24.4% (online survey), 2.1% (ICD-10), cocaine: 23.8% (clinical interview), illicit drugs: 11.6% (online survey), currently or had used cannabis: 31.4%, currently or had used cocaine: 12.1%, lifetime used cannabis but not currently using: 19%, currently using cannabis: 12.4%, used cocaine during lifetime but not currently using: 9.8%, current users of cocaine: 2.64% (clinical evaluation), drug dependence diagnosis: 13.6%, opioid: 1.3%, cocaine: 0.1% (ICD-10), injection drug use: 15%, non-injection drug use: 34% (questionnaire), illicit drugs in the past three months: 12%, ATS: 10.4%, heroin: 0.6%, marijuana: 0.3%, non-defined types: 0.4% (questionnaire), illicit drug use in the past 12 months for transgender women:	

						43.8% (interview), stimulant use: transgender women: 20.3% and transgender men: 6.8% (AUDIT, CUDIT-R), take a drug in the prior 12 months: transgender women 18% (survey), recent marijuana: 25.6%, recent methamphetamine use: 21.5%, lifetime injection drug or illegal hormone use: 66.3% (questionnaire), lifetime nonmedical prescription opioid use: 11.8% (questionnaire), use of drugs in the past year: 38% (AUDIT-10, DAST-10), injected speedball or methamphetamine in the last month: 1%, methamphetamine: 21%, marijuana: 12% (survey with interviewer), marijuana: 29%, methamphetamine: 20.1%, crack cocaine: 13.4%, club drugs: 13.1% (questionnaire), last	

						year drug use: 12.3% (Trans PULSE survey), history of drug use: 35.5% (interview), illicit drugs other than marijuana in the past 12 months: 18% (AUDIT-C), illicit drug use in the past month: 56.0% (self-report), at least one form of illicit drugs: 13.5%, amphetamine-type stimulants: 12.9% (structured questionnaire in face-to-face interviews) Cigarette use: Past 30-day use of any cigarette: 39.7%, higher current use of cigarettes: 35.5%, cigars: 26.8%, e-cigarettes: 21.3% (surveys), notably smoking: 32.5% (retrospective study), last month: 83%, daily smoking: 62.3% (questionnaires), current smoker: transwomen: 41.4% and transgender men: 6.8% (AUDIT, CUDIT-R), current smoker: 46%, ex-	

						smoker: 47.5% (interview)	
Other mental disorders							
de Freitas et al. (2020)	GD diagnosis	5 papers (577 subjects)	post-traumatic stress disorder, anorexia nervosa, schizophrenia, unspecified psychosis disorder, dissociative identity disorder.	cross-sectional, prospective, and retrospective, structured clinical interview	SCID-I MINI-Plus	0.8% (PTSD) 0.4% (anorexia nervosa) 0.4% (unspecified psychosis disorder) 0.4% (dissociative identity disorder) 1.0% (eating disorders) 0.8% (psychotic disorders) 0.5% (somatoform disorders) 0.1% (dissociative disorders)	None
Dhejne et. Al., 2016	TG	38	dissociative disorders	Cross-sectional, longitudinal	MINI, SCID-II DDIS, DES	29.6% (Dissociative disorders)	None
Drabish and Theeke (2022)	TG	15 (1093 trans people)	Somatization	Cross-sectional	Online self-report	27.5%	None
Hayek et al. (2022)	LGBTQ (data extracted for trans, gender queer, gender non-conforming)	7	PTSD	Cross-sectional, longitudinal	Post-traumatic Stress Disorder Checklist for DSM-V	64.9%.	None
Jones et. Al., 2016	TG	26	Eating disorders	Cross-sectional, longitudinal	BUT, EDI-2, Disordered eating measured by questions found by Silverstein et al. (1988)	0.7% (BUT: Body Uneasiness Test)	Trans people are not more dissatisfied with their bodies in comparison to homosexuals and controls.

							Trans women have more disordered eating than controls. In comparison to controls, trans individuals without Sex Reassignment Surgery (SRS) had higher levels of body uneasiness, similar to those with eating disorders. Additionally, trans individuals who had SRS reported body uneasiness levels that were not as low as controls, but they were lower than the trans people who had not had SRS and lower than the eating disorder participants' levels.
Lin et al. (2021)	TGNC	30	PTSD	Cross-sectional	PTSD (4 items)	24.0%	None
(Mark et al., 2019)	TG	30 (298 participants)	PTSD	Quantitative	No reported	41% screened positive for PTSD	None
(Pinna et al., 2022)	TG	165	Eating disorders, PTSD, Somatization	Cross-sectional	PTSD: structured self-reported questionnaire, PC-PTSD, PCL, ICD-9 Eating disorder: semi-structured in-depth interviews, EDI-2, EDE-Q, EAT-26, clinical interview, HBDS	Eating disorders: Past diagnosis All 10.6% (anorexia nervosa (4.2%), bulimia nervosa (3.2%), binge eating disorder (1.6%), or other/not specified (5.1%))	Transgender men had 3.92 times the odds of PTSD (corresponding to observed percentages of 62.5 % for transgender men and 28.1 % for cisgender men). When compared to cisgender women, transgender

					Somatization: BSI-18, SCL-90-R, DDIS, DES	Current MtF 23% - 33% FtM 22% PTSD Current All 8.6% - 45.3% Somatization Current All 27.5% (BSI-18)	women had 3.31 times the odds of PTSD (corresponding to observed percentages of 54.2 % for transgender women and 26.4 % for cisgender women).

Note: TG: transgender; BDI-II: Beck's Depression Inventory; HADS: Hospital Anxiety and Depression Scale; SCL-90-R: 90-item self-report symptom inventory; Zung SDS: Zung Self-Rating Depression Scale; MMPI: Minnesota Multiphasic Personality Inventory; CESD-R: Center for Epidemiological Studies Depression Rating; PHQ-9: Patient Health Questionnaire-9; GD: gender disorder; SCID-I: Structured clinical interview for DSM Disorders; CES-D: Center for Epidemiological Studies-Depression; FTM: female to male; MTF: male to female; BAI: Beck anxiety inventory; PROMIS: Patient-reported outcomes measurement information system; DASS-21: depression anxiety stress scale-21; C-SSRS: Columbia suicide severity rating scale; ZRS; SAS: self-rating anxiety scale; SADS: social avoidance and distress scale; STAI: Sate-trait anxiety inventory; BSI: Brief Symptom Inventory; GAD-7: generalized anxiety disorder assessment; GNC: gender non-conforming; NSSI: no suicidal self-injury; SIQ: suicidal ideation questionnaire; SSM; ISAS: inventory of statement about self-injury; SITBI: self-injurious thoughts and behaviors interview-revised; DSHI; DSM: Diagnostic and statistical manual of mental disorders; ICD: international classification of diseases; e-Cig: electronic cigarette; OR: odds ratio; CI: confidence interval; DCD; HIV: Human immunodeficiency virus; AUDIT: alcohol use disorders identification test; HED: heavy episodic drinking; BRFSS; USTS; DAST-10: drug abuse screen test; CUDIT-R: cannabis use disorders identification test; Trans PULSE; TGW: transgender women; DDIS; PTSD: Post-traumatic stress disorder; DES; BUT: Body Uneasiness Test; EDI; SRS: Sex Reassignment Surgery.