Differences in alcohol and other drug use and dependence between transgender and cisgender participants from the 2018 Global Drug Survey.

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Abstract

Purpose

The purpose of this study was to compare five gender groups (cisgender women, cisgender men, transgender women, transgender men, people with non-binary/other identities) on measures of use of and dependence on seven substances.

Methods

A two-stage approach to assessing gender allowed 126,648 participants from the 2018 Global Drug Survey to be classified to one of these five gender groups. Participants were asked to disclose use of each substance in the preceding 12 months. The Alcohol Use Disorder Identification Test and the Severity of Dependence Scale were used to assess dependence. Multivariable logistic regression generated odds ratios to measure the association between gender and each substance use/dependence outcome, with cisgender women as the reference group.

Results

The sample comprised 43,331 cisgender women, 81,607 cisgender men, 215 transgender women, 254 transgender men, and 1,241 people with non-binary/other identities. Relative to cisgender women, non-binary/other participants reported greater odds of last 12-month use of all substances (adjusted odds ratio (AOR)=1.66-2.93), except alcohol (lower odds; AOR=0.42), and greater odds of dependence on cannabis (AOR=2.39), 3,4-methylenedioxymethamphetamine (MDMA; AOR=1.64) and alcohol (AOR=3.28), adjusting only for age (all $p<0.05$).

Conclusion

Transgender 2018 Global Drug Survey respondents, particularly those with non-binary/other identities, had greater odds of reporting most substance use outcomes than cisgender women. These findings suggest a nuanced approach to gender reporting in surveys and treatment centres is required to understand the needs of transgender people who use substances.

Introduction

Transgender is an umbrella term which usually describes individuals for whom there is an incongruity between their experienced gender identity and the male/female sex they were assigned at birth.[1,2] Cisgender people are those whose gender identity matches their birth-assigned sex. While many transgender and cisgender people identify comfortably within the gender binary (man/woman), for an increasing number of people, collectively termed 'non-binary', this does not represent their experience.[3] While not all non-binary people identify as transgender and there is some variation in the definition of the term, all identities other than cisgender man and cisgender woman were considered transgender for the purposes of this paper, based on their shared gender minority status.

The population prevalence of transgender identity has not yet been accurately described. However, the few studies which report on regional and national estimates indicate that transgender people are a minority, making up between 0.3-1.2% of the adult population.[4–9] The Minority Stress Model asserts that minority or marginalised groups who are chronically exposed to discrimination will experience worse mental health outcomes, particularly related to suicidality and substance use.[10]

Gender Minority Stress Models contextualise this for transgender people and proposes that if transgender people have elevated rates of substance use, it is not because they are an inherently 'risky' population.[11,12] Instead, the consequence of coping with various stigma related to their marginalisation is the creation of psychosocial conditions leading to mental ill health and greater psychoactive

substance use.[10–14] Exclusion and trauma have been associated with excessive use of both alcohol[15–17] and other drugs[18–20] among transgender people.

Based on this association, one might expect that transgender people use substances more frequently or in greater quantities than cisgender counterparts who lack gender minority stress. However, the body of literature seeking to quantify substance use by transgender people has several limitations. The first relates to the studying of vulnerable subgroup populations and the associated complexity of capturing sufficiently large samples to allow generalisability of the data.

Most transgender substance use research draws on information from small convenience samples, not representative of the wider transgender community,[21] including studies of minority ethnic transgender women[22,23] with a history of sex work [23] or those with current gender dysphoria.[24] While estimates drawn from these studies are of value to their respective sub-groups, these sub-samples are too heterogeneous to make wider population inferences about patterns of substance use by transgender people.[25]

Few studies have directly compared the prevalence of substance use and/or dependence between transgender and cisgender participants. Among a representative sample of US-based transgender (n=274) and cisgender (n=1,162) parents, transgender participants were found to have a 2.5-fold greater mean Drug Use Disorders Identification Test score than cisgender participants.[26] Similarly, a study of United States (US) veterans found that, compared to cisgender participants, transgender participants had greater odds of amphetamine, cannabis, cocaine or

‘any drug’ use disorders.[27] These findings were corroborated by a recent US-based study which found an excess prevalence of substance use disorders among transgender participants relative to cisgender counterparts.[28]

Two further studies investigating alcohol outcomes reported that transgender people were more likely than cisgender people to engage in binge drinking[29] and three times as likely to report Alcohol Use Disorder Identification Test (AUDIT) scores indicating hazardous or harmful drinking.[30] However, neither study included cisgender participants and instead compared convenience and respondent-driven samples of transgender participants with nationally-representative samples of cisgender people.[29,30] These findings are corroborated by a study of 422,906 (989 transgender) US college students which found that transgender students reported more days drinking, total drinks consumed, alcohol-related blackouts and negative reasons for drinking.[31]

Moreover, a recent Global Drug Survey (GDS) study found that transgender people were more likely than cisgender people to require help to reduce their use of alcohol, cannabis and other substances, suggesting that problematic substance use may be more common among transgender people.[32] This study seeks to build on previous GDS work to address some of the aforementioned limitations by directly comparing transgender and cisgender respondents from GDS 2018. Specifically, five gender groups (cisgender women, cisgender men, transgender women, transgender men, people with non-binary/other identities) will be compared on the prevalence of 12-month use of and dependence on a range of psychoactive substances.

Methods

Study design

The GDS is an independent research organisation that develops cross-sectional surveys on an annual basis to monitor international patterns of drug use and associated behaviour.[33] Global harm reduction and media partners direct participants to an encrypted online platform that can be used anonymously by GDS participants to provide consent and participate in the survey.[33] While GDS does not claim to be a representative sample, prior work has demonstrated that cannabis and alcohol users recruited by GDS are similar to those recruited from population-based surveys in the US, Switzerland and Australia, in terms of sex and age.[33] A full account of GDS methodology is available elsewhere.[33]

Data from GDS 2018, which recruited between 8th November 2017 and 30th December 2017, were used in this study. GDS 2018 was available in 19 languages and recruited 130,761 participants from >40 countries. Ethical approval for GDS 2018 was received from The University of New South Wales (HREC HC17769), University College London 11671/001 and University of Queensland (No: 2017001452) Research Ethics Committees.

Variables

GDS adopts a two-stage approach to assess gender.[34,35] The first question asks participants to disclose their lived gender identity with the following response options: ‘female’, ‘male’, ‘non-binary’, ‘different identity’. Participants are then asked to report their birth-assigned gender and could choose ‘female’ or male’.

Available evidence suggests a greater prevalence of non-binary than binary trans identities (66.1% vs 33.8%),[36] particularly in young samples such as GDS 2018.[37] Moreover, greater heterogeneity in self-descriptors is reported by people who exist outside the gender binary.[36,38,39] This suggests that binary trans participants are fewer and less likely to use terms other than 'man' or 'woman' to define themselves. On this basis, it was agreed that the genders of participants reporting 'different identity' are more likely to be congruent with definitions of 'non-binary' genders and these groups were combined to increase power of subsequent analyses. Participants were assigned to one of the five aforementioned groups, based on criteria described in Supplementary Table S1. Transgender groups are marked with an asterisk.

This study used data pertaining to the use of and dependence on seven substances: alcohol, cannabis, ecstasy/3,4-methylenedioxymethamphetamine (MDMA), cocaine, amphetamine powder, amphetamine paste, methamphetamine. Participants were considered non-users if they indicated they had never used or had not used in the last 12 months. Participants who reported alcohol use in the last 12 months were asked to complete the AUDIT, which assesses alcohol consumption, harms and dependency.[40–42] The AUDIT is a ten-item questionnaire with a maximum score of 40, where scores ≥20 indicate probable dependence.[41]

When participants endorsed use of any drug (other than alcohol), they were invited to complete the Severity of Dependence Scale (SDS), reflecting specifically on their use of that drug in the preceding 12 months.[43] This five-item tool assesses the psychological aspects of drug dependence and has a maximum score of 15.[43–45]

Scores of ≥4 on the SDS were deemed a conservative estimate of dependence for each substance, based on previous literature.[46–51]

Several drugs had low or zero counts for 12-month use and/or dependence. Consequently, several drugs were combined to increase the statistical power of subsequent analyses. Amphetamine powder, amphetamine paste, and methamphetamine were combined to create an 'amphetamine' group. Participants had to report 12-month use of or dependence on at least one amphetamine drug to positively endorse the category. GDS 2018 also recorded participants' demographics and lifetime history of a mental health diagnosis (yes/no). Please see Supplementary Table S2 for the items used to assess each of the demographic variables.

Statistical analyses

The sample characteristics were described using counts and percentages. Percentages describe the proportion of respondents of each gender who endorsed 12-month use of and dependence on each drug (or drug group). For each drug (or drug group), likelihood ratio X^2 analyses were used as an omnibus measure of differences between genders on each of 12-month use and dependence.

Multivariable logistic regression was used to calculate odds ratios (ORs) for 12-month use and dependence. In each initial regression model, the association between gender and substance use or dependence was adjusted only for age. Gender was a five-level categorical variable, where cisgender women were chosen as the reference category because of their established lower risk for problematic

substance use, relative to cisgender men.[52–54] Age was a three-level categorical variable, and the lowest risk group (≥35 years) was the reference category.

Sensitivity analyses demonstrating the validity of combining 'non-binary' and 'different identity' groups comprised three parts. Counts and percentages followed by one-way analysis of variance (ANOVA) or likelihood ratio X^2 analyses described and compared the demographic then substance use and dependence characteristics of both groups. Following this, the 'different identity' group were omitted from repeated regression analyses. All analyses were conducted using IBM SPSS Statistics software, v25 and v27.[55,56]

Results

Sample characteristics and sensitivity analyses

Of 130,761 survey respondents, 126,648 responded to both questions relating to gender and so could be classified to one of five gender groups and included in the subsequent analyses. Of these, there were 81,607 (64.4%) cisgender men, 43,331 (34.2%) cisgender women, 254 (0.2%) transgender men, 215 (0.2%) transgender women and 1,241 (1.0%) people with non-binary/other identities. Sample characteristics are presented in Supplementary Table S2.

Demographic data was missing for >40% of participants on each variable (other than age). However, among those who did respond, most participants were white, highly educated and had never been diagnosed with a mental illness. More than half the sample was 18-25 years old. GDS also asks participants' country of origin. The largest number of respondents were from Germany (37.4%; n=48,915), Denmark

(11.6%; n=15,108), Poland (5.7%; n=7,390), United States (4.5%; 5,887) and Switzerland (4.4%; 5,703). A full breakdown of participants' country of origin is found in Supplementary Table S3.

Sensitivity analyses confirming the validity of combining 'non-binary' and 'different identity' groups are presented in Supplementary Tables S4 and S5. Other than 12-month cannabis use, there were no significant between-group differences on measures of substance use and dependence. Similarly, there were no significant changes to regression model effect sizes (other than for MDMA dependence) when participants reporting a 'different identity' were removed from the sample.

Substance use and dependence

Table 1 summarises data relating to 12-month use and dependence. Likelihood ratio X^2 values are reported for each measure. Table 2 reports the adjusted OR (AOR) for each gender endorsing each of 12-month use and dependence, for each drug (or drug group), controlling only for age. Cisgender women were the reference group. Age was significantly associated with most substance use measures, with younger respondents more likely to use and become dependent on substances.

Cannabis

Cannabis use, while common across all gender groups, was least likely to be reported by cisgender women (37.0%). People with non-binary/other identities had two-fold greater odds of reporting use of (55.1%, AOR: 2.06, 95% CI: 1.84-2.31, p<0.0001) and dependence on (12.7%, AOR: 2.39, 95% CI: 2.02-2.84, p<0.0001) cannabis, relative to cisgender women. Cisgender men were more likely to use and

become dependent on cannabis than cisgender women. While transgender men had greater odds of 12-month use than cisgender women, they were not significantly more likely to report dependence.

Other drugs

Twelve-month use of cocaine was reported by 14.1% of cisgender women. People with non-binary/other identities were more likely than cisgender women to report cocaine use (21.4%, AOR: 1.66, 95% CI: 1.44-1.91, p<0.0001). Cisgender men were the only group significantly more likely to report to cocaine dependence than cisgender women (1.7%, AOR: 1.23, 95% CI: 1.12-1.36, p<0.0001).

People with non-binary/other identities were more likely to report 12-month use (31.0%, AOR 1.94 95% CI: 1.72-2.20, p<0.0001) and dependence on MDMA (2.4%, AOR: 1.64 95% CI: 1.13-2.38, p<0.01) than cisgender women. Use of amphetamines was more commonly reported by people with non-binary/other identities (23.8%, AOR: 2.30, 95% CI: 2.01-2.63, p<0.0001) than cisgender women (11.9%, reference group). There were no significant differences in the rates of dependence between cisgender women and any other gender group.

Alcohol

Twelve-month alcohol use was reported by the majority of the whole sample (94.5%) and was more commonly reported by cisgender men (94.9%, AOR: 1.08, 95% CI: 1.02-1.14, p<0.01) and cisgender women (94.4%, reference group) than transgender participants (87.9-93.0%). People with non-binary/other identities (11.4%, AOR: 3.28, 95% CI: 2.73-3.94, p<0.0001), transgender women (8.4%, AOR: 2.24, 95% CI:

1.38-3.65, p<0.01) and transgender men (7.1%, AOR: 1.86, 95% CI: 1.15-3.01, p<0.05) all had greater odds of reporting alcohol dependence than cisgender women. Dependence was also more likely among cisgender men (5.5%, AOR: 1.48, 95% CI: 1.39-1.56, p<0.0001), relative to cisgender women.

Discussion

Key findings

The most consistent finding of this study was that participants with non-binary/other identities reported greater odds of 12-month use of all drugs (except alcohol), than cisgender women. In addition, participants with non-binary/other identities had greater odds of reporting dependence on alcohol, cannabis and MDMA, than cisgender women. While transgender women and transgender men also had significantly higher odds of alcohol dependence relative to cisgender women, there were fewer observed significant differences between binary transgender participants and cisgender women, on measures of use of other substances. However, there did appear to be a trend of increased likelihood of use among transgender people across most measures, despite many analyses lacking power.

Findings in context

The results of this study are supported by a systematic review which reported a high and excess prevalence of (problematic) substance use among transgender people, relative to cisgender people.[21] More specifically, our finding that transgender groups each had higher odds of alcohol dependence than cisgender women is supported by the substantial body of alcohol literature which suggests that transgender people have a high prevalence of hazardous or harmful drinking.[57]

A large study with a clinical sample corroborated our results for both alcohol and cocaine where disordered use of the former was almost three times as common and the latter half as common among transgender participants, relative to cisgender counterparts.[28] The more frequent reporting of amphetamine dependence by transgender women in this study is corroborated by recent work which found 2.2-fold greater odds of amphetamine use disorder among transgender compared with cisgender veterans.[27]

Non-binary people have largely been excluded from substance use research to date.[21] However, one study reported that while alcohol use severity was worse among cisgender men than any other gender group, drug use severity was worst among non-binary people assigned female at birth, thus supporting our findings. An extension of minority stress theory suggests that people with non-binary (or genderqueer) identities experience greater gender minority stress than do cisgender or other transgender counterparts.[58] This assertion is supported by studies which found that gender presentations incongruent with societal expectation are associated with increased substance use to cope with greater exposure to gender minority stress.[12,30,59]

Strengths and limitations

A limitation of the existing transgender substance use literature is that most studies focus on transfeminine people living in North America,[57] while those with non-binary/other identities, living elsewhere, remain understudied.[57,60] This study is unique in that GDS offers an international sample with a) 1,710 transgender

participants; b) >1000 participants with non-binary/other identities; c) cisgender comparators. Given the increased substance use and dependence reported by non-binary people, this disaggregated analysis was an important step forward in understanding substance use in the transgender community.

GDS has previously been criticised for its use of a non-probability-based sampling frame.[33] This approach means that the GDS sample is influenced by both non-response bias and volunteer bias.[61,62] In addition, the retrospective nature of GDS data means it is subject to recall bias.

Since it has been argued that a representative sample is only needed when estimating population prevalence, a purposive sample was adequate for this present study.[33,63–68] Indeed, the recruitment of such a large sample of transgender participants can be attributed to the sampling techniques employed by GDS.[33,69] Had a probability-based approach been used, one could expect a maximum of between 380-1,520 transgender participants.[7,9,70]

While GDS2018 asked about a wide range of drugs, several drug groups (opioids) and behaviours (non-medical use of prescription drugs), where one would expect similar differences, were not included in the survey. GDS 2018 is a largely Western European sample which limits generalisability. GDS is designed with demographic data collection at both the start and end of the survey. Therefore, one possible explanation for low response rate on important demographic variables such as ethnicity, sexual orientation and education level is that these items are asked when many participants have ended participation, before reaching the end of the survey.

This present analysis required the collation of ‘non-binary’ and ‘different identity’ respondents prior to statistical analysis. The rationale for this decision is described above. However, there remains a risk that participants have been miscategorised.

We were interested in current users and twelve-month use was chosen to ensure an adequate sample size. It also corresponded with the time frame used by the AUDIT and SDS. Consequently, a limitation of this study was that those who had never used and those who had used more than a year preceding the survey were collectively classified as ‘non-users’. Lastly, while it is possible that between-country differences exist, sub-samples of transgender participants from individual countries were too small to allow for meaningful comparison.

Clinical, policy and research recommendations

The most novel finding of this study was the increased risk of substance dependence faced by people with non-binary/other identities. Given the excess substance use-related harm reported in this and other studies,[28] there is a need for estimates of prevalence to inform the scale of clinical service provision. Estimates from studies such as *TransPop*[26,71] can begin to address such questions in the US. However, patterns of drug use are influenced by cultural, political, and legal factors which vary by both nation and region. Therefore, a representative US-based sample is not generalisable to other nations and representative samples outside of North America are needed.

Moreover, despite this being the largest international sample reported, the numbers of transgender men and transgender women were very small. Future GDS samples will aim to broaden participation in these as well as minority ethnic groups and low- and middle-income countries. Moving forward, research should explore the motivations and culture surrounding substance use and the experiences of harm among non-binary and other transgender people.

Currently in the UK, the National Drug Treatment Monitoring System only records each client's birth-registered sex and Adult Psychiatric Morbidity Survey reports make no comment on transgender people.[72,73] This and a previous GDS study indicate that there is a need for tailored substance use disorder treatment for transgender people.[32] To facilitate the abovementioned estimates, the two-stage approach to assessing gender, used by the GDS,[35] should be incorporated into all general population surveys. While there is evidence that this approach to measuring gender, which has high sensitivity and specificity, is generally acceptable to the community, further research is needed to understand the feasibility of offering an open-ended response option in large samples to maximise inclusivity.[68]

Further work is then needed to determine what types of support are most acceptable to transgender people and the barriers that might prevent engagement. In the interim, it is recommended that the two-stage approach to assessing gender should also be incorporated into substance use disorder services, so that clients can identify themselves as transgender if they wish.[35] There is an urgent need for treatment providers to be educated about gender and the needs of the transgender client, to

overcome the stigma and discrimination that currently prevents engagement with these services.[74–80]

Specialist services for transgender people who use drugs and/or specialist interventions in non-specialist settings may be indicated. However, a recent systematic review highlighted that these appear to be lacking.[81] The development of such interventions should be a priority for researchers and policymakers.

Conclusion

People with non-binary/other gender identities, transgender women and transgender men appear to be more likely to use and become dependent on psychoactive substances, relative to cisgender women. Researchers and clinicians must take these findings into account and a nuanced approach to gender reporting in surveys and by treatment centres is required to understand the needs of transgender people who use substances.

Author Contributions

Dean Connolly: Conceptualisation, Formal analysis, Writing – Original Draft, Writing – Review & Editing, Project administration **Emma Davies:** Conceptualisation, Methodology, Writing – Review & Editing **Michael Lynskey:** Conceptualisation, Formal analysis, Writing – Review & Editing, Supervision **Larissa Maier:** Conceptualisation, Methodology, Writing – Review & Editing **Jason Ferris:** Conceptualisation, Methodology, Writing – Review & Editing **Monica Barratt:** Conceptualisation, Methodology, Writing – Review & Editing **Adam Winstock:** Conceptualisation, Methodology, Writing – Review & Editing **Gail Gilchrist:** Conceptualisation, Formal analysis, Writing – Review & Editing, Supervision

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Author disclosures

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References

1. Lev AI. Transgender Emergence: Therapeutic Guidelines for Working with Gender-Variant People and their Families. The Haworth Clinical Practice Press: New York, NY; 2013.
2. Bockting W. From construction to context: Gender through the eyes of the transgendered. SIECUS Rep 1999;28(1):3-7.
3. Vincent B. Transgender Health: A Practitioner's Guide to Binary and Non-Binary Trans Patient Care. Jessica Kingsley Publishers: London; 2018.
4. Clark TC, Lucassen MFG, Bullen P, et al. The health and well-being of transgender high school students: Results from the New Zealand Adolescent Health Survey (Youth'12). J Adolesc Health 2014;55(1):93-99; https://doi.org/10.1016/j.jadohealth.2013.11.008.
5. Conron KJ, Scott G, Stowell GS et al. Transgender health in Massachusetts: Results from a household probability sample of adults. Am J Public Health 2012;102(1):118-122; https://doi.org/10.2105/AJPH.2011.300315.
6. Balarajan M, Gray M, Mitchell M. Research report 75: Monitoring equality - Developing a gender identity question & Technical note: Measuring gender identity. 2011. London, Equality and Human Rights Commission.
7. Meerwijk EL, Sevelius JM. Transgender population size in the United States: a meta-regression of population-based probability samples. Am J Public Health 2017;107(2):e1-e8; https://doi.org/10.2105/AJPH.2016.303578.
8. Van Caenegem E, Wierckx K, Elaut E, et al. Prevalence of gender nonconformity in Flanders, Belgium. Arch Sex Behav 2015;44(5):1281-1287; https://doi.org/10.1007/s10508-014-0452-6.

9. Winter S, Diamond M, Green J, et al. Transgender people: health at the margins of society. Lancet 2016;388(10042):390-400; https://doi.org/10.1016/S0140-6736(16)00683-8.
10. Meyer IH. Prejudice, social stress, and mental health in lesbian, gay, and bisexual populations: Conceptual issues and research evidence. Psychol Bull 2003;129(5):674-697; https://doi.org/10.1037/0033-2909.129.5.674.
11. Hatzenbuehler ML, Phelan JC, Link BG. Stigma as a fundamental cause of population health inequalities. Am J Public Health 2013;103(5):813-821; https://doi.org/10.2105/AJPH.2012.301069.
12. Hendricks ML, Testa RJ. A conceptual framework for clinical work with transgender and gender nonconforming clients: An adaptation of the Minority Stress Model. Prof Psychol Res Pr 2012;43(5):460-467; https://doi.org/10.1037/a0029597.
13. Bockting WO, Miner MH, Swinburne Romine RE, et al. Stigma, mental health, and resilience in an online sample of the US transgender population. Am J Public Health 2013;103(5):943-951; https://doi.org/10.2105/AJPH.2013.301241.
14. Testa RJ, Habarth J, Peta J, et al. Development of the Gender Minority Stress and Resilience Measure. Psychol Sex Orientat Gend Divers 2015;2(1):65-77; https://doi.org/10.1037/sgd0000081.
15. Arayasirikul S, Wilson EC, Raymond HF. Examining the effects of transphobic discrimination and race on HIV risk among transwomen in San Francisco. AIDS Behav 2017;21(9):2628-2633; https://doi.org/10.1007/s10461-017-1728-3.
16. Chakrapani V, Newman PA, Shunmugam M, et al. Syndemics of depression, alcohol use, and victimisation, and their association with HIV-related sexual risk among men who have sex with men and transgender women in India. Glob Public Health 2017;12(2):250-265; https://doi.org/10.1080/17441692.2015.1091024.

17. Nuttbrock L, Bockting W, Rosenblum A, et al. Gender abuse, depressive symptoms, and substance use among transgender women: A 3-year prospective study. Am J Public Health 2014;104(11):2199-2206; https://doi.org/10.2105/AJPH.2014.302106.
18. Budhwani H, Hearld KR, Milner AN, et al. Transgender women's drug use in the Dominican Republic. Trasngend Health 2017;2(1):288-194; https://doi.org/10.1089/trgh.2017.0032.
19. Scheim AI, Bauer GR, Shokoohi M. Drug use among transgender people in Ontario, Canada: Disparities and associations with social exclusion. Addict Behav 2017;72:151-158; https://doi.org/10.1016/j.addbeh.2017.03.022.
20. Shah HBU, Rashid F, Atif I, et al. Challenges faced by marginalized communities such as transgenders in Pakistan. Pan Afr Med J 2018;30:96; https://doi.org/10.11604/pamj.2018.30.96.12818.
21. Connolly D, Gilchrist G. Prevalence and correlates of substance use among transgender adults: A systematic review. Addict Behav 2020;111:106544; https://doi.org/10.1016/j.addbeh.2020.106544.
22. Nemoto T, Operario D, Keatley J, et al. HIV risk behaviors among male-to-female transgender persons of color in San Francisco. Am J Public Health 2004;94(7):1193-1199; https://doi.org/10.2105/ajph.94.7.1193.
23. Operario D, Nemoto T. Sexual risk behavior and substance use among a sample of Asian Pacific Islander transgendered women. AIDS Educ Prev 2005;17(5):430-443; https://doi.org/10.1521/aeap.2005.17.5.430.
24. Salas-Espinoza KJ, Menchaca-Diaz R, Patterson TL, et al. HIV prevalence and risk behaviors in male to female (MTF) transgender persons in Tijuana, Mexico. AIDS Behav 2017;21(12):3271-3278; https://doi.org/10.1007/s10461-017-1931-2.

25. Bowleg L. The Problem with the phrase w*omen and minorities:* Intersectionality—an important theoretical framework for public health. Am J Public Health 2012;102(7):1267-1273; https://doi.org/10.2105/AJPH.2012.300750.
26. Carone N, Rothblum ED, Bos HMW, et al. Demographics and health outcomes in a U.S. probability sample of transgender parents. J Fam Psychol 2021;35(1):57-68; https://doi.org/10.1037/fam0000776.
27. Frost MC, Blosnich JR, Lehavot K, et al. Disparities in documented drug use disorders between transgender and cisgender U.S. veterans health administration patients. J Addict Med 2021;15(4):334-340; https://doi.org/10.1097/ADM.0000000000000769.
28. Hughto JMW, Quinn EK, Dunbar MS, et al. Prevalence and co-occurrence of alcohol, nicotine, and other substance use disorder diagnoses among US transgender and cisgender adults. JAMA Netw Open 2021;4(2):e2036512; https://doi:10.1001/jamanetworkopen.2020.36512.
29. Scheim AI, Bauer GR, Shokoohi M. Heavy episodic drinking among transgender persons: Disparities and predictors. Drug Alcohol Depend 2016;167:156-162; https://doi.org/10.1016/j.drugalcdep.2016.08.011.
30. Staples JM, Neilson EC, George WH, et al. A descriptive analysis of alcohol behaviors across gender subgroups within a sample of transgender adults. Addict Behav 2018;76:355-362; https://doi.org/10.1016/j.addbeh.2017.08.017.
31. Tupler LA, Zapp D, DeJong W, et al. Alcohol-related blackouts, negative alcohol-related consequences, and motivations for drinking reported by newly matriculating transgender college students. Alcohol Clin Exp Res 2017;41(5):1012-1023; https://doi.org/10.1111/acer.13358.

32. Connolly D, Davies E, Lynskey M, et al. Comparing intentions to reduce substance use and willingness to seek help among transgender and cisgender participants from the Global Drug Survey. J Subst Abuse Treat 2020;112:86-91; https://doi.org/10.1016/j.jsat.2020.03.001.
33. Barratt MJ, Ferris JA, Zahnow R, et al. Moving on from representativeness: Testing the utility of the Global Drug Survey. Subst Abuse 2017;11:1-17; https://doi.org/10.1177/1178221817716391.
34. Bauer GR, Braimoh J, Scheim AI, et al.. Transgender-inclusive measures of sex/gender for population surveys: Mixed-methods evaluation and recommendations. PLoS One 2017;12(5):e0178043; https://doi.org/10.1371/journal.pone.0178043.
35. Sausa LA, Sevelius J, Keatley J, et al. Policy recommendations for inclusive data collection of trans people in HIV prevention, care & services. 2009. San Francisco, Centre of Excellence for Transgender HIV Prevention, University of California.
36. Callander D, Newman CE, Holt M, et al. The complexities of categorizing gender: A hierarchical clustering analysis of data from the first Australian Trans and Gender Diverse Sexual Health Survey. Transgend Health 2021;6(2):74-81; https://doi.org/10.1089/trgh.2020.0050.
37. Wilson BD, Meyer IH. Nonbinary LGBTQ adults in the United States. 2021. Los Angeles, Williams Institute, School of Law, University of California, Los Angeles.
38. Puckett JA, Brown NC, Dunn T, et al. Perspectives from transgender and gender diverse people on how to ask about gender. LGBT Health 2020;7(6):305-311; https://doi.org/10.1089/lgbt.2019.0295.
39. Suen LW, Lunn MR, Katuzny K, et al. What sexual and gender minority people want researchers to know about sexual orientation and gender identity questions: A

qualitative study. Arch Sex Behav 2020;49(7):2301-2318; https://doi.org/10.1007/s10508-020-01810-y.

40. Allen JP, Litten RZ, Fertig JB, et al. A review of research on the alcohol use disorders identification test (AUDIT). Alcohol Clin Exp Res 1997;21(4):613-619.
41. Babor TF, Higgins-Biddle JC, Saunders JB, et al. AUDIT : The Alcohol Use Disorders Identification Test : Guidelines for use in primary care, 2nd ed. 2001. Geneva, World Health Organization.
42. Saunders JB, Aasland OG, Babor TF, et al. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction 1993;88(6):791-804; https://doi.org/10.1111/j.1360-0443.1993.tb02093.x.
43. Gossop M, Darke S, Griffiths P, et al. The Severity of Dependence Scale (SDS): Psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. Addiction 1995;90(5):607-614; https://doi.org/10.1046/j.1360-0443.1995.9056072.x.
44. Ferri CP, Marsden J, de Araujo M, et al. Validity and reliability of the Severity of Dependence Scale (SDS) in a Brazilian sample of drug users. Drug Alcohol Rev 2000;19(4):451-455; https://doi.org/10.1080/713659418.
45. Gossop M, Best D, Marsden J, et al. Test-retest reliability of the Severity of Dependence Scale. Addiction 1997;92(3):353; https://doi.org/10.1111/j.1360-0443.1997.tb03205.x.
46. Bruno R, Matthews AJ, Topp L, et al. Can the Severity of Dependence Scale be usefully applied to 'ecstasy'? Neuropsychobiology 2009;60(3-4):137-147; https://doi.org/10.1159/000253550.

47. Kaye S, Darke S. Determining a diagnostic cut-off on the Severity of Dependence Scale (SDS) for cocaine dependence. Addiction 2002;97(6):727-731; https://doi.org/10.1046/j.1360-0443.2002.00121.x.

48. Martin G, Copeland J, Gates P, et al. The Severity of Dependence Scale (SDS) in an adolescent population of cannabis users: Reliability, validity and diagnostic cut-off. Drug Alcohol Depend 2006;83(1):90-93; ttps://doi.org/10.1016/j.drugalcdep.2005.10.014.

49. Steiner S, Baumeister SE, Kraus L. Severity of Dependence Scale: Establishing a cut-off point for cannabis dependence in the German adult population. SUCHT 2008;54:S57-S63; https://doi.org/10.1024/2008.07.07.

50. Swift W, Copeland J, Hall W. Choosing a diagnostic cut-off for cannabis dependence. Addiction 1998;93(11):1681-1692; https://doi.org/10.1046/j.1360-0443.1998.931116816.x.

51. Topp L, Mattick RP. Choosing a cut-off on the Severity of Dependence Scale (SDS) for amphetamine users. Addiction 1997;92(7):839-845.

52. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 alcohol use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry 2015;72(8):757-766; https://doi.org/10.1001/jamapsychiatry.2015.0584.

53. Nolen-Hoeksema S. Gender differences in risk factors and consequences for alcohol use and problems. Clin Psychol Rev 2004;24(8):981-1010; https://doi.org/10.1016/j.cpr.2004.08.003.

54. Wilsnack RW, Vogeltanz ND, Wilsnack SC, et al. Gender differences in alcohol consumption and adverse drinking consequences: Cross-cultural patterns. Addiction 2000;95(2):251-265; https://doi.org/10.1046/j.1360-0443.2000.95225112.x.

55. SPSS 25 [computer program]. Armonk, NY: IBM Corporation, 2015.

56. SPSS 27 [computer program]. Armonk, NY: IBM Corporation, 2020.

57. Gilbert PA, Pass LE, Keuroghlian AS, et al. Alcohol research with transgender populations: A systematic review and recommendations to strengthen future studies. Drug Alcohol Depend 2018;186:138-146; https://doi.org/10.1016/j.drugalcdep.2018.01.016.

58. Lefevor GT, Boyd-Rogers CC, Sprague BM, et al. Health disparities between genderqueer, transgender, and cisgender individuals: An extension of minority stress theory. J Couns Psychol 2019;66(4):385-395; https://doi.org/10.1037/cou0000339.

59. Reisner SL, Pardo ST, Gamarel KE, et al. Substance use to cope with stigma in healthcare among U.S. female-to-male trans masculine adults. LGBT Health 2015;2(4):324-332; https://doi.org/10.1089/lgbt.2015.0001.

60. Flentje A, Bacca CL, Cochran BN. Missing data in substance abuse research? Researchers' reporting practices of sexual orientation and gender identity. Drug Alcohol Depend 2015;147:280-284; https://doi.org/10.1016/j.drugalcdep.2014.11.012.

61. Eysenbach G, Wyatt J. Using the Internet for surveys and health research. J Med Internet Res 2002;4(2):e13; https://doi.org/10.2196/jmir.4.2.e13.

62. Zhao J, Stockwell T, MacDonald S. Non-response bias in alcohol and drug population surveys. Drug Alcohol Rev 2009;28(6):648-657; https://doi.org/10.1111/j.1465-3362.2009.00077.x.

63. Ebrahim S, Davey Smith G. Commentary: Should we always deliberately be non-representative? Int J Epidemiol 2013;42(4):1022-1026; https://doi.org/10.1093/ije/dyt105.

64. Elwood JM. Commentary: On representativeness. Int J Epidemiol 2013;42(4):1014-1015; https://doi.org/10.1093/ije/dyt101.

65. Nohr EA, Olsen J. Commentary: Epidemiologists have debated representativeness for more than 40 years--has the time come to move on? Int J Epidemiol 2013;42(4):1016-1017; https://doi.org/10.1093/ije/dyt102.

66. Richiardi L, Pizzi C, Pearce N. Commentary: Representativeness is usually not necessary and often should be avoided. Int J Epidemiol 2013;42(4):1018-1022; https://doi.org/10.1093/ije/dyt103.

67. Rothman KJ, Gallacher JE, Hatch EEL. Rebuttal: When it comes to scientific inference, sometimes a cigar is just a cigar. Int J Epidemiol 2013;42(4):1026-1028; 1026–1028. https://doi.org/10.1093/ije/dyt124.

68. Rothman KJ, Gallacher JE, Hatch EE. Why representativeness should be avoided. Int J Epidemiol 2013;42(4):1012-1014; https://doi.org/10.1093/ije/dys223.

69. Topp L, Barker B, Degenhardt L. The external validity of results derived from ecstasy users recruited using purposive sampling strategies. Drug Alcohol Depend 2004;73(1):33-40; https://doi.org/10.1016/j.drugalcdep.2003.09.001.

70. Flores AR, Herman, JL, Gates GJ, et al. How many adults identify as transgender in the United States? 2016. Los Angeles, Williams Institute, School of Law, University of California, Los Angeles.

71. Meyer IH, Wilson BD, O'Neill K. LGBTQ People in the US: Select findings from the Generations and TransPop studies. 2021. Los Angeles, Williams Institute, School of Law, University of California, Los Angeles.

72. Appleby L, Asherson, P, Ashtarikiani, A, et al. Mental health and wellbeing in England: Adult Psychiatric Morbidity Survey 2014. 2016. Leeds, NHS Digital.

73. Hughes L, Smith H. National Drug Treatment Monitoring System (NDTMS) Reference Data Core Dataset O. 2019. London, Public Health England.
74. Cochran BN, Cause AM. Characteristics of lesbian, gay, bisexual, and transgender individuals entering substance abuse treatment. J Subst Abuse Treat 2006;30(2):135-146; https://doi.org/10.1016/j.jsat.2005.11.009.
75. Cochran BN, Peavy KM, Cauce AM. Substance abuse treatment providers' explicit and implicit attitudes regarding sexual minorities. J Homosex 2007;53(3):181-207; https://doi.org/10.1300/J082v53n03_10.
76. Eliason MJ. Substance abuse counselor's attitudes regarding lesbian, gay, bisexual, and transgendered clients. J Subst Abuse 2000;12(4):311-328; https://doi.org/10.1016/s0899-3289(01)00055-4.
77. Lombardi EL, van Servellen G. Building culturally sensitive substance use prevention and treatment programs for transgendered populations. J Subst Abuse Treat 2000;19(3):291-296; https://doi.org/10.1016/s0740-5472(00)00114-8.
78. Nuttbrock LA. Culturally competent substance abuse treatment with transgender persons. J Addict Dis 2012;31(3):236-241; https://doi.org/10.1080/10550887.2012.694600.
79. Rachlin K, Green J, Lombardi E. Utilization of health care among female-to-male transgender individuals in the United States. J Homosex 2008;54(3):243-258; https://doi.org/10.1080/00918360801982124.
80. Sperber J, Landers S, Lawrence S. Access to health care for transgendered persons: Results of a needs assessment in Boston. International Journal of Transgenderism 2005;8(2-3):75-91; https://doi.org/10.1300/J485v08n02_08.

81. Glynn TR, van der Berg JJ. A Systematic review of interventions to reduce problematic substance use among transgender individuals: A call to action. Transgend Health 2017;2(1):45-59; https://doi.org/10.1089/trgh.2016.0037.

Table 1: 12-month substance use and dependence, by gender group

Outcome		Cisgender men (n=81,607)	Cisgender women (n=43,331)	Transgender men (n=254)	Transgender women (n=215)	Non-binary/other identity (n=1,241)	X^2 (df = 4)
Substance	**Measure**	%	%	%	%	%	
Cannabis	Last 12-month use	50.6%	37.0%	47.2%	50.7%	55.1%	2182.8**
	SDS ≥4	9.4%	5.7%	7.9%	9.3%	12.7%	594.7**
Cocaine	Last 12-month use	19.2%	14.1%	14.6%	17.2%	21.4%	544.0**
	SDS ≥4	1.7%	1.4%	1.6%	0.5%	1.7%	18.8*
MDMA	Last 12-month use	23.6%	18.7%	18.5%	20.0%	31.0%	471.4**
	SDS ≥4	1.1%	1.4%	0.8%	1.9%	2.4%	32.2**
Amphetamines	Last 12-month use	16.2%	11.9%	14.6%	16.7%	23.8%	503.5**
	SDS ≥4	1.5%	1.6%	1.6%	3.3%	2.3%	8.9^{ns}
Alcohol	Last 12-month use	94.9%	94.4%	89.0%	93.0%	87.9%	112.32**
	AUDIT ≥20	5.5%	3.7%	7.1%	8.4%	11.4%	292.1**

Notes: *p<0.001 **p<0.0001; AUDIT: alcohol use disorders identification test; df: degrees of freedom; MDMA: 3,4-methylenedioxymethamphetamine; ^{ns}: not significant; SDS: severity of dependence scale.

Table 2: Multivariable logistic analysis of the association between gender group, age and 12-month substance use and dependence

Outcome		Gender (reference category: cisgender women)			
Substance	**Measure**	**Transgender men**	**Cisgender men**	**Transgender women**	**Non-binary/other identity**
		AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Cannabis	Last 12-month use	1.37 (1.07-1.76)*	1.72 (1.68-1.76)****	1.60 (1.22-2.10)***	2.06 (1.84-2.31)****
	SDS ≥4	1.34 (0.85-2.12)^{ns}	1.71 (1.63-1.79)****	1.61 (1.02-2.56)*	2.39 (2.02-2.84)****
Cocaine	Last 12-month use	1.01 (0.71-1.44)^{ns}	1.46 (1.41-1.50)****	1.22 (0.86-1.74)^{ns}	1.66 (1.44-1.91)****
	SDS ≥4	1.16 (0.43-3.12)^{ns}	1.23 (1.12-1.36)****	0.33 (0.05-2.38)^{ns}	1.24 (0.80-1.93)^{ns}
MDMA	Last 12-month use	0.91 (0.66-1.25)^{ns}	1.33 (1.29-1.37)****	1.00 (0.71-1.40)^{ns}	1.94 (1.72-2.20)****
	SDS ≥4	0.47 (0.12-1.90)^{ns}	0.75 (0.68-0.83)****	1.14 (0.42-3.09)^{ns}	1.64 (1.13-2.38)**
Amphetamines	Last 12-month use	1.19 (0.84-1.69)^{ns}	1.42 (1.37-1.47)****	1.40 (0.98-2.01)^{ns}	2.30 (2.01-2.63)****
	SDS ≥4	0.93 (0.35-2.51)^{ns}	0.93 (0.85-1.02)^{ns}	1.95 (0.91-4.15)^{ns}	1.43 (0.98-2.08)^{ns}
Alcohol	Last 12-month use	0.43 (0.29-0.63)****	1.08 (1.02-1.14)**	0.71 (0.42-1.20)^{ns}	0.42 (0.35-0.50)****
	AUDIT ≥20	1.86 (1.15-3.01)*	1.48 (1.39-1.56)****	2.24 (1.38-3.65)**	3.28 (2.73-3.94)****

Notes: AOR: adjusted odds ratio; CI: confidence intervals; *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; ns: not significant; SDS: severity of dependence scale; AUDIT: alcohol use disorders identification test

Supplementary Table S1: Classification of gender categories

Birth-assigned sex	Gender identity	Gender category
Female	Female	Cisgender woman
Male	Male	Cisgender man
Male	Female	Transgender woman*
Female	Male	Transgender man*
Female	Non-binary	Non-binary/other identity*
Male	Non-binary	
Female	Different identity	
Male	Different Identity	

Notes: *transgender

Supplementary Table S2: Demographic questions, groups used for analysis and participants' responses

Demographic question	Response options	Groups for analysis	N=126,648 n (%)
How old are you?	16-85 years	18-25 years	67,453 (53.5%)
		26-34 years	35,293 (27.9%)
		≥35 years	23,902 (18.9%)
	Missing	*Missing*	*0 (0%)*
What is your sexual orientation?	Bisexual	Bisexual	6,939 (5.5%)
	Heterosexual	Heterosexual	55,445 (43.8%)
	Homosexual	Homosexual	2,852 (2.3%)
	Prefer not to answer	Prefer not to answer	1,422 (1.1%)
	Other	Other	972 (0.8%)
	Missing	*Missing*	*59,018 (46.6%)*
Your ethnicity?	Black African/Black Caribbean Black American	Black	238 (0.2%)
	South East Asian Asian (Pakistani, Indian, Bangladeshi)	Asian	550 (0.4%)
	Hispanic/Latino	Hispanic	1,472 (1.2%)
	Aboriginal/Maori Native American Other	Other	1,382 (1.1%)
	White	White	62,813 (49.6%)
	Mixed	Mixed	1,839 (1.5%)
	Missing	*Missing*	*58,354 (46.1%)*
Highest academic qualification attained?	No formal schooling	No formal schooling	375 (0.3%)
	Primary school	Primary school	1,468 (1.2%)
	Lower secondary school/school certificate/intermediate certificate Technical or trade certificate Higher secondary school/HSC/VCE/leaving certificate	Secondary school	25,191 (19.9%)
	College certificate/diploma Undergraduate degree	Undergraduate degree	34,711 (27.4%)
	Postgraduate degree	Higher degree	5,220 (4.1%)
	Don't know	*Missing*	*59,683 (47.1%)*
	Missing	*Missing*	
Have you ever been diagnosed with a mental illness?	Yes	Yes	15,293 (12.1%)
	No	No	56,918 (44.9%)
	Missing	*Missing*	*54,437 (43.0%)*

Notes: The above questions and response options are taken from Global Drug Survey 2018, with permission from CEO Adam Winstock. HSC: High School Certificate; VCE: Victorian Certificate of Education

Supplementary Table S3: Global Drug Survey 2018 respondents' country of origin, by gender identity

	Gender	Total

		Cisgender women	Transgender men	Cisgender men	Transgender women	Non-binary/other identity	
Which country do you currently live in?	Afghanistan	11	5	30	0	26	72
	Algeria	0	3	6	1	3	13
	American Samoa	5	1	6	1	9	22
	Andorra	2	1	6	0	10	19
	Angola	2	0	5	2	4	13
	Anguilla	3	0	0	0	3	6
	Antarctica	1	0	6	0	7	14
	Antigua and Barbuda	0	1	2	1	3	7
	Argentina	30	1	93	2	4	130
	Armenia	5	0	4	1	5	15
	Aruba	0	0	1	1	1	3
	Australia	788	7	1,735	10	32	2,572
	Austria	1,519	4	2,338	4	29	3,894
	Azerbaijan	7	0	10	0	6	23
	Bahamas	1	0	5	1	5	12
	Bahrain	1	0	4	0	4	9
	Bangladesh	3	0	4	0	8	15
	Barbados	0	0	4	0	3	7
	Belarus	11	0	10	0	0	21
	Belgium	237	1	544	0	2	784
	Belize	0	0	4	0	0	4
	Benin	0	0	1	0	0	1
	Bermuda	0	0	3	0	0	3
	Bhutan	0	0	1	0	0	1
	Bolivia	5	0	11	0	1	17
	Botswana	0	0	2	0	1	3
	Bouvet Island	0	0	1	0	1	2
	Brazil	675	4	1,234	2	14	1,929

British Indian Ocean Territory	2	0	1	0	2	5
Brunei Darussalam	0	0	1	0	0	1
Burkina Faso	1	0	2	0	1	4
Burundi	1	0	1	0	0	2
Cambodia	2	0	6	0	2	10
Cameroon	1	0	1	0	1	3
Canada	511	10	998	6	44	1,569
Cape Verde	2	0	0	0	0	2
Cayman Islands	0	0	0	0	1	1
Central African Republic	0	0	3	0	0	3
Chad	2	0	0	0	0	2
Chile	36	1	73	0	2	112
China	18	0	34	0	2	54
Christmas Island	0	0	4	0	0	4
Cocos (Keeling) Islands	0	1	0	0	0	1
Colombia	413	1	1,017	2	19	1,452
Congo	2	0	4	0	1	7
Congo, The Democratic Republic of The	0	0	2	0	1	3
Cook Islands	0	0	2	0	1	3
Costa Rica	15	0	27	1	1	44
Cote Divoire	1	0	2	0	1	4
Cuba	0	0	5	0	0	5
Cyprus	11	0	19	0	0	30
Czech Republic	298	2	672	4	14	990
Denmark	5,266	30	9,669	11	98	15,074
Djibouti	1	0	3	0	2	6

Dominica	0	0	1	0	0	1
Dominican Republic	5	0	8	0	0	13
Ecuador	17	0	40	0	0	57
Egypt	2	0	7	0	2	11
El Salvador	2	0	1	0	1	4
England	1,144	8	2,489	7	48	3,696
Equatorial Guinea	1	0	0	0	0	1
Eritrea	0	0	3	0	1	4
Estonia	32	0	73	1	0	106
Ethiopia	0	0	4	0	0	4
Falkland Islands (Malvinas)	2	0	0	0	0	2
Faroe Islands	15	1	28	0	0	44
Fiji	1	0	1	0	1	3
Finland	381	3	944	2	28	1,358
France	235	3	413	5	12	668
French Guiana	0	0	0	0	1	1
French Polynesia	1	0	0	0	1	2
French Southern Territories	1	0	4	0	0	5
Gabon	1	0	1	0	0	2
Gambia	2	0	5	0	0	7
Georgia	12	0	9	0	1	22
Germany	18,713	67	29,413	56	367	48,616
Ghana	5	0	14	0	0	19
Gibraltar	2	0	3	0	0	5
Greenland	26	0	34	0	0	60
Grenada	2	0	1	0	0	3
Guadeloupe	0	0	0	0	1	1
Guam	0	0	3	0	0	3
Guatemala	4	0	10	0	0	14

Guernsey (Bailiwick of Guernsey)	25	0	18	0	1	44
Guinea	0	0	1	0	0	1
Haiti	0	0	1	0	0	1
Heard Island and Mcdonald Islands	0	0	1	0	1	2
Holy See (Vatican City State)	0	0	2	0	0	2
Honduras	1	0	1	0	0	2
Hong Kong	12	0	25	0	1	38
Hungary	579	0	2,088	0	13	2,680
Iceland	39	0	37	0	3	79
India	17	0	45	0	0	62
Indonesia	3	0	29	0	0	32
Iran, Islamic Republic of	7	0	21	0	0	28
Iraq	7	0	14	0	1	22
Ireland	129	4	333	1	4	471
Israel	27	0	39	0	0	66
Italy	619	3	1,443	0	22	2,087
Jamaica	6	0	7	0	1	14
Japan	12	0	26	0	0	38
Jersey (Bailiwick of Jersey)	0	0	6	0	0	6
Jordan	1	0	7	0	0	8
Kazakhstan	2	0	3	0	0	5
Kenya	7	0	6	0	2	15
Kiribati	0	0	2	0	0	2
Korea, Republic of	7	0	14	1	1	23
Kuwait	1	0	0	1	0	2
Kyrgyzstan	1	0	1	0	0	2

Lao Peoples Democratic Republic	1	0	1	0	0	2
Latvia	13	0	30	0	2	45
Lebanon	6	0	8	0	0	14
Liberia	0	0	1	0	0	1
Libyan Arab Jamahiriya	1	0	1	0	0	2
Liechtenstein	5	0	27	0	1	33
Lithuania	21	0	32	0	2	55
Luxembourg	80	0	113	0	2	195
Macao	0	0	3	0	0	3
Madagascar	0	0	1	0	1	2
Malaysia	3	0	13	0	1	17
Maldives	1	0	4	0	0	5
Malta	8	0	13	0	0	21
Martinique	0	0	1	0	0	1
Mauritius	0	0	4	0	0	4
Mayotte	0	0	1	0	0	1
Mexico	146	1	276	2	8	433
Micronesia, Federated States of	1	0	1	0	0	2
Moldova, Republic of	2	0	2	0	0	4
Monaco	1	0	2	0	0	3
Mongolia	2	0	2	0	2	6
Morocco	6	0	10	0	0	16
Mozambique	3	0	3	0	0	6
Myanmar	1	0	2	0	1	4
Namibia	7	0	1	0	0	8
Nepal	2	0	5	0	0	7
Netherlands	1,646	5	1,763	1	17	3,432
Netherlands Antilles	1	0	1	0	0	2

New Caledonia	1	0	0	0	0	1
New Zealand	1,363	3	1,834	3	21	3,224
Nicaragua	4	0	3	0	0	7
Nigeria	0	0	1	0	0	1
Northern Ireland	17	0	43	0	0	60
Norway	92	0	274	1	3	370
Oman	0	0	2	0	0	2
Pakistan	7	0	17	0	0	24
Palau	1	0	0	0	0	1
Palestinian Territory, Occupied	6	0	12	0	0	18
Panama	2	0	6	0	0	8
Papua New Guinea	0	0	1	0	0	1
Paraguay	1	0	4	0	0	5
Peru	14	0	18	0	0	32
Philippines	7	1	17	0	0	25
Pitcairn	1	0	2	0	0	3
Poland	1,201	18	6,090	9	37	7,355
Portugal	169	0	155	1	1	326
Puerto Rico	2	0	4	0	0	6
Qatar	3	0	4	0	0	7
Reunion	1	0	2	0	0	3
Russian Federation	234	3	286	3	11	537
Saint Kitts and Nevis	0	0	1	0	0	1
Saint Vincent and The Grenadines	0	0	2	0	0	2
San Marino	0	0	1	0	0	1
Saudi Arabia	0	0	6	0	0	6
Scotland	331	2	996	3	8	1,340
Seychelles	0	0	1	0	0	1
Sierra Leone	0	0	0	0	1	1

Singapore	6	0	17	0	0	23
Slovakia	1,176	8	2,510	6	23	3,723
Somalia	4	0	7	0	0	11
South Africa	81	0	158	1	2	242
South Georgia and The South Sandwich Islands	1	0	0	0	0	1
Spain	175	1	246	0	6	428
Sri Lanka	2	0	3	0	0	5
Sudan	1	0	1	0	0	2
Suriname	0	0	3	0	0	3
Swaziland	2	0	4	0	0	6
Sweden	136	0	429	1	6	572
Switzerland	1,819	8	3,823	7	20	5,677
Syrian Arab Republic	1	0	3	0	1	5
Taiwan, Province of China	4	0	11	0	1	16
Tanzania, United Republic of	2	0	3	0	0	5
Thailand	18	0	27	0	1	46
Timor-leste	1	0	0	0	0	1
Togo	0	0	1	0	1	2
Tonga	0	0	1	0	0	1
Trinidad and Tobago	4	0	5	0	0	9
Tunisia	2	0	7	0	0	9
Turkey	110	0	188	0	3	301
Turkmenistan	0	0	1	0	0	1
Tuvalu	0	0	1	0	0	1
Uganda	3	0	1	0	1	5
Ukraine	103	0	129	2	2	236
United Arab Emirates	8	0	13	0	1	22

	United States	1,412	32	4,239	45	131	5,859
	United States Minor Outlying Islands	0	0	1	0	1	2
	Uruguay	15	0	7	0	0	22
	Uzbekistan	0	0	1	0	1	2
	Venezuela	5	0	8	0	0	13
	Viet Nam	7	0	16	0	0	23
	Virgin Islands, British	0	0	3	0	1	4
	Wales	31	0	65	0	5	101
	Wallis and Futuna	0	0	1	0	0	1
	Yemen	1	0	0	0	1	2
	Zambia	0	0	4	0	0	4
	Zimbabwe	2	0	5	0	3	10
	Balkans	788	10	1,267	6	23	2,094
Total		43,331	254	81,607	215	1,241	12,6648

Supplementary Table S4: Comparison of sample characteristics between participants reporting non-binary and different identity as their gender identity

Variable	Category	Non-binary (n=750)	Different identity (N=539)	Omnibus test
Age (years)	Median (IQR)	23 (20-31)	23 (19-30)	F = 2.097, df=1, p=0.148
	<25	418 (55.7%)[a]	297 (55.1%)[a]	
	25-34	192 (25.6%)[a]	155 (28.8%)[a]	X^2 = 2.323, df=2, p=0.313
	≥35	140 (18.7%)[a]	87 (16.1%)[a]	
Sexual orientation	Bisexual	169 (22.5%)[a]	68 (12.6%)[b]	
	Heterosexual	34 (4.5%)[a]	45 (8.3%)[b]	
	Homosexual	40 (5.3%)[a]	36 (6.7%)[a]	X^2 = 41.191, df=5, p<0.001
	Prefer not to answer	20 (2.7%)[a]	31 (5.8%)[b]	
	Other	123 (16.4%)[a]	62 (11.5%)[a]	
	Missing	*364 (48.5%)[a]*	*297 (55.1%)[b]*	
Highest education level	No formal schooling	7 (0.9%)[a]	1 (0.2%)[a]	
	Primary school	13 (1.7%)[a]	4 (0.7%)[a]	
	Secondary school*	160 (21.3%)[a]	85 (15.8%)[b]	X^2 = 17.242, df=5, p<0.01
	Undergraduate degree	160 (21.3%)[a]	133 (24.7%)[a]	
	Higher degree	36 (4.8%)[a]	16 (3.0%)[a]	
	Missing	*374 (49.9%)*	*300 (55.7%)*	
Ethnicity	White	309 (41.2%)[a]	205 (38.0%)[a]	
	Black	5 (0.7%)[a]	1 (0.2%)[a]	
	Asian	9 (1.2%)[a]	2 (0.4%)[a]	
	Hispanic	14 (1.9%)[a]	5 (0.9%)[a]	X^2 = 10.795, df=6, p=0.095
	Other	18 (2.4%)[a]	9 (1.7%)[a]	
	Mixed	29 (3.9%)[a]	19 (3.5%)[a]	
	Missing	*366 (48.8%)*	*298 (55.3%)*	
Mental health diagnosis (ever)	Yes	259 (34.5%)[a]	109 (20.2%)[b]	X^2 = 36.159, df=2, p<0.001
	Missing	*345 (46.0%)*	*276 (51.2%)*	

Notes: *including technical or trade certificates; df: degrees of freedom; each superscript letter (a,b) indicates a group which differs significantly from any group not denoted with the same superscript letter, at the level p<0.05; IQR: interquartile range; SD: standard deviation

Supplementary Table S5: Multivariable logistic analysis of the association between gender group, age and 12-month substance use and dependence excluding participants disclosing “different [gender] identity”

Outcome		Gender (reference category: cisgender women)			
Substance	**Measure**	**Transgender men**	**Cisgender men**	**Transgender women**	**Non-binary**
		AOR (95% CI)	AOR (95% CI)	AOR (95% CI)	AOR (95% CI)
Cannabis	Last 12-month use	1.37 (1.07-1.76)*	1.72 (1.68-1.76)****	1.60 (1.22-2.10)**	2.35 (2.02-2.73)****
	SDS ≥4	1.34 (0.85-2.12)^{ns}	1.71 (1.63-1.79)****	1.61 (1.02-2.56)*	2.67 (2.15-3.31)****
Cocaine	Last 12-month use	1.01 (0.71-1.44)^{ns}	1.46 (1.41-1.50)****	1.22 (0.86-1.74)^{ns}	1.80 (1.51-2.15)****
	SDS ≥4	1.16 (0.43-3.13)^{ns}	1.23 (1.12-1.36)****	0.33 (0.05-2.39)^{ns}	1.22 (0.69-2.18)^{ns}
MDMA	Last 12-month use	0.91 (0.66-1.25)^{ns}	1.33 (1.29-1.37)****	1.00 (0.71-1.40)^{ns}	2.18 (1.86-2.56)****
	SDS ≥4	0.47 (0.12-1.90)^{ns}	0.75 (0.68-0.83)****	1.14 (0.42-3.09)^{ns}	2.09 (1.35-3.22)**
Amphetamines	Last 12-month use	1.19 (0.84-1.69)^{ns}	1.42 (1.37-1.47)****	1.40 (0.98-2.01)^{ns}	2.51 (2.12-2.98)****
	SDS ≥4	0.93 (0.35-2.51)^{ns}	0.93 (0.85-1.02)^{ns}	1.95 (0.91-4.15)^{ns}	1.53 (0.95-2.45)^{ns}
Alcohol	Last 12-month use	0.43 (0.29-0.63)****	1.08 (1.02-1.14)**	0.71 (0.42-1.20)^{ns}	0.43 (0.34-0.54)****
	AUDIT ≥20	1.85 (1.15-3.00)*	1.48 (1.39-1.56)****	2.24 (1.38-3.65)**	3.45 (2.74-4.35)****

Notes: *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001; AOR: adjusted odds ratio; AUDIT: alcohol use disorders identification test; CI: confidence intervals; MDMA: 3,4-methylenedioxymethamphetamine; ns: not significant; SDS: severity of dependence scale