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Medical gender affirmation appears protective against problematic substance use among transgender women and transfeminine adults: Findings from The LITE Study study

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Abstract

Objective: To estimate the association between medical and legal gender affirmation with problematic substance use among transfeminine adults.

Methods: Data from a longitudinal cohort (The LITE Study) were analyzed (n = 1186). Participants were enrolled between March 2018 and August 2020 and followed for 2 years. We tested the association between baseline medical and legal gender affirmation with problematic drug use (DAST-10 ≥ 3) and problematic alcohol use (AUDIT-C ≥ 4) at 12-months. We used Poisson regression to estimate adjusted prevalence ratios (aPR) and 95% confidence intervals (CI).

Results: Mean age was 31.0 years (standard deviation=11.2). For race and ethnicity, 55.8% were non-Latinx, white, 13.0% were non-Latinx Black/African American, 17.1% were Latinx, and 14.1% were Asian, American Indian/Alaskan Native, Native Hawaiian/Pacific Islander, or multiracial. For exposures, 75.1% had met need for medical gender affirmation, 16.4% did not seek medical gender affirmation, 8.5% had unmet need for medical gender affirmation, and 19.5% had all IDs match their chosen name/gender. At follow-up, 24.1% had problematic drug use, and 27.6% had problematic alcohol use. Participants with met need for medical gender affirmation were less likely to have problematic drug use at follow-up (aPR = 0.70, 95% CI = 0.49–0.99) compared to those with unmet need. Compared to those who did not seek medical gender affirmation, those with met need (aPR = 0.72, 95% CI = 0.57–0.91) and unmet need (aPR = 0.68, 95% CI = 0.47–0.97) were less likely to have problematic alcohol use.

Conclusion: Medical gender affirmation appears protective against problematic substance use. Increasing access to medical gender affirmation may improve substance use outcomes among transfeminine adults who desire such services.

Keywords

transgender; medical gender affirmation; legal gender affirmation; problematic drug use; problematic alcohol use

1 Introduction

Transgender women and nonbinary transfeminine people may experience disproportionate risk for substance use as a result of systemic cisgenderism, including policy restrictions or other barriers to accessing gender affirming services (Grant et al., 2011; Reisner et al., 2016a; White Hughto et al., 2015; Zubizarreta et al., 2024). Studies suggest transgender adults have a higher prevalence of substance use, and alcohol, nicotine, and other substance use disorders compared to cisgender adults (Connolly and Gilchrist, 2020; Hughto et al., 2021). Transfeminine people may also experience unique risk and protective factors for substance use. A better understanding of such factors can inform prevention efforts.

Medical and legal gender affirmation may be considered transgender-specific social determinants of health (Reisner et al., 2016b). Medical affirmation relates to hormones, surgery, and other body modifications to align one's physical self with one's gender identity.

Legal affirmation refers to having documents such as a birth certificate or identification cards that reflect a person's chosen name and gender. Gender affirmation is a multifaceted process, and transgender people may desire some but not all aspects of affirmation. The Gender Affirmation Framework describes how unmet need for gender affirmation can negatively impact substance use and HIV outcomes (Sevelius, 2013). Systematic reviews have examined the impact of gender affirmation, primarily medical gender affirmation, on health outcomes finding improvements in psychological functioning, anxiety, depression, suicidality, quality of life, and social distress (Akhavan et al., 2021; King and Gamarel, 2021; Nguyen et al., 2018; Passos et al., 2020; Swan et al., 2023; White Hughto and Reisner, 2016). Given the importance of gender affirmation for transgender people and the recent rise in anti-transgender legislation and policies across the United States (US) which seek to restrict transgender people's access to healthcare, education, legal recognition, and the right to publicly exist (Trans Legislation Tracker, n.d.), an understanding of how medical and legal gender affirmation are associated with substance use may provide insights into the potential negative impact of such legislation, and inform prevention efforts.

Studies that have investigated the association between gender affirmation and substance use behaviors have mixed results, particularly for medical gender affirmation. Six studies estimated associations between receipt of or met need for medical gender affirmation and substance use including 20 comparisons. Of these, two from cross-sectional studies found positive associations (Keuroghlian et al., 2015; Lelutiu-Weinberger et al., 2020), five were inversely associated (Almazan and Keuroghlian, 2021; Beckwith et al., 2017), and 13 reported no association with substance use (Almazan and Keuroghlian, 2021; Beckwith et al., 2017; Kidd et al., 2018; Tomita et al., 2019). Three cross-sectional studies estimated associations between receipt of or met need for legal gender affirmation and substance use outcomes including five comparisons. Of these, one was positively associated (Lelutiu-Weinberger et al., 2020) and four were inversely associated (Kidd et al., 2018; Yee et al., 2022) with substance use.

Aspects of study designs limit inference in the extant substance use literature. Each of the studies reviewed above was cross-sectional, which limits the ability to establish temporal ordering of exposure and outcome. No studies used a prospective design to assess the longitudinal relationship between gender affirmation and substance use behaviors. Additionally, measures of substance use in these studies varied widely, with some combining measures of alcohol, cannabis, and/or illicit substance use (Keuroghlian et al., 2015; Lelutiu-Weinberger et al., 2020). Only one study used validated measures of problematic substance use (e.g., Drug Abuse Screening Test 10 [DAST-10]) (Tomita et al., 2019), while two studies measured alcohol and substance use disorders through medical record review (Beckwith et al., 2017; Yee et al., 2022). Another consideration is that gender affirmation was measured using different approaches, with three studies assessing both need for and receipt of gender affirmation (Almazan and Keuroghlian, 2021; Lelutiu-Weinberger et al., 2020; Tomita et al., 2019) while four studies assessed receipt only (Beckwith et al., 2017; Keuroghlian et al., 2015; Kidd et al., 2018; Yee et al., 2022). While many transfeminine people need gender affirmation services, these needs are not universal. Thus, assuming need for gender affirmation is universal may result in the misclassification of some transfeminine people as having unmet need.

To begin addressing these gaps in the literature, we examined associations between baseline medical and legal gender affirmation with problematic drug and problematic alcohol use at 12-months follow-up among a cohort of transfeminine adults. We hypothesized that access to medical and legal gender affirmation would be associated with lower likelihood of problematic drug use and problematic alcohol use at follow-up compared to those with unmet gender affirmation needs.

2 Methods

2.1 The LITE Study

The main objective of the parent study, The LITE Study, was to estimate HIV incidence among transgender women in the Eastern and Southern US and associated individual, social, and structural risk factors including substance use and gender affirmation (Wirtz et al., 2021; Wirtz et al., 2019). The LITE Study was a hybrid longitudinal cohort comprised of two modes: a site-based mode that permitted in-person data collection across six cities (Atlanta, Baltimore, Boston, Miami, New York City, Washington DC), and a fully remote, digital mode (geotargeted to 72 metropolitan areas with population sizes greater than 100,000 people selected based on similar demographic characteristics to the six site-based cities). Enrollment occurred between March 2018 and August 2020 and follow-up occurred for up to 24 months. The site-based mode enrolled 745 participants and the digital mode enrolled 587 participants. Data were collected every three months in the site-based mode and every six months in the digital mode. For the site-based mode, in-person data collection was required for baseline and 6-, 12-, and 24-month visits with the option for in-person or web-based data collection for all other assessments. Participants completed a self-administered survey and HIV testing.

2.2 Sample

Recruitment methods included advertising on geosocial networking apps (e.g., Grindr), peer and clinic-based referrals, and venue-based recruitment at community events and conferences (e.g., Philadelphia Trans Health Conference). Eligibility criteria for participation included: ages ≥ 18 years-old; identified as a transgender woman or transfeminine individual (i.e., assigned male sex at birth and identifying as women or along the transfeminine spectrum, assessed using a two-step method) (Tate et al., 2013); spoke or understood English or Spanish; resided within 50 miles of one of the study cities. Cohort enrollment was restricted to individuals with a negative baseline HIV test.

2.3 Measures

2.3.1 Outcomes: problematic substance use: Participants completed the DAST-10 and the Alcohol Use Disorders Identification Test-Concise (AUDIT-C). These measures have been previously used with transgender populations, including in the US TransPOP Survey (Meyer et al., 2016). The DAST-10 measures problems associated with controlled substance use (hereafter, drug use) across 10 items and has yielded satisfactory levels of reliability and sensitivity for measuring maladaptive drug use in adults (Santos et al., 2020; Yudko et al., 2007), with a 0 indicating no problems, 1–2 low level, 3–5 moderate level, 6–8 substantial level, and 9–10 severe level of problematic drug use. For analytic purposes, the

DAST-10 was recoded to a binary variable with ≥ 3 as an indicator for moderate, substantial, or severe problematic drug use versus a score < 3 as no or low problematic drug use. At baseline, the recall period for the DAST-10 was past 12 months. After baseline, the recall period for the DAST-10 was past of 3 months in the site-based mode, and past 6 months in the digital mode. For the site-based mode, we used two consecutive past 3-month timepoints (i.e., 9-month and 12-month follow-up) to construct a recall period of 6 months to align with the digital mode at 12-months follow-up. Participants in the site-based mode were coded as moderate, substantial, or severe problematic drug use if they scored ≥ 3 at either 9- or 12-months follow-up, no or low drug use if they scores < 3 at both, and missing if they did not respond to one or both timepoints. Internal consistency for the DAST-10 in the sample was sufficient ($\alpha = 0.88$).

The AUDIT-C has demonstrated satisfactory sensitivity in measuring problematic alcohol use (Bush et al., 1998; Santos et al., 2020). The AUDIT-C was coded as an indicator for current problematic alcohol use (score ≥ 4) (Bush et al., 1998). Internal consistency for the AUDIT-C in the sample was sufficient ($\alpha = 0.76$). The AUDIT-C is considered “current” with no recall period specified in the measure. Participants who selected prefer not to answer to all items on the DAST-10 or AUDIT-C items were coded as missing for the summed measure.

2.3.2 Exposures: medical and legal gender affirmation at baseline. Measures of gender affirmation were drawn from the US TransPop Survey (Meyer et al., 2016). For medical gender affirmation, participants were asked, “Have you tried to get gender transition-related care (for example, hormones or surgery) in the past 12 months?” with response options yes, no, and prefer not to answer. Participants who selected yes were then asked, “When you tried to get transition related care (for example, hormones or surgery) in the past 12 months, were you able to get it?” with response options yes, no, and prefer not to answer. Responses to these two questions were recoded as met medical gender affirmation need, unmet need, or did not try to access medical gender affirmation.

For legal gender affirmation, participants were asked, “To what extent do your IDs list the name that you prefer?” and “To what extent is your preferred gender listed on all of your IDs?” Response options for each item were none, some, most, or, all of my IDs and records list the name/gender I prefer, as well as prefer not to answer. Response options to these two questions were recoded as all IDs match chosen name and gender (i.e., responded all to both items) versus some (i.e., responded some, most or all to one item but not all to both), or no IDs match chosen name or gender (i.e., responded none to both). Participants who selected prefer not to answer to the medical or legal gender affirmation items were treated as missing.

2.3.3 Covariates: sociodemographic measures at baseline: Self-reported demographics included gender identity, age, race, and ethnicity were drawn from the US TransPop Survey (Meyer et al., 2016). In multivariable analyses, gender was recoded as binary (i.e., female or woman, trans female, trans woman, male-to-female (MTF), woman of trans experience) versus nonbinary (i.e., transfeminine, trans femme, nonbinary, agender, gender fluid, gender variant, gender nonconforming, person of trans experience, two-spirit, & other) due to a small number of participants in some groups. Similarly, race and ethnicity

were coded as: non-Latinx white; non-Latinx Black or African American; Latinx; or non-Latinx Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, multiracial, and other. Age was treated as continuous in regression models. Participants who selected prefer not to answer to any demographic questions were coded as missing on that specific measure.

We created an indicator for participating in the site-based versus digital mode, to account for the hybrid cohort design. We include the covariate US Census Division based on self-reported zip codes.

2.3.4 Covariates: COVID 19-pandemic: To assess the impact of the onset of the COVID-19 pandemic on our outcome, we created an indicator for whether our outcome data were collected after the onset of the COVID-19 pandemic (approximated as March 13th, 2020).

2.3.5 Covariates: indicators of retention: We collected information on potential causes of selection bias including currently homeless, and current food insecurity at baseline. We also created an indicator for HIV seroconversion between baseline and 12-months follow-up.

2.4 Analysis

Analyses were performed using SAS (version 9.4). Participants with missing data on any exposure or covariate at baseline ($n = 128$) were excluded from the analysis, leaving an analytic sample of 1186 participants. First, we assessed the distribution of baseline exposures and covariates. We then assessed the distribution of baseline exposures and covariates by our outcomes at follow-up. We also assessed the distribution of baseline exposures and covariates by censoring at follow-up (see online Supplementary Table 1). We also assessed the joint distributions of our exposures at baseline and the co-occurrence of our outcomes at baseline. For legal gender affirmation, the distribution of our outcomes at follow-up among those with none or some legal gender affirmation was nearly identical and thus we combined these groups in our regression analyses to increase power. To further contextualize our finding, we assess the joint distributions of problematic drug use at follow-up by types of drug use at baseline and polydrug use (see online Supplementary Table 2).

To inform our analysis, we created directed acyclic graphs (DAGs). Figure 1 displays the DAG depicting our assumptions of the causal structure for our exposures and outcomes including back door confounders and causes censoring which contribute to selection bias.

Missing data at 12-month follow-up was substantial for problematic drug use ($n = 363$; 30.6%) and problematic alcohol use ($n = 371$; 31.3%). To address potential selection bias, we used stabilized inverse probability-of-censoring weights (sIPCW) (Hernán et al., 2002; Hernán et al., 2004). Participants were censored for missing outcome data, with separate indicators of censoring for each outcome. Separate weights were estimated for each exposure/outcome pair.

sIPCW numerators were constructed using logistic regression to estimate the probability of retention (censored = 0) conditioned on the exposure to which the weight was applied. sIPCW denominators were constructed using logistic regression to estimate the probability of retention (censored = 0) conditioned on exposure and covariates deemed likely causes of censoring including: baseline problematic substance use, medical gender affirmation, legal gender affirmation, age, gender, race, ethnicity, US Census Division, cohort mode, indicators for data collection before the start of the COVID 19-Pandemic at baseline and 12-month follow-up, currently homelessness, food insecurity, and HIV-seroconversion between baseline and 12-months. After dividing the numerator by the denominator to generate exposure/outcome-specific sIPCW, the weights were applied to our models estimating the association between that exposure and the outcome. Weighted distributions of baseline covariates were approximately equal to the unweighted distributions. Figure 2 and Figure 3 display the DAGs for the pseudo-populations created by applying sIPCW for medical gender affirmation and legal gender affirmation respectively.

Models were estimated using the PROC GEE command in SAS using the Poisson distribution with robust standard errors to estimate prevalence ratios (PR), given our outcomes are not rare (< 10%) (Zou, 2004). We used separate models for each exposure-outcome relationship. In the first set of models, we regressed our outcome on our exposure and outcome measures at baseline, and we reported PR and 95% confidence intervals (95% CI). In the second set of models, we adjust for confounders including: age, gender, race, ethnicity, US Census Division, cohort mode, baseline problematic drug use, baseline problematic alcohol use, and an indicator of whether the baseline data was collected before or after the start of COVID and we reported adjusted prevalence ratios (aPR) and 95% CIs. For medical gender affirmation, we used “ESTIMATE” statements to assess all pairwise comparisons among exposure levels. We did not adjust for baseline homelessness or food insecurity as these may be confounders or mediators, and the data structure did not allow us to differentiate the temporal order between exposures and these covariates.

Figure 2 and Figure 3 depict confounder adjustment for medical gender affirmation and legal gender affirmation respectively. In our DAGs, we include a node “U” for unmeasured confounding to denote possible residual confounding between our exposures and outcome. As a sensitivity analysis, we calculate e-values for the point estimates (E-PE) to understand the strength of the relationship a confounder would need to have with the exposure and outcome to explain away the association above and beyond measured confounders (VanderWeele and Ding, 2017). We also calculate e-values for the confidence limit (E-CL) closest to the null value to understand the strength of the relationship a confounder would need to have with the exposure and outcome to explain away the confidence limit above and beyond measured confounders (VanderWeele and Ding, 2017).

3. Results

Among participants with complete data at baseline, the mean age was 31.0 years (standard deviation=11.2). Most participants reported a binary gender identity (83.6%), were non-Latinx, White (55.8%), and were in the site-based mode (54.4%). As shown in Table 1, 75.1% obtained medical gender affirmation, 16.4% did not seek medical gender affirmation,

8.5% had unmet medical gender affirmation needs, and 19.5% had all their IDs match their chosen name/gender.

At follow-up, 24.1% had past 6-month problematic drug use and 27.6% had current problematic alcohol use. Table 2 displays the distribution of baseline covariates by outcomes at follow-up. The highest proportions of problematic drug use were among participants who were nonbinary (34.3%), ages 21 to 24 years old (34.9%), homeless (38.2%), and participants with unmet need for medical gender affirmation (33.8%). The highest proportions of problematic alcohol use were among participants ages 21 to 24 years old (34.1%), and those who did not seek medical gender affirmation (34.9%).

At baseline, those with met need for and those who did not seek medical gender affirmation reported all IDs matched their name and gender more frequently (20.2% and 23.2% respectively) than those with unmet need (5.9%). At baseline, 13.9% of participants had both problematic drug use and problematic alcohol use, 14.8% had problematic drug use only, 19.1% had problematic alcohol use only, and 52.3% had neither.

Table 3 displays the results of unadjusted and adjusted models regressing problematic drug use and problematic alcohol use at follow-up on baseline medical gender affirmation and baseline legal gender affirmation, using separate models for each exposure-outcome pair. Participants with met need for medical gender affirmation were less likely to have problematic drug use at follow-up than those with unmet needs (aPR = 0.70, 95% CI = 0.49–0.99, E-PE = 2.21, E-CL = 1.11). Participants with met need for medical gender affirmation were less likely to have problematic alcohol use compared to those who did not seek medical gender affirmation (aPR = 0.72, 95% CI = 0.57–0.91, E-PE = 2.12, E-CL = 1.43). Similarly, participants with unmet need for medical gender affirmation were less likely to have problematic alcohol use compared to those who did not seek medical gender affirmation (aPR = 0.68, 95% CI = 0.47–0.97, E-PE = 2.30, E-CL = 1.21). Legal gender affirmation did not appear to be associated with either outcome, with aPRs approximately equal to the null value.

4. Discussion

In this prospective analysis of a cohort of transfeminine people across the Eastern and Southern US, we found medical gender affirmation may be protective against problematic drug use and problematic alcohol use. Our findings counter previous research that suggests medical gender affirmation is positively associated with substance use (Keuroghlian et al., 2015; Lelutiu-Weinberger et al., 2020). Prior studies were cross-sectional, potentially explaining this incongruence. Further, these studies used different measures of substance use including a composite measures of drug use and alcohol use or substance use disorder treatment and recent substance use. Those with met and unmet need for medical gender affirmation had similar prevalence estimates of problematic alcohol use at follow-up similar to what other have found (Almazan and Keuroghlian, 2021; Tomita et al., 2019). However, both those with met and unmet need for medical gender affirmation had lower prevalence estimates of problematic alcohol use than those who did not seek such services. It is unclear if those who did not seek medical gender affirmation services had met or unmet need or

simply did not need them and qualitative and quantitative analysis unpacking these findings may be warranted. The nuance in these findings suggests drug use (i.e., use of controlled substances) and alcohol use should be measured and analyzed as distinct constructs when assessing associations with medical gender affirmation. However, 13.9% of participants had both problematic drug and alcohol use at baseline, and future investigations should assess the association of medical gender affirmation with the co-occurrence of these outcomes.

Counter to our hypothesis and previous research (Yee et al., 2022), legal gender affirmation did not appear to be associated with either outcome. In our DAGs, we placed the node for legal gender affirmation after the node for medical gender affirmation, as some states require proof of medical gender affirmation to change gender markers on IDs (Movement Advancement Project, n.d.). At baseline, those with met need for medical gender affirmation reported all IDs matched their name and gender over 3 times more frequently than those with unmet need. It is possible the relationship between legal gender affirmation and problematic substance is moderated by medical gender affirmation. Our sample size was too restrictive to test for such moderation effects, and this maybe an important consideration for future work.

Certain subgroups of transfeminine adults may also face greater barriers to healthcare, which could impact both medical gender affirmation and substance use outcomes. For example, transgender migrants experience simultaneous anti-transgender and anti-immigrant stigma which limits their access to healthcare (Castro et al., 2022). People with nonbinary genders, older adults, emerging adults, people outside of urban city centers, and people with disabilities, among other groups, may also face additional and/or unique challenges to accessing healthcare including medical gender affirmation and substance use prevention services. Future qualitative and quantitative research could inform prevention efforts among such subgroups of transfeminine adults who may be more vulnerable to problematic substance use and other negative health outcomes.

Previous research suggests substance use may be a coping mechanism for stigma in healthcare (Reisner et al., 2015), which contextualizes our findings. While increasing access to medical gender affirmation may have a protective or health-promoting effect on substance use for transgender people, barriers to medical gender affirmation, such as laws prohibiting provision of medical gender affirmation, health insurance denials of medical gender affirmation, and other barriers may ultimately have adverse effects on substance use. In the US, over 600 anti-transgender bills were introduced in the first three months of 2025 alone, which often seek to limit access to gender affirmation services (Barbee et al., 2022; Trans Legislation Tracker, n.d.). Indeed, critical legal scholars have called for a focus on policies governing access to medical and legal gender affirmation services (Spade, 2022). Our findings suggest meeting individual needs for medical gender affirmation is associated with lower prevalence of problematic substance use. Thus, in theory, federal, state, local, and institutional policies that increase/decrease access to gender affirmation services may improve/worsen substance use outcomes. While these hypotheses are not addressed in our analyses, our findings can inform future studies on policies and other barriers to gender affirmation services, which are warranted given the frequency at which bills targeting transgender rights are being introduced across the US.

It is important to consider both need for and access to gender affirmation when estimating their associations with health outcomes (Goldenberg et al., 2021; Sevelius, 2013). We were able to distinguish between those who attempted to but were not able to obtain medical gender affirmation, in which need for affirmation may be inferred. However, we are unable to infer need for those who did not seek medical gender affirmation as they may or may not have had unmet need. Those who did not seek medical gender affirmation had similar prevalence estimates of problematic drug use and greater prevalence estimates of problematic alcohol use compared to those with met and unmet need. These findings are difficult to interpret, emphasizing the importance of measuring both need for and access to gender affirmation. Additionally, we did not assess need for legal gender affirmation, and could not classifying those with no or some IDs matching their chosen name/gender as having an unmet need.

4.1 Limitations and strengths

Our study used convenience sampling methods, and thus, the extent that findings are generalizable is unclear. However, The LITE Study used robust sampling methods with two modes which expanded the geographical reach and diversity of the study sample beyond a single mode. While censoring at 12-months follow-up was substantial, we used sIPCW to mitigate the impact of selection bias. However, as depicted in our DAGs via the node “S” additional variables not included in our models used to estimate sIPCW may be related to censoring and our exposures which could result in residual selection bias. For our outcomes, we used measures with well-established valid and reliable psychometric properties in diverse populations (Bush et al., 1998; Santos et al., 2020; Yudko et al., 2007). However, as previously noted measurement error may be present in our exposures.

We adjust for several possible confounders at baseline as depicted in our DAG, yet unmeasured confounding may be present as represented by the node “U.” E-values for our point estimates for statistically significant findings ranged from 2.1 to 2.2. Given the number of confounders we adjust for in our analysis, we feel it is possible but not highly likely an unmeasured confounder would explain away our findings above and beyond measured confounders. However, E-values for the confidence limits ranged from 1.1 to 1.4 and thus, the likelihood of an unmeasured confounder moving the confidence limit to include the null value given no other gains in statistical efficiency is highly likely. If such confounders exist, future studies investigating these associations adjusting for such confounders likely require larger samples to retain statistical significance under similar conditions. Given overlapping recall periods for our exposures and baseline outcome measures, adjusting for baseline outcome measures may result in over adjustment (i.e., bias towards the null).

4.2 Implications

Prevention efforts for substance use among transfeminine people may benefit from increasing access to gender affirmation services, as described by the Gender Affirmation Framework (Sevelius, 2013), similar to studies of gender affirmation and HIV, mental health, quality of life, and social distress (Akhavan et al., 2021; Andrzejewski et al., 2021; King and Gamarel, 2021; Nguyen et al., 2018; Passos et al., 2020; Sevelius et al., 2021; Swan et al., 2023; White Hughto and Reisner, 2016). Patient navigators are one approach that

may be used in treatment settings to increase access to services (Budde et al., 2021), and navigators should be trained on the specific needs of transfeminine people, including gender-affirming local resources. Community-based interventions that address substance use may also benefit from the inclusion of strategies to increase access to gender affirmation services. For example, two pilot studies adapted *Seeking Safety*, a group-based, cognitive behavioral therapy intervention targeting substance use and mental health for transgender women, showed improvement in substance use and mental health outcomes (Empson et al., 2017; Takahashi et al., 2022). Still, there is a dearth of research on interventions that address substance use among transfeminine adults. At baseline, 28.7% of participants in our study had problematic drug use and 33.0% had problematic alcohol use, underscoring the need for interventions, as others have noted (Gilbert et al., 2018; Glynn and van den Berg, 2017; Kidd et al., 2022). Additionally, research is needed to assess the impacts of structural cisgenderism, such as policies governing access to medical and legal gender affirmation, on substance use outcomes.

4.3 Conclusions

Medical gender affirmation may be protective against problematic substance use among transfeminine adults. Thus, increasing access to medical gender affirmation in substance use treatment, in community health settings, and through policy changes may bolster efforts to improve substance use outcomes. Interventions that address substance use among transfeminine people are needed, and researchers and practitioners should consider gender affirmation in the development and implementation of such work.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- About 24 % of transfeminine people in this cohort study had problematic drug use.
- About 27 % of transfeminine people in this cohort study had problematic alcohol use.
- Medical gender affirmation may be protective for problematic drug and alcohol use.

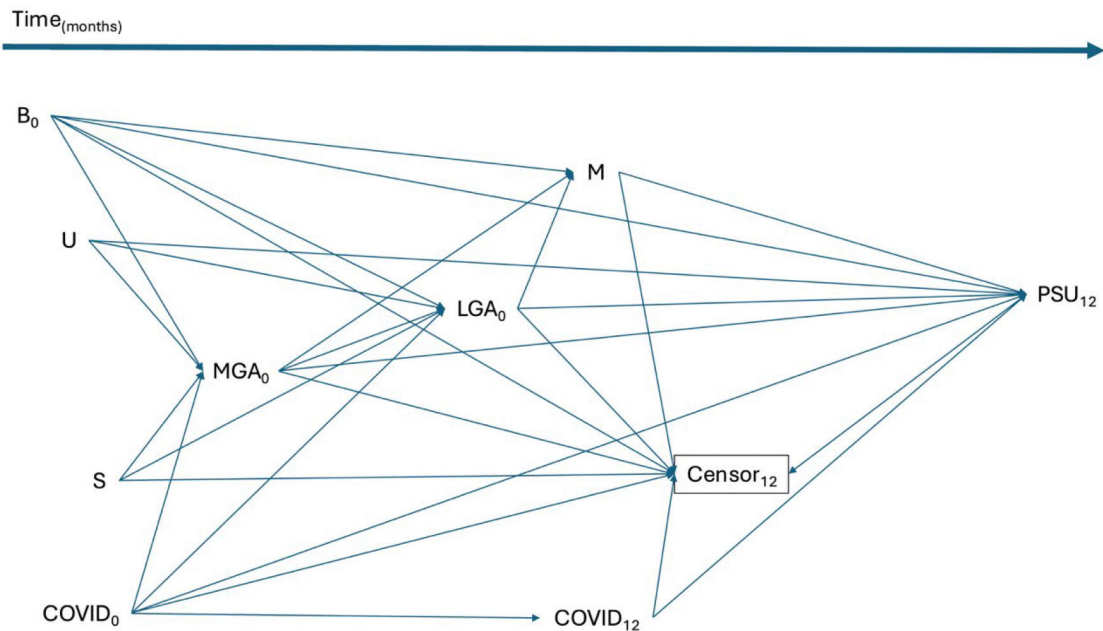


Figure 1.

DAG for the association between baseline medical gender affirmation, legal gender affirmation, and outcomes at follow-up. MGA = Medical Gender Affirmation (past 12 months), LGA = Legal Gender Affirmation (current), B = Time independent confounders (age, gender, race, ethnicity, US Census Division, & cohort mode), baseline problematic drug use (past 12-months), & baseline problematic alcohol use (current), U = Unmeasured confounding, S = Unmeasured covariates causing censoring, M = Mediators causing censoring: currently homeless (past 3 months), food Insecurity (current), & HIV acquisition between baseline and 12-month follow-up, COVID = Indicator for data collection before or after the start of the COVID-19 Pandemic starting on March 13th, 2020, Censor = Censored at 12-month follow-up, & PSU = Either problematic drug use (past 6 months) or problematic alcohol use (current).

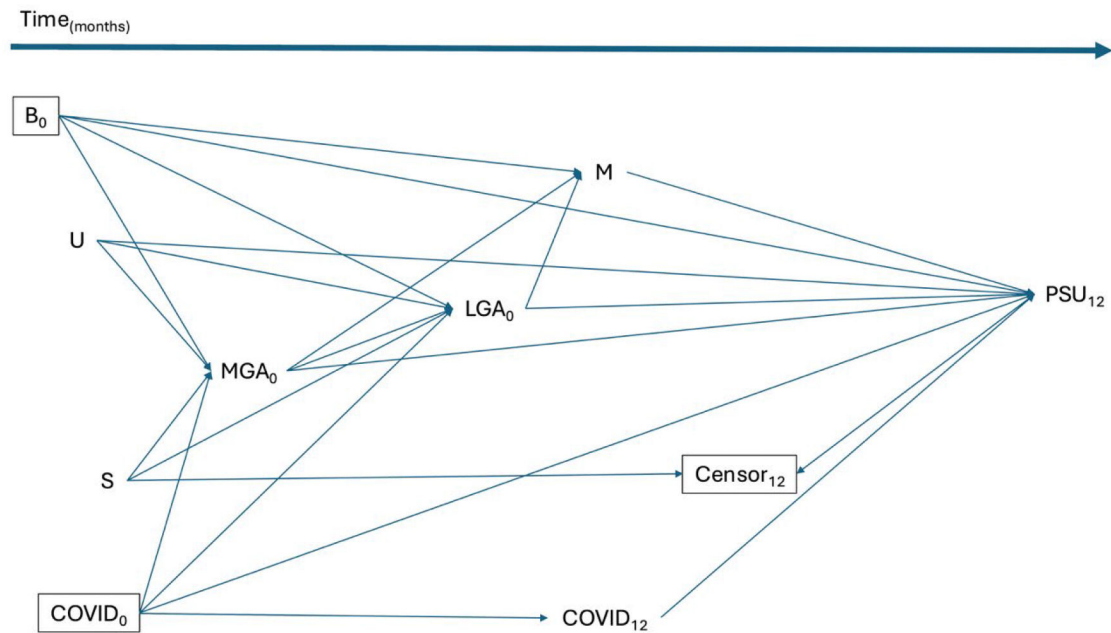
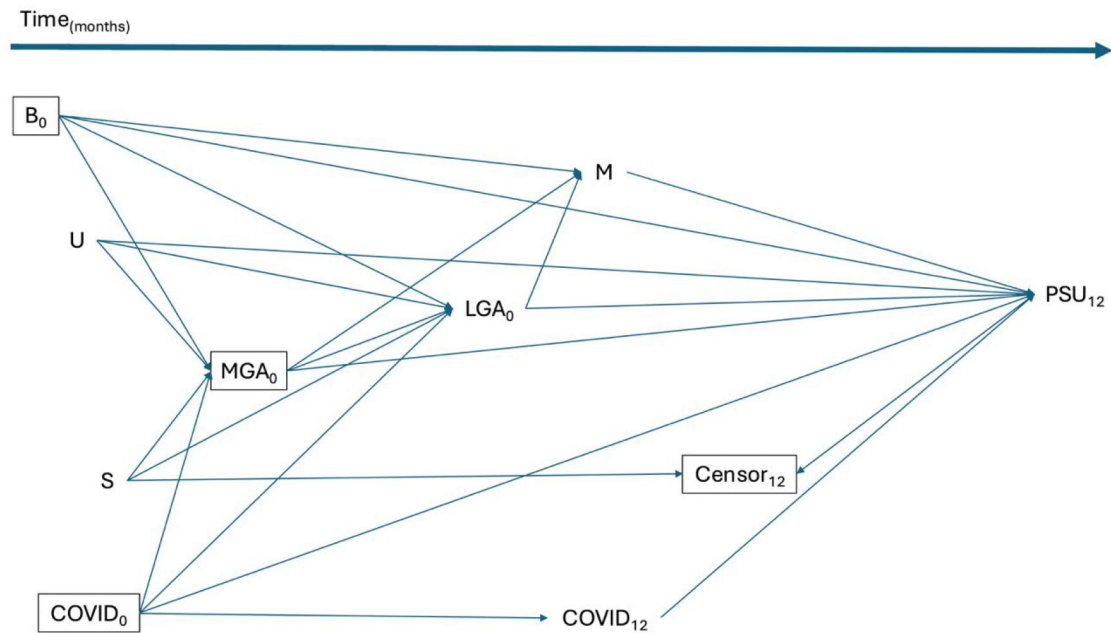


Figure 2.

DAG depicting analysis of the association between baseline medical gender affirmation and outcomes at follow-up controlling for measured confounders and using stabilized inverse probability of censor weights to account for selection bias. MGA = Medical Gender Affirmation (past 12 months), LGA = Legal Gender Affirmation (current), B = Time independent confounders (age, gender, race, ethnicity, US Census Division, & cohort mode), baseline problematic drug use (past 12-months), & baseline problematic alcohol use (current), U = Unmeasured confounding, S = Unmeasured covariates causing censoring, M = Mediators causing censoring: currently homeless (past 3 months), food Insecurity (current), & HIV acquisition between baseline and 12-month follow-up, COVID = Indicator for data collection before or after the start of the COVID-19 Pandemic starting on March 13th, 2020, Censor = Censored at 12-month follow-up, & PSU = Either problematic drug use (past 6 months) or problematic alcohol use (current).

**Figure 3.**

DAG depicting analysis of the association between baseline legal gender affirmation and outcomes at follow-up controlling for measured confounders and using stabilized inverse probability of censor weights to account for selection bias. MGA = Medical Gender Affirmation (past 12 months), LGA = Legal Gender Affirmation (current), B = Time independent confounders (age, gender, race, ethnicity, US Census Division, & cohort mode), baseline problematic drug use (past 12-months), & baseline problematic alcohol use (current), U = Unmeasured confounding, S = Unmeasured covariates causing censoring, M = Mediators causing censoring: currently homeless (past 3 months), food Insecurity (current), & HIV acquisition between baseline and 12-month follow-up, COVID = Indicator for data collection before or after the start of the COVID-19 Pandemic starting on March 13th, 2020, Censor = Censored at 12-month follow-up, & PSU = Either problematic drug use (past 6 months) or problematic alcohol use (current).

Table 1.
Distribution of baseline measures (March 2018 to August 2020) in The LITE Study Cohort.

	N (%)
Total	1186 (100)
Gender identity	
Female or woman	326 (27.5)
Trans female, trans woman, male-to-female (MTF)	619 (52.2)
Transfeminine, trans femme	104 (8.8)
Nonbinary, agender, gender fluid, gender variant, gender nonconforming	63 (5.3)
Woman of trans experience	47 (4.0)
Person of trans experience	4 (0.3)
Two-spirit	14 (1.2)
Other identity ^a	9 (0.8)
Race and ethnicity	
Latinx	203 (17.1)
Non-Latinx, Asian	29 (2.5)
Non-Latinx, American Indian or Alaska Native	3 (0.3)
Non-Latinx, Black or African American	154 (13.0)
Non-Latinx, Native Hawaiian or Pacific Islander	1 (0.1)
Non Latinx, White	662 (55.8)
Non-Latinx, multiracial	120 (10.1)
Other ^b	14 (1.2)
Age group in years	
18–20	141 (11.9)
21–24	251 (21.2)
25–29	243 (20.5)
30–39	344 (29.0)
40+	207 (17.5)
US Census Division	
Northeast	508 (42.8)
Midwest	136 (11.5)
South	542 (45.7)
Cohort mode	
Site-based	645 (54.4)
Digital	541 (45.6)
Food insecurity	
Never	492 (41.5)
Seldom, rarely, or sometimes	485 (40.9)
Most of the time or always	209 (17.6)
Homeless	
Yes	122 (10.3)

	N (%)
No	1064 (89.7)
Data collected before start of COVID-19 pandemic	
Yes	1,153 (97.2)
No	33 (2.8)
Medical gender affirmation	
Met need	891 (75.1)
Did not try	194 (16.4)
Unmet need	101 (8.5)
Legal gender affirmation	
All match name and gender	231 (19.5)
Some match name or gender	451 (38.0)
None match name and gender	504 (42.5)
Problematic drug use (past 12 months)	
Yes	340 (28.7)
No	846 (71.3)
Problematic alcohol use (current)	
Yes	391 (33.0)
No	795 (67.0)

^a Other gender identities primarily included nonbinary identities and denoting the identity of transgender woman and nonbinary.

^b Other included ethnic and religious identities not included as options in our survey measures, for example Caribbean, Middle Eastern, and Jewish.

Table 2.

Distribution of baseline measures (March 2018 to August 2020) by past 6-month problematic drug use and current problematic alcohol use at 12-months follow-up in The LITE Study Cohort.

	Past 6-month problematic drug use at 12-months follow-up		Current problematic alcohol use at 12-months follow-up	
	No, N (%)	Yes, N (%)	No, N (%)	Yes, N (%)
Total	625 (75.9)	198 (24.1)	590 (72.4)	225 (27.6)
Gender identity ^a				
Binary	533 (78.0)	150 (22.0)	496 (72.8)	185 (27.2)
Nonbinary	92 (65.7)	48 (34.3)	94 (70.2)	40 (29.8)
Race and ethnicity				
Non-Latinx, white	368 (74.5)	126 (25.5)	344 (70.4)	145 (29.6)
Non-Latinx, Black or African American	70 (78.7)	19 (21.3)	68 (77.3)	20 (22.7)
Latinx	95 (74.2)	33 (25.8)	94 (75.2)	31 (24.8)
Non-Latinx Asian, American Indian or Alaska Native, Native Hawaiian or Pacific Islander, multiracial, and other ^b	92 (82.1)	20 (17.9)	84 (74.3)	29 (25.7)
Age group in years				
18–20	66 (68.8)	30 (31.2)	61 (67.0)	30 (33.0)
21–24	110 (65.1)	59 (34.9)	110 (65.9)	57 (34.1)
25–29	126 (75.9)	40 (24.1)	119 (73.0)	44 (27.0)
30–39	193 (80.1)	48 (19.9)	181 (74.8)	61 (25.2)
40+	130 (86.1)	21 (13.9)	119 (78.3)	33 (21.7)
US Census Division				
Northeast	255 (67.4)	79 (23.6)	249 (74.1)	87 (25.9)
Midwest	78 (69.0)	35 (31.0)	77 (68.1)	36 (31.9)
South	292 (77.7)	84 (22.3)	264 (72.1)	102 (27.9)
Cohort mode				
Site-based	276 (75.0)	92 (25.0)	271 (74.7)	92 (25.3)
Digital	349 (76.7)	106 (23.3)	319 (70.6)	133 (29.4)
Food insecurity				
Never	283 (81.3)	65 (18.7)	264 (75.9)	84 (24.1)
Seldom, rarely, or sometimes	253 (73.8)	90 (26.2)	239 (70.1)	102 (29.9)
Most of the time or always	89 (67.4)	43 (32.6)	87 (69.1)	39 (30.9)
Homeless				
Yes	47 (61.8)	29 (38.2)	46 (67.7)	22 (32.3)
No	578 (77.4)	169 (22.6)	544 (72.8)	203 (27.2)
Data collected before start of COVID-19 pandemic				
Yes	603 (75.5)	196 (24.5)	570 (72.2)	220 (27.8)
No	22 (91.7)	2 (8.3)	20 (80.0)	5 (20.0)
Medical gender affirmation				
Met need	477 (76.8)	144 (23.2)	455 (73.5)	164 (26.5)

	Past 6-month problematic drug use at 12-months follow-up		Current problematic alcohol use at 12-months follow-up	
Did not try	99 (77.3)	29 (22.7)	82 (65.1)	44 (34.9)
Unmet need	49 (66.2)	25 (33.8)	53 (75.7)	17 (24.3)
Legal gender affirmation				
All match name and gender	128 (83.7)	25 (16.3)	117 (77.5)	34 (22.5)
Some match name or gender	237 (74.3)	82 (25.7)	227 (71.6)	90 (28.4)
None match name or gender	260 (74.1)	91 (25.9)	246 (70.9)	101 (29.1)
Baseline problematic drug use (past 12 months)				
Yes	94 (39.7)	143 (60.4)	134 (60.4)	88 (39.6)
No	531 (90.6)	55 (9.4)	456 (76.9)	137 (23.1)
Baseline problematic alcohol use (current)				
Yes	173 (63.8)	98 (36.2)	90 (34.5)	171 (65.5)
No	452 (81.9)	100 (18.1)	500 (90.3)	54 (9.7)

^aGender identity was recoded as binary (i.e., female or woman, trans female, trans woman, male-to-female (MTF), woman of trans experience) and nonbinary (i.e., transfeminine, trans femme, nonbinary, agender, gender fluid, gender variant, gender nonconforming, person of trans experience, two-spirit, & other) due to a small number of participants in some groups.

^bCombined due to a small number of participants in each group.

Table 3.

Results from models regressing past 6-month problematic drug use and current problematic alcohol use at 12-months follow-up on baseline medical gender affirmation and baseline legal gender affirmation in The LITE Study Cohort.

	Past 6-month problematic drug use N1=823		Current problematic alcohol use N2=815	
	PR (95% CI)	aPR (95% CI)	PR (95% CI)	aPR (95% CI)
Medical gender affirmation				
Met need versus (ref) unmet need	0.77 (0.54, 1.09)	0.70 (0.49, 0.99)	1.06 (0.76, 1.48)	1.07 (0.77, 1.49)
Met need versus (ref) did not try	0.87 (0.64, 1.18)	0.84 (0.62, 1.15)	0.78 (0.63, 0.96)	0.72 (0.57, 0.91)
Unmet need versus (ref) did not try	1.14 (0.74, 1.75)	1.20 (0.79, 1.84)	0.73 (0.51, 1.05)	0.68 (0.47, 0.97)
Legal gender affirmation				
All ^a versus (ref) some or none ^b	0.84 (0.59, 1.19)	0.94 (0.66, 1.35)	0.98 (0.74, 1.29)	1.02 (0.77, 1.35)

Baseline data were collected from March 2018 to August 2020. N1 = number of study participants who were retained at follow-up in the analysis of problematic drug use. N2 = number of study participants who were retained at follow-up in the analysis of problematic alcohol use. Total sample size, N = 1186. PR = prevalence ratio. 95% CI = 95% confidence interval. aPR = adjusted prevalence ratio. All models were weighted using stabilized inverse probability of censor weights (sIPCW) to account for selection bias due to missing data at follow-up. The distributions of weighted baseline measures were approximately equal to the distribution of unweighted baseline measures. We used Poisson regression with robust standard errors to estimate model parameters. To address the confounding depicted in our DAG, multivariable models were adjusted for: baseline problematic drug use or problematic alcohol use age, gender identity, race, ethnicity, US Census Division, cohort mode, baseline food insecurity and an indicator for the baseline data being collected after the start of COVID.

^a All IDs match name and gender.

^b Some or no IDs match name and/or gender