therapeutics

MDPI

Article

The Impact of Prior Substance Use on Postoperative Outcomes Following Gender-Affirming Surgery

Chrishaun Alexander [1,†], Akeem Henry [2,†], Derek Nuamah [3], Joshua Lewis [4,*], Bryce Gantt [5], Kelsey M Green [5], Malory Alexis [6] and Oyetokunbo Ibidapo-Obe [7]

[1] School of Medicine, Morehouse College, 720 Westview Dr SW, Atlanta, GA 30310, USA; cdalexander@msm.edu
[2] School of Medicine, Meharry Medical College, 1005 Dr DB Todd Jr Blvd, Nashville, TN 37208, USA; ahenry24@mmc.edu
[3] Miller School of Medicine, University of Miami, 1600 NW 10th Ave #1140, Miami, FL 33136, USA
[4] School of Medicine, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77554, USA
[5] College of Medicine, Howard University, 520 W St NW, Washington, DC 20059, USA
[6] College of Medicine, Florida State University, 1115 W Call St, Tallahassee, FL 32304, USA
[7] Department of Family Medicine, Memorial Hermann Hospital, 6411 Fannin St., Houston, TX 77030, USA
* Correspondence: jelewis114@gmail.com
† These authors contributed equally and can be considered as co-first authors.

Abstract

Background/Objectives: Gender-affirming surgery (GAS) is associated with improved mental health outcomes in transgender and gender-diverse (TGD) individuals. However, TGD populations experience disproportionately high rates of substance use disorders (SUDs), which are established risk factors for surgical complications. Despite this, the relationship between preoperative SUDs and postoperative outcomes following GAS has not been studied. Our objective was to evaluate how specific SUD subtypes, including tobacco, alcohol, and cannabis, impact short- and medium-term postoperative complications following GAS. **Methods:** A retrospective cohort study was conducted using the TriNetX Research Network, which includes de-identified electronic health records from over 100 million U.S. patients. Adults with documented gender dysphoria who underwent GAS between April 2015 and April 2025 were included. Patients were divided into four groups: no SUD, tobacco use, alcohol use, and cannabis use. Propensity score matching was used to control for demographic variables. Postoperative complications were assessed at 30 days and 6 months. **Results:** Alcohol use was significantly associated with increased rates of delayed wound healing, wound dehiscence, gastrointestinal symptoms, and postoperative pain at both 30 days and 6 months. Cannabis use was linked to higher rates of wound dehiscence, infections, GI symptoms, and pain. Tobacco use showed the broadest impact, significantly associated with nearly all complications measured except pain at 30 days. These associations persisted at six months. **Conclusions:** This is the first study to quantify the relationship between substance use and GAS outcomes. Preoperative use of tobacco, alcohol, and cannabis was independently associated with increased postoperative complications. These findings underscore the need for systematic preoperative screening and the development of SUD-specific perioperative care pathways to improve outcomes and advance equity in surgical care for TGD patients.

Keywords: gender-affirming surgery; transgender health; substance use disorder; postoperative complications

Academic Editor: Nejat Düzgüneş

Received: 17 June 2025
Revised: 6 August 2025
Accepted: 12 August 2025
Published: 21 August 2025

Citation: Alexander, C.; Henry, A.; Nuamah, D.; Lewis, J.; Gantt, B.; Green, K.M.; Alexis, M.; Ibidapo-Obe, O. The Impact of Prior Substance Use on Postoperative Outcomes Following Gender-Affirming Surgery. *Therapeutics* **2025**, 2, 14. https://doi.org/10.3390/therapeutics2030014

1. Introduction

Gender-affirming surgery (GAS) is a critical intervention for transgender and gender-diverse (TGD) individuals, with well-documented reductions in psychological distress and suicidality [1]. However, TGD populations face disproportionately high rates of substance use disorders (SUDs); their rate is 30% greater than their cisgender peers, driven by systemic inequities and minority stress [2]. A 2023 cohort study of 200,816 surgical patients found that the co-occurrence of smoking and risky alcohol use increased postoperative complications (e.g., infections and wound dehiscence) by 1.5–2.9 times compared to non-users, highlighting the urgency of addressing SUDs in surgical populations [3]. While surgical access expands, preoperative risk stratification remains underdeveloped, particularly regarding SUDs as modifiable predictors of postoperative outcomes.

Substance use disorders are established risk factors for surgical complications, including infections, prolonged recovery, and readmissions. It has been established that opioid use heightens thromboembolic risks, while chronic alcohol consumption impairs wound healing and immune function [4,5]. Despite these established risks, no studies have examined how SUDs influence outcomes in GAS, where unique anatomical factors (e.g., estrogen-associated hypercoagulability in transfeminine patients) and psychosocial stressors may exacerbate vulnerabilities.

This study addresses this gap by analyzing a national cohort, via the TriNetX Research Network, to test the hypothesis that preoperative substance use will independently predict adverse outcomes following GAS. Unlike prior research emphasizing mental health outcomes, we identify modifiable surgical risks and high-impact SUD subtypes (e.g., cannabis and alcohol) to inform tailored perioperative protocols. The objectives are to (1) quantify complication rates associated with SUD subtypes, (2) identify high-risk procedures, and (3) inform tailored perioperative protocols to improve equity in surgical care for TGD patients. We hypothesize that the presence of any SUDs will be independently associated with increased postoperative complications following GAS, with variability expected in magnitude across substance types.

2. Methods

2.1. Data Source

This study was a retrospective observational cohort study utilizing the TriNetX Research Network, a global federated health research platform that provides de-identified electronic health record (EHR) data from over 69 healthcare organizations (HCOs) across the United States. The network includes hospitals, outpatient centers, and academic institutions, covering more than 113 million unique patients. Available data include demographics, diagnoses, procedures, medications, and laboratory results. Because the data are de-identified and aggregated at the institutional level, this study qualified as being exempt from Institutional Review Board (IRB) approval.

2.2. Study Design and Population

The study population consisted of patients treated between 1 April 2015 and 1 April 2025. Inclusion criteria required patients to be 18 years or older, have a documented diagnosis of gender dysphoria, and have undergone gender-affirming surgery. Gender dysphoria was identified using ICD-10 codes F64.0 (transsexualism), F64.1 (dual-role transvestism), F64.2 (gender identity disorder of childhood), F64.8 (other gender identity disorders), and F64.9 (gender identity disorder, unspecified). Gender-affirming surgical procedures were identified using validated CPT codes, including mastectomy (19303 and 19304), breast augmentation (19325), vaginoplasty (55970), metoidioplasty (55980), phalloplasty (55899), hysterectomy (58150 and 58260), and orchiectomy (54530). Surgical

procedures were confirmed through provider-entered CPT codes within the electronic health records.

2.3. Cohort Definition

Patients were divided into four non-overlapping groups based on their documented substance use and transgender status before surgery. The control group had no history of substance use. The tobacco group included patients diagnosed with tobacco use using ICD-10 codes such as F17.200, F17.201, F17.210, F17.211, F17.220, and similar. The cannabis group included patients with cannabis use identified by ICD-10 codes such as F12.10, F12.20, F12.21, and related codes. The alcohol group included patients diagnosed with alcohol use with codes such as F10.10, F10.20, F10.21, and similar. Each patient was assigned to only one group to avoid overlap.

2.4. Outcome Measures

We evaluated complications occurring within 30 days and 6 months after gender-affirming surgery using ICD-10 codes. Delayed wound healing was captured with codes T81.89XA, L89.90, and L98.8. Wound dehiscence was identified using T81.30XA to T81.32XA. Surgical site infection was recorded using T81.4XXA and L08.9. Postoperative nausea, vomiting, and diarrhea were assessed with R11.0, R11.2, R11.10, and K52.9. Surgical site pain was recorded using G89.18 and G89.28.

2.5. Statistical Analysis

To reduce the effects of confounding variables, propensity score matching was performed. Patients were matched 1:1 based on age, race, ethnicity, and sex documented in the EHRs using a nearest neighbor algorithm with a caliper of 0.1 pooled standard deviations. Risk ratios and p-values were calculated to compare the incidence of complications between cohorts. Statistical significance was determined at a two-tailed p-value threshold of less than 0.05. Analyses were conducted using the statistical modules available through the TriNetX platform. Because of the retrospective design and use of observational data, the findings represent associations rather than causal relationships.

3. Results

Thirty days following gender-affirming surgery, alcohol use was associated with a significantly increased risk of delayed wound healing (RR: 2.198, $p = 0.0139$); wound dehiscence (RR: 1.398, $p = 0.0419$); nausea, vomiting, and diarrhea ($p = 0.0046$); and postoperative surgical site pain (RR: 1.488, $p = 0.0431$). Alcohol use was not significantly associated with surgical site infections at 30 days (RR: 1.487, $p = 0.1148$). Cannabis use was significantly associated with higher rates of wound dehiscence (RR: 1.694, $p = 0.0002$), surgical site infection ($p = 0.0138$), and nausea, vomiting, and diarrhea (RR: 2.488, $p = 0.0089$), but it was not significantly associated with delayed wound healing (RR: 0.977, $p = 0.9857$) or postoperative surgical site pain (RR: 1.039, $p = 0.7685$). Tobacco use demonstrated a significant association with delayed wound healing (RR: 1.526, $p = 0.0034$), wound dehiscence (RR: 1.423, $p = 0.0001$), surgical site infection (RR: 1.506, $p < 0.0001$), and nausea, vomiting, and diarrhea (RR: 2.603, $p < 0.0001$), but was not significantly associated with postoperative surgical site pain (RR: 0.854, $p = 0.1766$) (Table 1).

Six months following surgery, alcohol use continued to show significant associations with delayed wound healing (RR: 2.682, $p = 0.0217$); wound dehiscence (RR: 1.598, $p = 0.0019$); nausea, vomiting, and diarrhea (RR: 2.427, $p < 0.0001$); and postoperative surgical site pain (RR: 1.698, $p = 0.0002$). However, no significant association was found with surgical site infections (RR: 1.703, $p = 0.3331$). Cannabis use was associated with significantly higher rates of wound dehiscence (RR: 2.012, $p = 0.0004$); surgical site infec-

tion (RR: 1.651, $p < 0.0001$); nausea, vomiting, and diarrhea (RR: 3.719, $p < 0.0001$); and postoperative surgical site pain (RR: 1.842, $p = 0.0006$). However, cannabis use was not significantly associated with delayed wound healing (RR: 1.284, $p = 0.4497$). Tobacco use remained significantly associated with delayed wound healing (RR: 1.738, $p < 0.0001$); wound dehiscence (RR: 1.709, $p = 0.0265$); surgical site infection (RR: 2.004, $p < 0.0001$); nausea, vomiting, and diarrhea (RR: 2.572, $p < 0.0001$); and postoperative surgical site pain (RR: 1.512, $p = 0.0002$) at six months (Table 2).

Table 1. Regression analysis evaluating associations between substance use and complications 30 days following gender-affirming surgery.

Outcomes	Risk Ratio	95% Confidence Interval	*p*-Value
Delayed wound healing			
Cannabis	0.977	(0.388, 2.461)	0.9857
Tobacco	1.526	(1.185, 1.846)	0.0034
Alcohol	2.198	(1.147, 4.986)	0.0139
Wound dehiscence after procedure			
Cannabis	1.694	(1.297, 2.296)	0.0002
Tobacco	1.423	(1.203, 1.763)	0.0001
Alcohol	1.398	(1.021, 1.805)	0.0419
Surgical site infection			
Cannabis	1.369	(1.034, 1.859)	0.0138
Tobacco	1.506	(1.326, 1.701)	<0.0001
Alcohol	1.487	(0.885, 2.627)	0.1148
Nausea, vomiting, and diarrhea			
Cannabis	2.488	(1.215, 5.103)	0.0089
Tobacco	2.603	(1.729, 3.584)	<0.0001
Alcohol	2.571	(1.273, 5.299)	0.0046
Postoperative surgical site pain			
Cannabis	1.039	(0.671, 1.684)	0.7685
Tobacco	0.854	(0.623, 1.105)	0.1766
Alcohol	1.488	(1.008, 2.272)	0.0431

Table 2. Regression analysis evaluating associations between substance use and complications six months following gender-affirming surgery.

Outcomes	Risk Ratio	95% Confidence Interval	*p*-Value
Delayed wound healing			
Cannabis	1.284	(0.604, 2.728)	0.4497
Tobacco	1.738	(1.503, 2.080)	<0.0001
Alcohol	2.682	(1.019, 6.892)	0.0217
Wound dehiscence after procedure			
Cannabis	2.012	(1.372, 2.951)	0.0004
Tobacco	1.709	(1.559, 1.911)	0.0265
Alcohol	1.598	(1.199, 2.133)	0.0019

Table 2. *Cont.*

Outcomes	Risk Ratio	95% Confidence Interval	*p*-Value
Surgical site infection			
Cannabis	1.651	(1.532, 1.780)	<0.0001
Tobacco	2.004	(1.812, 2.249)	<0.0001
Alcohol	1.703	(0.611, 4.818)	0.3331
Nausea, vomiting, and diarrhea			
Cannabis	3.719	(2.281, 6.266)	<0.0001
Tobacco	2.572	(2.109, 3.113)	<0.0001
Alcohol	2.427	(1.662, 3.512)	<0.0001
Postoperative surgical site pain			
Cannabis	1.842	(1.287, 2.646)	0.0006
Tobacco	1.512	(1.217, 1.862)	0.0002
Alcohol	1.698	(1.271, 2.271)	0.0002

4. Discussion

Substance use was associated with a range of complications following gender-affirming surgery, both in the short term and at six months. At 30 days, alcohol use was significantly linked to delayed wound healing, wound dehiscence, gastrointestinal symptoms, and postoperative pain. Cannabis was associated with wound dehiscence, surgical site infections, and gastrointestinal symptoms. Tobacco use showed the broadest impact, with significant associations across nearly all complications except postoperative pain. These patterns remained consistent at six months. Cannabis became significantly associated with postoperative pain, and both alcohol and tobacco continued to show strong links to delayed healing, wound complications, and gastrointestinal symptoms.

Transgender and gender-diverse (TGD) individuals in the U.S. experience disproportionately high rates of substance use, often shaped by stigma, discrimination, and limited access to affirming care. A systematic review found substance use in up to 40% of TGD samples, frequently alongside elevated rates of depression, suicidality, and trauma exposure [6]. In one study, over a quarter of transmasculine adults reported using substances to cope with mistreatment in healthcare settings, with direct experiences of discrimination—such as being refused care—strongly linked to this behavior [6]. Anticipated stigma also contributed to avoiding care, compounding the challenge. Structural stigma, including systemic exclusion, provider bias, and institutional neglect, has been increasingly recognized as a determinant of poor health outcomes and elevated substance use among TGD populations [7]. As Costa (2023) notes, these barriers operate across multiple levels of society and healthcare systems, reinforcing patterns of minority stress that contribute to self-medication, disengagement from care, and worsened surgical recovery [8]. These findings highlight how social stressors can shape patterns of substance use in this population. Given these overlapping risks and barriers, more research is needed to understand how substance use may affect clinical outcomes in TGD individuals, particularly in the context of gender-affirming procedures.

TGD individuals who are contemplating GAS may face elevated biological and physiological risk when undergoing GAS, particularly in connection with substance use. Substances such as tobacco, alcohol, and cannabis are associated with higher use within this population, each posing distinct risks that may compromise surgical outcomes. The pathological effects tobacco use has been shown to have include vasoconstrictive effects and reduction in tissue perfusion, increasing the likelihood of ischemia during and after

surgery [6]. In our study, a six-month postoperative follow-up revealed a 1.7-fold increased risk of wound dehiscence among tobacco users. National data further aids this premise; a national study found that transgender adults were associated with a higher frequency of tobacco products in a 30-day period (39.7% vs. 25.1%) and current use of cigarettes (35.5% vs. 20.7%), cigars (26.8% vs. 9.3%), and e-cigarettes (21.3% vs. 5.0%) than cisgender adults [7]. These increased levels of substance use reflect the role of social determinants, including structural discrimination, marginalization, and participation in sex work—settings where tobacco and other substance use may be more prevalent [9,10].

The consumption of alcohol poses additional risks, especially concerning negative effects on the immune system and the prolonged post-surgical recovery process. Excessive alcohol consumption can result in decreased immune function which, on the other hand, decreases the body's ability to combat postoperative infections [11]. Ultimately, in our study, we saw a higher risk ratio (2.5) for alcohol-related outcomes regarding gastrointestinal symptoms 30 days following GAS compared to other outcome categories measured. Other studies indicate that transgender individuals exhibit elevated levels of alcohol use, complicating surgical interventions [12]. For transgender individuals with higher alcohol use interested in GAS, our findings support the need for careful management of substance consumption pre- and post-surgery [11].

It is essential to understand the association between SUD and hormone therapy in TGD patients. Hormones used in gender-affirming hormone therapy, such as estrogen and testosterone, have to be examined as they present different risks that can be exacerbated by substance use, especially during recovery and medical treatments. Research has demonstrated that estrogen is associated with increased coagulation; thus, the extravasation of a thrombotic risk is a major concern [13]. This risk is particularly alarming for those who may be prone to hypercoagulable states, such as those with higher substance use, which can alter normal physiological reactions and recovery [14,15]. Estrogen therapy is commonly prescribed to transgender women, which raises the risk of venous thromboembolism (VTE), a major health concern for patients with underlying conditions that affect normal physiological responses [16]. For individuals with SUD, particularly those who may already have compromised vascular health due to substance use, the potential for thrombotic events becomes significantly alarming [17].

The role of testosterone in metabolism and inflammation can be distinguished as a metabolic factor (in the sense of causing obesity or other obesity-related conditions) that might complicate surgical outcomes. Elevated testosterone levels disturb lipid metabolism, which in turn leads to dyslipidemia that has an association with high cardiovascular probabilities like stroke and myocardial infarction [17,18]. Furthermore, research showed that testosterone can be the cause of fat redistribution, in particular visceral fat, which speeds up disease development when combined with drug and alcohol dependence [19]. This interplay suggests that TGD individuals undergoing testosterone treatment may have an increased risk of complicated conditions if they are also handling higher levels of substance use. This, in turn, forms a cycle of both physical and psychological stress, which hinders the recovery process.

There is an urgent need for the systematic assessment and implementation of interventions that aim to reduce and screen for substance-use-related risk and consequently improve recovery results. Preoperative substance use screening and early identification are the primary steps to attaining this goal. By embedding these practices into the surgical protocol, healthcare providers can proactively identify the possible complications that are likely to be encountered, resulting in a more precise and effective perioperative scheme for patients with SUD.

4.1. Preoperative SUD Screening and Identification

Implementing a standardized substance use screening protocol would enable healthcare providers to diagnose at-risk patients in the preoperative setting. Evidence shows that the transgender population has higher rates of substance use, likely due to stress factors such as discrimination, social stigma, and mental health concerns [20,21]. Foreknowledge of these social factors ensures more accurate risk factoring and better preoperative planning. As a result, standardized mental health assessments and routine surgical evaluations would aid in prompt interventions, which in turn would lower the possibility of surgical complications associated with substance use [22,23].

4.2. Specific Plans After Surgery

After identifying high levels of substance use, the next step is to implement specific postoperative plans that are meant for management. An example could be the launching of a tobacco cessation program, which would have the most profound effect in reducing the risks associated with impaired wound healing and increased thrombotic events [23,24]. Interventions that provide behavioral health support and educational resources concerning alcohol and illicit drug use could likewise improve outcomes for TGD individuals with SUD [25]. Taking into consideration individual patient histories can also personalize postoperative care plans while implementing the comprehensive management of both surgical and substance use needs.

4.3. Limitations

The present research has several limitations. One major challenge stems from our reliance on existing electronic health records (EHRs) and ICD-10 coding, which may lack uniformity or completeness. Specifically, ICD-10 codes may not fully capture the frequency, duration, timing, or severity of substance use, and underreporting may occur due to patient stigma or clinician bias. Our classification of substance use was based solely on diagnosis codes, which do not reliably differentiate between active use at the time of surgery and historical or resolved use. This limitation may lead to misclassification and bias the magnitude of associations observed.

Additionally, while the dataset is large, the population sample size for each subgroup may limit generalizability to all transgender and gender-diverse (TGB) patients. Our retrospective design introduces potential for confounding variables not fully controlled in our analysis, such as socioeconomic status, comorbidities, and access to care. Although we used propensity score matching to mitigate demographic imbalances such as age, sex, race, and ethnicity, important clinical variables such as diabetes, body mass index (BMI), psychiatric illness, and hormone therapy status were not available and may confound the observed associations. These clinical factors have known impacts on wound healing, immune function, and surgical recovery and should be included in future analyses when data availability allows.

While we used matching to mitigate demographic imbalance, future studies should employ multivariate regression models and sensitivity analyses to strengthen causal inference. Another key limitation is the absence of hormone therapy data; this is a potentially important modifier of surgical risk, given its impact on vascular and metabolic health. Future investigations should explore the interaction between substance use and gender-affirming hormone therapy on surgical outcomes.

Finally, we recommend future prospective studies with larger, more diverse samples and longer-term follow-ups to better capture the nuances of substance use and postoperative complications in this high-risk population. Therefore, these drawbacks indicate the necessity for a more inclusive approach in future studies. This may include increasing the

sample size, encouraging cross-site collaboration between databases, and improving data collection methods. Additionally, patients may underestimate their substance use in order to avoid shame or guilt in fear of judgment or biases from their clinicians. Longer studies with extensive follow-ups examining this important topic regarding SUDs and GAS are necessary to further report factors that can impede recovery and surgery outcomes among this vulnerable population.

4.4. Future Research Directions

There exists a gap in the prospective research efforts that seek to evaluate the performance of SUD interventions perioperatively, which are organized and applied in the context of GAS. Contingency management is a behavioral cognitive tool used by mental health clinicians to help individuals with heavy alcohol consumption [26]. Perhaps future studies can examine how TGD patients who have SUD may benefit from contingency management and how it may influence SUD and GAS. Creating a personalized and tailored approach to treating and optimizing the treatment of SUD before patients undergo GAS is vital. Future research can prioritize studies that aim to identify the effects of unique programs pertaining to behavioral counseling methods [21,27]. Examples of such programs would promote positive reinforcement in achieving abstinence goals. Additionally, the research by Tuten et al. demonstrates the great possibilities of reinforcement strategies that can support populations to work towards abstinence [28]. In the modern age of apps and personalization of algorithms, Alessi and Petry investigated the implementation of mobile technology-based contingency management for alcohol abstinence, which shows that the method can bring new perspectives to the healing process, especially for people battling addiction and mental and social health challenges [29]. With this, experts can look at the benefits of how an app-based therapy approach could influence the outcomes for TGD patients who have undergone SUD in both pre and postop periods. The results of these studies would be crucial in determining the most effective ways to handle the distinct and complex challenges that TGD patients with SUDs encounter. These studies would aid in creating tailored, evidence-based approaches solely directed at this vulnerable population.

5. Conclusions

This study is the first to quantify the association between specific substance use and postoperative complications in patients undergoing gender-affirming surgery. Our findings reveal that preoperative substance use—particularly tobacco, alcohol, and cannabis—is independently associated with an increased risk of adverse outcomes both 30 days and 6 months after surgery. Notably, tobacco use was consistently linked to the broadest spectrum of complications, including impaired wound healing and infection, while cannabis use showed the strongest association with gastrointestinal symptoms. These results underscore the urgent need for systematic preoperative screening and targeted perioperative protocols that address substance use in transgender and gender-diverse patients. Tailoring surgical care through early identification, harm reduction strategies, and SUD-specific interventions can improve postoperative outcomes and promote equitable care delivery. Future prospective studies are essential to evaluate the effectiveness of these interventions and develop best practices for optimizing surgical recovery in this high-risk population.

Author Contributions: J.L.: Conceptualization, methodology, writing—original draft preparation, writing—review and editing, and data curation. C.A.: Writing—original draft preparation and writing—review and editing. A.H.: Writing—original draft preparation and writing—review and editing. D.N.: Writing—original draft preparation and writing—review and editing. B.G.: Writing—original draft preparation and writing—review and editing. K.M.G.: Writing—original draft preparation and writing—review and editing. M.A.: Writing—original draft preparation and

writing—review and editing. O.I.-O.: Reviewing and editing, supervision, and conceptualization. All authors have read and agreed to the published version of the manuscript.

Funding: This research was supported by the Institute for Translational Sciences at the University of Texas Medical Branch. It was supported in part by the Clinical and Translational Science Award (UL1 TR001439) from the National Center for Advancing Translational Sciences at the National Institutes of Health (NIH). The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH. This project was funded in part by the Department of Health and Human Services, Health Resources and Services Administration (HRSA), through its grant to the UTMB Center of Excellence for Professional Advancement and Research (grant number 1 D34HP49234-01-00). The HRSA had no role in decisions related to the research, authorship, or publication of this article.

Institutional Review Board Statement: This study was reviewed and determined to be exempt from full Institutional Review Board (IRB) review by the University of Texas Medical Branch (UTMB) IRB as it involved an analysis of de-identified, retrospective data in accordance with federal regulations.

Informed Consent Statement: The database used in this study contains de-identified patient information. All patients provided informed consent at the time of data entry for their information to be used for research purposes in a de-identified manner. Therefore, individual informed consent for this specific study was waived.

Data Availability Statement: The data used in this study were obtained from the TriNetX database, a secure, federated network that provides access to de-identified patient data from participating healthcare organizations. Due to data sharing agreements and privacy regulations, direct access to the TriNetX data is limited to authorized users within the network. Researchers interested in accessing similar data can request access through TriNetX, subject to institutional and ethical approvals.

Conflicts of Interest: The authors declare no potential conflicts of interest during the completion, authorship, and/or publication of this article.

References

1. Lewis, J.E.; Patterson, A.R.; Effirim, M.A.; Patel, M.M.; Lim, S.E.; Cuello, V.A.; Phan, M.H.; Lee, W.-C. Examining gender-specific mental health risks after gender-affirming surgery: A national database study. *J. Sex. Med.* **2025**, *22*, 645–651. [CrossRef]
2. Hughto, J.M.W.; Quinn, E.K.; Dunbar, M.S.; Rose, A.J.; Shireman, T.I.; Jasuja, G.K. Prevalence and Co-occurrence of Alcohol, Nicotine, and Other Substance Use Disorder Diagnoses Among US Transgender and Cisgender Adults. *JAMA Netw. Open* **2021**, *4*, e2036512. [CrossRef]
3. Fernandez, A.C.; Bohnert, K.M.; Bicket, M.C.; Weng, W.; Singh, K.; Englesbe, M. Adverse Surgical Outcomes Linked to Co-occurring Smoking and Risky Alcohol Use Among General Surgery Patients. *Ann. Surg.* **2023**, *278*, 201–207. [CrossRef]
4. Radek, K.A.; Ranzer, M.J.; DiPietro, L.A. Brewing complications: The effect of acute ethanol exposure on wound healing. *J. Leukoc. Biol.* **2009**, *86*, 1125–1134. [CrossRef]
5. Sodhi, N.; Anis, H.K.; Acuña, A.J.; Vakharia, R.M.; Piuzzi, N.S.; Higuera, C.A.; Roche, M.W.; Mont, M.A. The Effects of Opioid Use on Thromboembolic Complications, Readmission Rates, and 90-Day Episode of Care Costs After Total Hip Arthroplasty. *J. Arthroplast.* **2020**, *35*, S237–S240. [CrossRef]
6. Reisner, S.L.; Pardo, S.T.; Gamarel, K.E.; Hughto, J.M.W.; Pardee, D.J.; Keo-Meier, C.L. Substance Use to Cope with Stigma in Healthcare Among U.S. Female-to-Male Trans Masculine Adults. *LGBT Health* **2015**, *2*, 324–332. [CrossRef] [PubMed]
7. Buchting, F.O.; Emory, K.T.; Scout; Kim, Y.; Fagan, P.; Vera, L.E.; Emery, S. Transgender Use of Cigarettes, Cigars, and E-Cigarettes in a National Study. *Am. J. Prev. Med.* **2017**, *53*, e1–e7. [CrossRef]
8. Costa, D. Transgender Health between Barriers: A Scoping Review and Integrated Strategies. *Societies* **2023**, *13*, 125. [CrossRef]
9. de Blok, C.J.M.; Wiepjes, C.M.; Nota, N.M.; van Engelen, K.; Adank, M.A.; Dreijerink, K.M.A.; Barbé, E.; Konings, I.R.H.M.; den Heijer, M. Breast cancer risk in transgender people receiving hormone treatment: Nationwide cohort study in the Netherlands. *BMJ* **2019**, *365*, l1652. [CrossRef] [PubMed]
10. Cotaina, M.; Peraire, M.; Boscá, M.; Echeverria, I.; Benito, A.; Haro, G. Substance Use in the Transgender Population: A Meta-Analysis. *Brain Sci.* **2022**, *12*, 366. [CrossRef]
11. Connolly, D.J.; Davies, E.; Lynskey, M.; Maier, L.J.; Ferris, J.A.; Barratt, M.J.; Winstock, A.R.; Gilchrist, G. Differences in Alcohol and Other Drug Use and Dependence Between Transgender and Cisgender Participants from the 2018 Global Drug Survey. *LGBT Health* **2022**, *9*, 534–542. [CrossRef] [PubMed]

12. Ezeh, E.; Perdoncin, M.; Al-Hiari, M.; Ogbu, C.; Marcum, M.; Saunders, E.; Mader, J. Abstract 18471: Cardiovascular Risks Among the Transgender Population in Rural United States: Spotlight on the Appalachian Region. *Circulation* **2023**, *148* (Suppl. 1), A18471. [CrossRef]
13. Goldstein, Z.; Khan, M.; Reisman, T.; Safer, J.D. Managing the risk of venous thromboembolism in transgender adults undergoing hormone therapy. *J. Blood Med.* **2019**, *10*, 209–216. [CrossRef] [PubMed]
14. Maraka, S.; Singh Ospina, N.; Rodriguez-Gutierrez, R.; Davidge-Pitts, C.J.; Nippoldt, T.B.; Prokop, L.J.; Murad, M.H. Sex Steroids and Cardiovascular Outcomes in Transgender Individuals: A Systematic Review and Meta-Analysis. *J. Clin. Endocrinol. Metab.* **2017**, *102*, 3914–3923. [CrossRef]
15. Martinelli, I.; Lensing, A.W.A.; Middeldorp, S.; Levi, M.; Beyer-Westendorf, J.; van Bellen, B.; Bounameaux, H.; Brighton, T.A.; Cohen, A.T.; Trajanovic, M.; et al. Recurrent venous thromboembolism and abnormal uterine bleeding with anticoagulant and hormone therapy use. *Blood* **2016**, *127*, 1417–1425. [CrossRef]
16. Rytz, C.L.; Pattar, B.S.B.; Mizen, S.J.; Lieb, P.; Parsons Leigh, J.; Saad, N.; Dumanski, S.M.; Beach, L.B.; Marshall, Z.; Newbert, A.M.; et al. Transgender and Nonbinary Individuals' Perceptions Regarding Gender-Affirming Hormone Therapy and Cardiovascular Health: A Qualitative Study. *Circ. Cardiovasc. Qual. Outcomes* **2024**, *17*, e011024. [CrossRef]
17. Masumori, N.; Baba, T.; Abe, T.; Niwa, K. What is the most anticipated change induced by treatment using gender-affirming hormones in individuals with gender incongruence? *Int. J. Urol.* **2021**, *28*, 526–529. [CrossRef]
18. Asscheman, H.; Giltay, E.J.; Megens, J.A.J.; de Ronde, W.P.; van Trotsenburg, M.A.A.; Gooren, L.J.G. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. *Eur. J. Endocrinol.* **2011**, *164*, 635–642. [CrossRef]
19. Velho, I.; Fighera, T.M.; Ziegelmann, P.K.; Spritzer, P.M. Effects of testosterone therapy on BMI, blood pressure, and laboratory profile of transgender men: A systematic review. *Andrology* **2017**, *5*, 881–888. [CrossRef]
20. Frost, M.C.; Blosnich, J.R.; Lehavot, K.; Chen, J.A.; Rubinsky, A.D.; Glass, J.E.; Williams, E.C. Disparities in Documented Drug Use Disorders Between Transgender and Cisgender U.S. Veterans Health Administration Patients. *J. Addict. Med.* **2021**, *15*, 334–340. [CrossRef] [PubMed]
21. Keuroghlian, A.S.; Reisner, S.L.; White, J.M.; Weiss, R.D. Substance Use and Treatment of Substance Use Disorders in a Community Sample of Transgender Adults. *Drug Alcohol. Depend.* **2015**, *152*, 139–146. [CrossRef] [PubMed]
22. Rifkin, W.J.; Daar, D.A.; Cripps, C.N.; Mars, G.; Zhao, L.C.; Levine, J.P.; Bluebond-Langner, R. Gender-affirming Phalloplasty: A Postoperative Protocol for Success. *Plast. Reconstr. Surg. Glob. Open* **2022**, *10*, e4394. [CrossRef]
23. Glynn, T.R.; van den Berg, J.J. A Systematic Review of Interventions to Reduce Problematic Substance Use Among Transgender Individuals: A Call to Action. *Transgend Health* **2017**, *2*, 45–59. [CrossRef]
24. Flentje, A.; Heck, N.C.; Sorensen, J.L. Characteristics of transgender individuals entering substance abuse treatment. *Addict. Behav.* **2014**, *39*, 969–975. [CrossRef]
25. Miller, P.J.; Grinberg, D.; Wang, T.D. Midline Cleft. *Arch. Facial Plast. Surg.* **1999**, *1*, 200–203. [CrossRef]
26. Dougherty, D.M.; Lake, S.L.; Hill-Kapturczak, N.; Liang, Y.; Karns, T.E.; Mullen, J.; Roache, J.D. Using contingency management procedures to reduce at-risk drinking in heavy drinkers. *Alcohol. Clin. Exp. Res.* **2015**, *39*, 743–751. [CrossRef] [PubMed]
27. Singh, S.; Ninan, R.T.; Ambooken, G.C.; Dhiman, M. Challenges in provision of anesthesia to transgender patients in India: A scoping review. *J. Anaesthesiol. Clin. Pharmacol.* **2025**, *41*, 15–19. [CrossRef]
28. Hill Weller, L.; Rubinsky, A.D.; Shade, S.B.; Liu, F.; Cheng, I.; Lopez, G.; Robertson, A.; Smith, J.; Dang, K.; Leiva, C.; et al. Lessons learned from implementing a diversity, equity, and inclusion curriculum for health research professionals at a large academic research institution. *J. Clin. Trans. Sci.* **2024**, *8*, e22. [CrossRef]
29. Alessi, S.M.; Petry, N.M. A randomized study of cellphone technology to reinforce alcohol abstinence in the natural environment. *Addiction* **2013**, *108*, 900–909. [CrossRef] [PubMed]