mhc MENTAL HEALTH CLINICIAN

ORIGINAL RESEARCH Open Access

Antidepressant prescribing in transgender and nonbinary individuals diagnosed with gender dysphoria and mood or anxiety disorders

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How to cite: Tiefenthaler CM, Lee KC. Antidepressant prescribing in transgender and nonbinary individuals diagnosed with gender dysphoria and mood or anxiety disorders. Ment Health Clin [Internet]. 2023;13(6):298-302. DOI: 10.9740/mhc.2023.12.298.

Submitted for Publication: March 30, 2023; **Accepted for Publication:** August 24, 2023

Abstract

Introduction: Transgender and nonbinary (TGNB) individuals are highly stigmatized members of society and are significantly at higher risk of having mood or anxiety-related disorders compared to non-TGNB individuals.

Methods: In this retrospective cohort study, antidepressant prescribing data were collected from TGNB adults diagnosed with gender dysphoria (GD) and mood or anxiety-related disorder between January 2005 and October 2021. The primary outcome was to compare the number of active outpatient antidepressant prescriptions at the time of GD diagnosis between gender identities. The secondary outcomes were to compare antidepressant class utilization between gender identities as well as the prevalence of concurrent mood or anxiety-related disorder diagnoses between gender identities.

Results: Of 131 patients who met inclusion criteria, there was no significant difference in number of active antidepressant prescriptions between gender identities at the time of the GD diagnosis ($p = .357$). However, transgender females were prescribed bupropion at significantly higher rates than other gender identities ($p = .046$). Approximately 38% of patients did not have an active antidepressant prescription at the time of GD diagnosis despite concurrent mood or anxiety-related diagnoses. The prevalence of generalized anxiety disorder was significantly greater among transgender males ($p = .044$).

Discussion: Although the number of active antidepressant prescriptions between gender identities were similar in this study, we found 38% of patients were not prescribed any antidepressants at time of GD and mood or anxiety-related disorders. This serendipitous finding elucidates a potential gap in mental health care among transgender adults.

Keywords: antidepressants, antipsychotics, anxiolytics, gender dysphoria, transgender mental health, mood disorders, anxiety disorders

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Introduction

Gender incongruence (GI) is an umbrella term used to describe people whose gender identity does not align with their physical phenotype.[1] Individuals who experience significant distress and impairment in daily functioning as a result of GI meet the diagnostic criteria for gender dysphoria (GD) as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[2] In 2016, Flores and colleagues estimated that 0.6% (~1.4 million) of adults in the United States self-identified as transgender, which increased 2-fold from a prior 2011 estimate of 0.3%.[3,4] However, these numbers are likely underestimates given that transgender and nonbinary (TGNB) individuals are highly stigmatized and face discrimination in a variety of settings.[5,6] Consequently, this community is highly vulnerable to facing

various health disparities with a recent study showing that transgender individuals are four times more likely to have major depressive disorder (MDD) or generalized anxiety disorder (GAD) than cisgender people (defined as someone whose sex assigned at birth aligns with their gender identity).[7] Additionally, 40% of TGNB individuals reported attempting suicide, which is alarmingly 9 times higher than cisgender people reporting attempting suicide.[8]

Psychotherapy and gender-affirming medical interventions demonstrate significant reductions in symptoms of depression, anxiety, and number of suicide attempts in TGNB individuals experiencing GD.[9,10] Therefore, psychotherapy and gender-affirming interventions are often considered essential treatment modalities when addressing mood and anxiety symptoms in patients experiencing GD.[9,11] However, high out-of-pocket costs as well as variability in length of time (months to years) before noticeable improvement of psychiatric symptoms remain significant challenges to gender-affirming care.[12] In the general population, antidepressants are the treatments of choice for mood and anxiety-related disorders with selective serotonin reuptake inhibitors (SSRIs) being the most commonly prescribed class of antidepressants. SSRIs and serotonin norepinephrine reuptake inhibitors (SNRIs) may also be augmented with additional psychotropic medications, including bupropion, mirtazapine, second generation antipsychotics (SGAs), buspirone, lithium, and thyroid supplementation.[13,14] Despite being first-line pharmacotherapy for treating depression and anxiety-related disorders in the general population, there is little to no antidepressant prescribing data in TGNB individuals with depression and anxiety symptoms, many of whom experience dysphoria secondary to GI.

Given the gap in literature, this exploratory study evaluated gender identity differences in antidepressant prescribing among TGNB individuals with a diagnosis of GD and a concurrent mood or anxiety-related disorder.

Methods

This was a single-center, retrospective cohort study among TGNB adults diagnosed with GD in the inpatient or outpatient setting at a large academic health system between January 1, 2005, and October 31, 2021. Patients were identified via a data abstraction tool that utilized International Classification of Diseases 9th Revision (ICD-9) or ICD 10th Revision (ICD-10) diagnostic codes. Inclusion criteria were any TGNB adults ($\geq$ 18 years old) with an ICD-9 gender identity disorder (GID) or ICD-10 GD diagnostic code. In addition, patients were included if antidepressant prescribing predated or occurred at the time of their GD diagnosis. ICD-9 and ICD-10 codes were used to identify TGNB patients with at least 1 concurrent mood (MDD, premenstrual dysphoric disorder, dysthymic disorder, disruptive mood dysregulation disorder) or anxiety-related disorders (GAD, social anxiety disorder, panic disorder, posttraumatic stress disorder). Patients with a diagnosis for bipolar disorder or cyclothymia were excluded given antidepressants are not indicated for these mood disorders. The study protocol was reviewed and designated exempt by the institutional review board.

All data were retrieved from the institution's electronic health record, EPIC (Epic Systems Corporation, Verona, WI). Demographic characteristics included current age, sex assigned at birth (male, female), gender identity (transgender female, transgender male, nonbinary or genderqueer), and race or ethnicity (white, black, Hispanic, Asian, Native American, and mixed).

The primary outcome was to compare the number of active outpatient antidepressant prescriptions at the time of GD diagnosis between gender identities. The secondary outcomes were to compare antidepressant class use as well as the prevalence of concurrent mood or anxiety disorders between gender identities. For the purposes of this study, antidepressants were defined as SSRI, SNRI, mirtazapine, bupropion, SGAs, and lithium. Additionally, the number of individual gender identity–related diagnoses (GID and/or GD) within a given year were tallied to compare diagnostic trends pre- and post-DSM-5 publication (2005-2013 and 2014-2021, respectively).

All data were collected by a single investigator and stored on an encrypted, password-protected Microsoft Excel spreadsheet. Descriptive statistics were used to describe demographic characteristics. Categorical data for primary and secondary outcomes were summarized as number and percentage and analyzed using chi-square or Fisher exact test as appropriate. IBM SPSS Version 28 (Armonk, NY) was used for all statistical analyses.

Results

Upon completion of the retrospective review of inpatient and outpatient data between January 1, 2005, and October 31, 2021, a total of 131 patients met the inclusion criteria. Baseline demographics consisted of a mean age of 34 years (range: 18 to 75 years) and a relatively even distribution of transgender males ($n = 54$, 41%) and females ($n = 56$, 43%) followed by nonbinary individuals ($n = 21$, 16%) (Table 1). The most common concurrent diagnoses were unipolar depression ($n = 96$, 73%) and GAD ($n = 67$, 51%).

Whereas 40% of patients were prescribed antidepressant monotherapy, 38% of patients were not prescribed any antidepressant therapy at time of GD and concurrent mood or anxiety-related diagnoses (Table 2). Additionally, SSRIs were the most commonly prescribed class of antidepressants across the total study sample ($n = 52$, 40%). For the primary outcome, there was no significant difference in number of antidepressants prescribed

TABLE 1: Baseline characteristics

	Total
Mean age, years (±SD, range)	34 (14.5, 18-75)
Gender Identity, no. (%)	
Male	54 (41.2)
Female	56 (42.7)
Nonbinary	21 (16.0)
Race, no. (%)	
White	77 (58.8)
Mixed race	34 (26.0)
Black/Asian/American Indian	20 (15.3)
Concurrent psychiatric diagnosis, no. (%)	
Unipolar depression	96 (73.3)
GAD	67 (51.1)
PTSD/SAD/panic disorder	26 (19.9)

GAD = generalized anxiety disorder; PTSD = posttraumatic stress disorder; SAD = social anxiety disorder.

between gender identities ($p = .357$). In terms of antidepressant class use, bupropion was prescribed at significantly high rates among transgender females compared with transgender males and nonbinary individuals (16%, 11%, 0%, respectively; $p = .046$). However, no additional gender identity differences were observed between the other antidepressant classes.

Unipolar depression was found to be the most prevalent across all gender identities; however, there were no statistical differences between individual gender identities ($p = .447$) (Figure 1). The second most prevalent diagnosis across all gender identities was GAD with transgender males exhibiting significantly higher rates of concurrent GAD compared with transgender females and nonbinary patients (63%, 39%, 52%, respectively; $p = .044$). Moreover, 86% ($n = 112$) of gender identity-related diagnoses (GID or GD) during the study time frame were in the years following the publication of the DSM-5 (2014-2021), whereas 14% ($n = 19$) of diagnoses were between the years 2005-2013 (Figure 2).

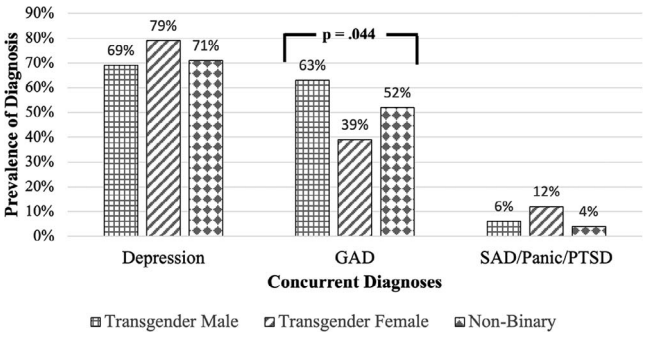

FIGURE 1: Gender identity differences in prevalence of concurrent diagnoses

Discussion

In this retrospective cohort study of TGNB patients with concurrent mood or anxiety-related disorders, there were no observable differences in the number of active antidepressants prescribed between gender identities. This finding may suggest that gender identity differences have minimal influence on a prescriber's decision to initiate antidepressant therapy or add adjunctive antidepressant agents. In terms of antidepressant class utilization, SSRIs were the most commonly prescribed antidepressant class among TGNB patients, which is in line with antidepressant prescribing data for the general population.[13] With the exception of bupropion, there was no significant difference in antidepressant class utilization between gender identities. In the case of bupropion, transgender females were prescribed bupropion at significantly higher rates than that seen among transgender males and nonbinary patients. Although this finding may be coincidental in nature, it should be noted that transgender females (male sex) had the lowest rate of GAD diagnoses among all gender identities. Increased anxiety is a reported side effect of bupropion.[15] Therefore, the lower rates of GAD diagnoses seen in transgender females may possibly explain the higher rate of bupropion prescribing in this patient population. As such, future studies should consider further exploring the

TABLE 2: Active outpatient antidepressant prescription(s) at time of gender dysphoria diagnosis

	Total (n = 131)	Transgender Male	Transgender Female	Nonbinary	p-value
Antidepressants, no. (%)					.357
None	50 (38.1)	24 (44.4)	19 (33.9)	7 (33.3)	
1	53 (40.1)	23 (42.6)	21 (37.5)	9 (42.9)	
2	24 (21.4)	5 (9.3)	15 (26.8)	4 (19.0)	
≥3	4 (3.1)	2 (3.7)	1 (1.8)	1 (4.8)	
Antidepressant class, no. (%)					
SSRI	52 (39.7)	21 (38.9)	23 (41.1)	8 (38.1)	.960
SNRI	16 (12.2)	6 (11.1)	6 (10.7)	4 (19.0)	.611
Bupropion	15 (11.5)	6 (11.1)	9 (16.1)	0 (0)	.046
Mirtazapine or Lithium	7 (5.3)	0 (0)	5 (8.9)	2 (9.5)	.191
SGA	22 (16.8)	6 (13.0)	11 (19.6)	5 (23.8)	.060

SGA = second generation antipsychotic; SNRI = serotonin norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

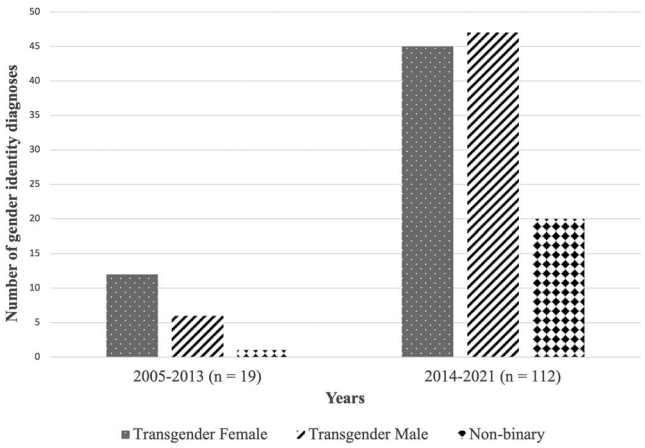

FIGURE 2: Number of gender identity-related diagnoses by year

possible reasons for the higher rates of bupropion prescription in transgender females.

Transgender males (female sex) exhibited significantly higher rates of GAD compared with other gender identities. This finding is in concordance with numerous studies that found cisgender females having significantly higher rates of GAD compared with the male sex.[16–18] This may suggest that a TGNB person's biological sex is an associated risk factor for developing GAD as opposed to gender identity.

Moreover, there was a 6-fold increase in the number of gender identity–related diagnoses (GD or GID) in the years following the publication of the DSM-5 in 2013 with 112 (86%) diagnoses occurring between the years 2014-2021 and 19 (14%) diagnoses between the years 2005-2013 (when DSM-4 was the current publication). This follows a similar trend seen in previous studies, which show an increasing number of patients with GD presenting to specialty clinics with referrals for gender-affirming interventions, which has been increasing by an average of 18% per year.[19–21] This substantial annual increase in individuals who identify as TGNB is likely a result of the increasing societal awareness and acceptance toward TGNB individuals and underscores the urgent and imminent need for clinicians to address health care disparities faced by this community.[10,22]

To our knowledge, this was the first study to investigate antidepressant prescribing characteristics among TGNB individuals experiencing GD and concurrent mood or anxiety-related disorders over a 17-year study time frame. One of the most noteworthy findings was the 38% of patients not having an active antidepressant prescription at time of their GD diagnosis despite having concurrent mood or anxiety-related disorder. This serendipitous finding may elucidate a potential gap in mental health care in TGNB adults. This, coupled with the increasing annual prevalence of patients identifying as TGNB, highlights the essential need for health care professionals to recognize and address the health disparities faced by this highly stigmatized patient population.

This study has several limitations that should be addressed. First, given the novelty and exploratory nature of the study design, there was lack of a comparator group needed to calculate the study's power. Second, the research project was conducted at a single institution, which may make the findings less generalizable. Therefore, more robust, multicenter studies are warranted to further explore the possible role antidepressant prescribing plays in treating mood or anxiety disorders in TGNB individuals with GD. Third, given this was a retrospective study, we were unable to confirm whether or not GD was an underlying etiology for a person's mood and anxiety symptoms, which may have confounded the results. However, it should be noted that regardless of study design, demonstrating causality between GD and psychiatric disorders remains a challenging endeavor given the many confounding biochemical, genetic, epigenetic, and social factors involved with mood and anxiety-related disorders.[22] Last, we were unable to account for the potential confounding variables of patients receiving gender-affirming care (eg, hormonal or surgical interventions), psychotherapy, or somatic treatments (eg, electroconvulsive therapy) in alleviating symptoms of depression and anxiety, which may have contributed to the 38% of study subjects not being on an antidepressant at the time of their GD diagnosis. Therefore, it is essential that future studies aim to compare and further explore the relationship between gender-affirming, psychotherapy, and somatic interventions on antidepressant prescribing and deprescribing in those with GD.

Conclusion

Our findings suggest that an individual's gender identity does not influence antidepressant prescribing in TGNB individuals with mood and anxiety-related disorders. Most notably, this study elucidates the increasing need for psychiatric health care professionals, including psychiatric pharmacists, to be at the forefront of addressing mental health disparities faced by the TGNB community with the ultimate goal of fostering advancements that will positively impact the care of TGNB individuals in the future.

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