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Comparison of inpatient psychiatric medication management in gender diverse youth with cisgender peers

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Abstract

Introduction: The primary objective was to determine if gender diverse (GD) youth receive different psychotropic prescribing compared with cisgender (CG) peers with the same diagnosis. Secondary objectives include evaluation of readmission rates and the effect of gender-affirming hormone therapy (GAHT) on psychiatric outcomes in transgender (TG) patients.

Methods: A total of 255 GD youth patients were retrospectively matched to CG controls based on age, primary discharge diagnosis, and year of admission. Data collection included psychotropic medications at admission and discharge, baseline demographics, time to readmission, and total number of readmissions within 6 months. Use of GAHT was also documented. Wilcoxon signed rank test was used for continuous and χ^2 for nominal data with an a priori α of 0.05.

Results: MDD was the primary discharge diagnosis in 74% of patients. GD youth were more likely to present on antidepressants ($P = .031$) and antipsychotics ($P = .007$), and to be discharged with antipsychotics ($P = .003$). They were additionally more likely to be readmitted within 30 days of discharge ($P = .032$). TG youth on GAHT (13%) had fewer readmissions ($P = .046$) than those not on GAHT, but there were no differences in psychotropic prescribing.

Discussion: Higher antipsychotic and antidepressant prescribing were seen in the GD population despite the same mental health diagnosis. Despite higher prescribing in the GD population, patients presented for readmission within 30 days more frequently, which may represent a need for more rigorous transitions-of-care practices in this population.

Keywords: gender diverse, transgender, adolescence, medications, major depressive disorder, antidepressant, antipsychotic

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Introduction

Gender diverse (GD) youth, defined as transgender (TG) and nonconforming (NC) adolescents, have a 2- to 3-fold increased risk of having a mental health diagnosis, particularly a depressive or anxiety disorder, compared with cisgender (CG) peers.[1,2] Additionally, psychologic distress is commonly reported in GD youths due to harassment, victimization, and bullying by peers.[3,4] Approximately 30% to 50% of GD patients report serious psychologic distress leading to attempted suicide, with the

highest risk in transmasculine patients.[5-7] Mental health evaluations should be routine care for all adolescents.[8] However, GD individuals often report stigma and discrimination in health care services secondary to lack of insurance coverage for gender-affirming care, and negative experiences with health care providers.[3,9-11]

Studies evaluating the treatment of psychiatric disorders in GD youth are limited. Hisle-Gorman et al[12] conducted a large retrospective study assessing psychotropic prescribing in GD youth. Researchers identified 3754 military-dependent GD youth (ages <18 years) and matched them to CG siblings (N = 6603) to assess differences in mental health diagnoses, mental health visits, and outpatient psychotropic prescriptions. They found GD youth were approximately 5 times more likely to have a mental health diagnosis and at least 2 times more likely to use mental health services and be prescribed psychotropics.

Literature suggests that gender-affirming care, addressing psychologic, surgical, and hormonal therapies, is medically necessary to alleviate gender dysphoria and reduce psychiatric comorbidities.[13-16] In the study by Hisle-Gorman et al,[12] researchers additionally assessed the effects of gender-affirming hormone therapy (GAHT) on mental health outcomes in the TG subgroup.[12] Among the 963 TG youth receiving GAHT, mental health care use did not significantly change after initiation of GAHT; however, psychotropic medication use increased in all categories except stimulants, migraine agents, and lithium.[12]

Psychotropic medications are not benign agents and can have short- and long-term effects in children and adolescents. Antidepressants have been associated with reduced growth velocity, reduced bone mineral density, and a potential risk for diabetes mellitus secondary to weight gain in pediatric patients.[17] All antidepressants carry a black box warning for increased suicidality in adolescent patients.[18] Additionally, antipsychotics have increased risks for metabolic syndromes, specifically hyperlipidemia, diabetes mellitus, and cardiovascular disease.[19-22] Our study aims to compare psychotropic prescribing in GD youth to their CG peers with the same primary psychiatric diagnosis during an inpatient psychiatric hospitalization.

Methods

Study Design

This case-control study was a retrospective chart review evaluating psychotropic medication use in hospitalized GD youth (ages <18 years) compared with matched controls admitted to a Midwest, academic, child and adolescent psychiatric hospital from January 1, 2017, to August 1, 2021. Readmission data within 6 months of discharge from index admission were also evaluated to assess mental health outcomes. Patients were identified through the Healthcare Enterprise Repository for Ontological Narration (HERON) data set (CTSA award UL1TR002366), an internal research database.[23,24] This research was approved by the Institutional Review Board.

Study Participants

Patients with a diagnosis of gender dysphoria identified through HERON with admission to our child and adolescent psychiatric hospital were assessed for study inclusion in the GD group (cases). Cases were further reviewed for self-reported and provider-documented gender diversity. GD cases were matched to CG controls based on (1) sex assigned at birth, (2) age at index admission, (3) primary discharge diagnosis of index admission, and (4) year of index admission. The index admission was defined as the first admission to this institution with documented gender diversity. Cases were excluded if (1) admission prior to study period with documented GD or a diagnosis of gender dysphoria, (2) insufficient documentation of GD, (3) inability to match to control based on criteria, (4) not yet 6 months out from index admission at time of data collection.

Study Procedures

Demographic, ICD-10 diagnostic codes at index discharge date, admission and discharge prescriptions, and readmission data were pulled from HERON and the electronic health record. Demographic data collected included age, assigned sex at birth, race, foster status, individualized education program (IEP), and insurance. The primary discharge diagnoses were categorized and based on the following ICD-10 codes: MDD without psychotic features (F32, F33), MDD with psychotic features (F32.3, F33.3), posttraumatic stress disorders (F43), anxiety spectrum (F40, F41, F42), disruptive mood spectrum (F34.81, F43.9), adjustment disorders (F43.21, F43.23, F43.25), attention deficit hyperactivity disorder (ADHD) spectrum (F90), and bipolar disorders (F31). For purposes of matching, individuals were paired, to the best ability, to specific ICD-10 coding; however, if not available, they were paired with a similar ICD-10 code within the same spectrum. For example, F32.1 and F33.1 were paired for MDD without psychotic features. Readmission data were evaluated for total number of readmissions and days to first readmission within 6 months of index discharge date.

Medications were classified into the following groups: antidepressants, antipsychotics, mood stabilizer, stimulants, anxiolytics, and other. Agents categorized as other included nonstimulant ADHD medications, benztropine, cyproheptadine, and prazosin. Agents with other therapeutic indications, such as antiepileptics, were evaluated and included if prescribed by a psychiatrist.

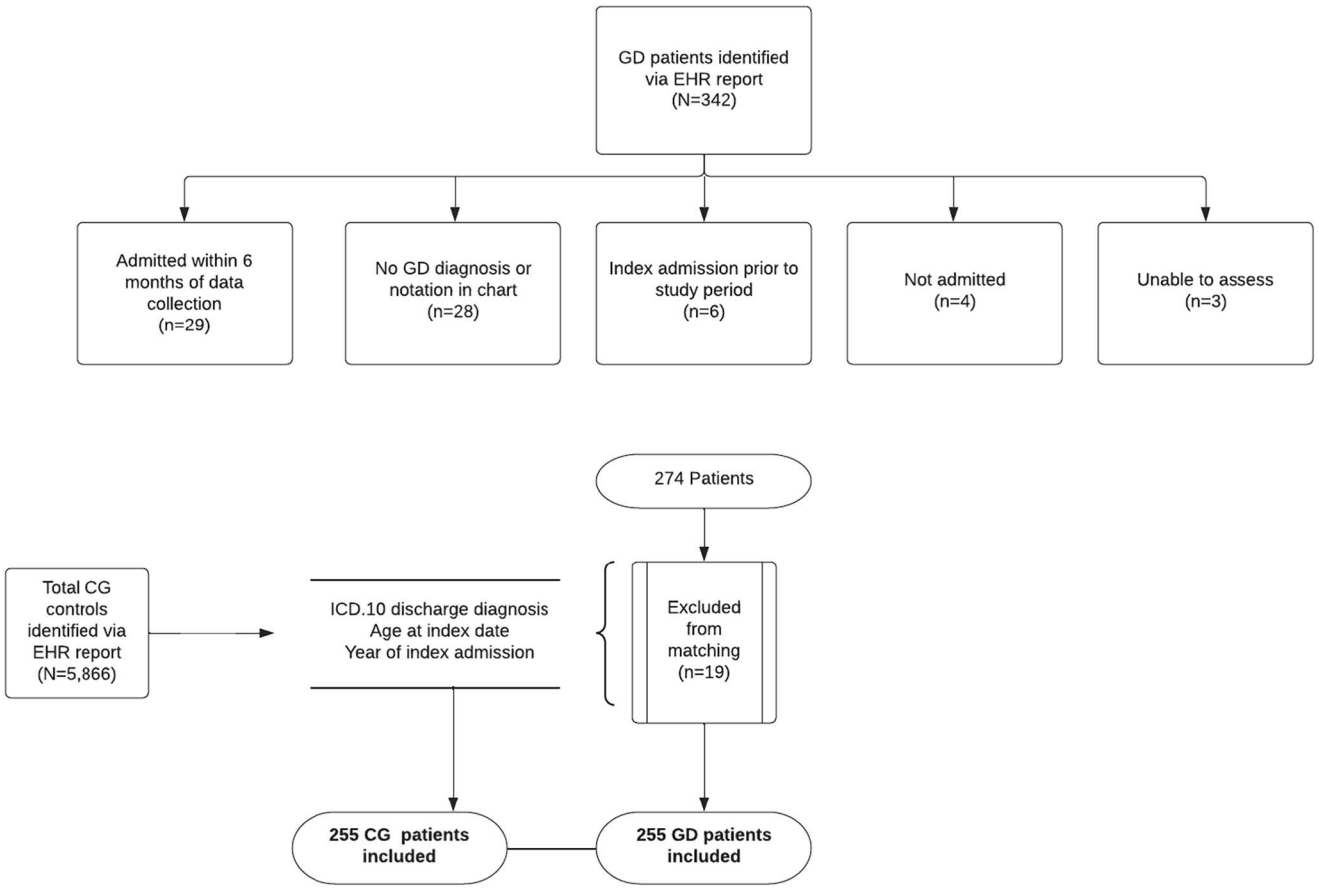

FIGURE: Exclusion criteria. CG = cisgender; EHR = electronic health record; GD = gender diverse.

A subgroup analysis was performed in TG patients (nonbinary patients not included in this group) for the use of GAHT. Patients were identified to be on GAHT if they were reported to be on pubertal blockers, antiandrogens, or hormone analogs at time of admission. All psychotropic and readmission outcomes were similarly compared between TG patients on GAHT to TG patients not on GAHT.

Statistical Analysis

IBM SPSS (version 27, Armonk, New York) was used for analyses. Descriptive statistics were used for demographics and to assess classes of psychotropic medications, duplicate and combinations of these classes, and total number of psychotropics at both admission and discharge. Comparisons were run using Wilcoxon signed rank test and Mann-Whitney *U* test for continuous variables, and χ^2 for nominal data. Percent changes were calculated by comparing the total number of patients on a specific medication at discharge to the number at admission. Statistical significance was defined a priori as a *P* value of $<.05$.

Results

A total of 255 GD patients were included in this study and matched to 255 CG patients (Figure). The demographics of our population is included in Table 1. Most were transmasculine (89.8%) and had a primary diagnosis of MDD without psychotic features (74.5%).

Psychotropic medication patterns are highlighted in Table 2. A significantly higher number of psychotropics were prescribed per patient in the GD group compared with the CG group at both admission (1.31 versus 1.01; $P = .008$) and discharge (1.86 versus 1.58; $P = .002$). At admission, the percentage of antidepressants (54.9% versus 44.3%; $P = .031$), antipsychotics (24.7% versus 15.3%; $P = .007$), and combination of antidepressants and antipsychotics (17.6% versus 10.9%; $P = .011$) were significantly higher in the GD group compared with their peers. At discharge, the percentage of antipsychotics prescribed remained significantly higher in the GD group compared with their peers and increased in percentage from admission (31.4% versus 20.4%; $P = .003$). Similarly, GD patients discharged on both an antidepressant and antipsychotic were higher than CG peers (24.3% versus 15.2%; $P = .002$).

When looking at percent changes in medication classes from admission to discharge, CG patients had higher percentage increases in all medication classes. The highest percent increase occurred with antidepressants (58.6% versus 91.2%)

TABLE 1: Demographic data

	All Patients, n (%)	GD Group (Case), n (%)	CG Group (Control), n (%)
N	510	255	255
Age, median (IQR), y	14 (13–16)	14 (13–16)	14 (13–16)
Sex at birth, female	458 (89.8)	229 (89.8)	229 (89.8)
Race			
White	402 (78.8)	218 (85.5)	184 (72.2)
Black	43 (8.4)	11 (4.3)	32 (12.5)
Other/unknown	65 (12.7)	26 (10.2)	39 (15.3)
Foster status	20 (3.9)	11 (4.3)	9 (3.5)
IEP	110 (21.6)	60 (23.5)	50 (19.6)
Insurance			
Commercial	223 (43.7)	121 (47.5)	102 (40)
Public	239 (46.8)	110 (43.1)	129 (50.6)
Self-pay	33 (6.5)	16 (6.3)	17 (6.7)
Other	15 (2.9)	8 (3.1)	7 (2.7)
Primary diagnosis			
MDD without psychotic features	380 (74.5)	190 (74.5)	190 (74.5)
MDD with psychotic features	34 (6.7)	17 (6.7)	17 (6.7)
Posttraumatic stress disorders	26 (5.1)	13 (5.1)	13 (5.1)
Other	70 (13.7)	35 (13.7)	35 (13.7)
Adjustment disorders	24 (4.7)	12 (4.7)	12 (4.7)
Anxiety spectrum	20 (3.9)	10 (3.9)	10 (3.9)
Disruptive mood spectrum	16 (3.1)	8 (3.1)	8 (3.1)
ADHD spectrum	8 (1.6)	4 (1.6)	4 (1.6)
Bipolar disorders	2 (0.4)	1 (0.4)	1 (0.4)

ADHD = attention deficit hyperactive disorders; CG = cisgender; GD = gender diverse; IEP = individualized education program; IQR = interquartile range.

and anxiolytics (63.6% versus 81.8%) in the GD and CG groups, respectively. Only 1 class of medication, mood stabilizers, had a decrease in prescribing that occurred in the GD group.

Table 3 highlights secondary readmission outcomes for the study. Patients in the GD group had an increased number of readmissions within 30 days of discharge (54.4% versus 28.3%; $P = .003$), and shorter median time to readmission compared with CG peers.

Subgroup Analysis

Twenty-one TG patients were receiving GAHT at time of admission. No significant differences were found in total number of medications prescribed within medication classes at admission and discharge between patients on GAHT and those not on GAHT. However, fewer total readmissions occurred in the GAHT group compared with those not on GAHT ($P = .046$).

Discussion

To our knowledge, this is the first study to match subjects based on primary diagnosis, and it assesses medication outcomes after initial psychiatric admission. Although several studies have evaluated mental health diagnoses, minimal studies have assessed psychotropic medication use in GD patients. Our study found that more GD patients were prescribed psychotropics, particularly antidepressants and antipsychotics, when matched to CG peers with the same primary mental health diagnosis. In this study, despite the higher use of psychotropics, GD patients returned for readmission in less time than their peers.

Our study population's increased use of psychotropic medication and high prevalence of MDD aligns with previously reported literature.[1,2,12,25,26] Becerra-Culqui et al[1] found that GD youth had longer courses of psychiatric symptoms, particularly depression and anxiety, before first presentation identifying as gender diverse to a health care provider, which may be an explanation for the higher amount of antidepressant prescribing on admission in our study population. Similarly to our study, Hisle-Gorman et al[12] assessed psychotropic prescribing and found higher rates of antidepressant and antipsychotic medications in GD patients. However, patients were matched to sibling controls regardless of mental health diagnoses, with only 50% of CG siblings receiving any diagnosis

TABLE 2: Psychotropic prescribing at admission and discharge in gender diverse (GD) youth compared with cisgender (CG) controls

	Admission Medications			Discharge Medications		
	GD (n = 255)	CG (n = 255)	*P* Value[a]	GD (n = 255)	CG (n = 255)	*P* Value[a]
Total No. of medications	333	257	—	475	403	—
No. of medications per patient, mean (SD)	1.31 (1.36)	1.01 (1.25)	.008	1.86 (1.05)	1.58 (1.04)	.002
Medication classes: patients prescribed, n (%)						
Antidepressants	140 (54.9)	113 (44.3)	.031	222 (87.1)	216 (84.7)	.405
Antipsychotics	63 (24.7)	39 (15.3)	.007	80 (31.4)	52 (20.4)	.003
Mood stabilizers	20 (7.8)	11 (4.3)	.117	15 (5.9)	12 (4.7)	.549
Stimulants	26 (10.2)	26 (10.2)	1.000	33 (12.9)	29 (11.4)	.579
Anxiolytics	33 (12.9)	22 (8.6)	.123	54 (21.2)	40 (15.7)	.090
Other	26 (10.2)	25 (9.8)	.876	42 (16.5)	33 (12.9)	.233
Duplicate medication classes: patients prescribed, n (%)						
>1 antidepressant	21 (8.2)	14 (5.5)	.303	23 (9.0)	13 (5.1)	.077
>1 antipsychotic	1 (0.4)	1 (0.4)	1.000	0 (0.0)	1 (0.4)	.317
>1 mood stabilizer	3 (1.2)	2 (0.8)	.655	3 (1.2)	2 (0.8)	.157
AD + AP	45 (17.6)	28 (10.9)	.011	62 (24.3)	39 (15.2)	.002
AD + MS	8 (3.1)	2 (0.8)	.159	3 (1.2)	4 (1.6)	.086

AD = antidepressant; AP = antipsychotic; MS = mood stabilizer.

[a]Statistical significance $P < .05$.

during the 8.5-year study. Despite the higher psychotropic prescribing, their research showed that GD youth had more than twice as many mental health visits and were more than 7 times as likely to have suicidal ideation or self-harm.

The high prevalence of antipsychotic prescribing in the GD group at admission and discharge is concerning, mainly because the GD group was matched with CG patients with the same primary diagnosis. The adverse effects associated with long-term use of antipsychotics are well documented, particularly movement disorders and metabolic syndromes.[19-22] Although antipsychotics can be prescribed for depression augmentation, it is important to note this is an off-label indication in pediatric and adolescent patients and literature to support this use is scarce.[17,27-30] Careful consideration of the adverse risk of antipsychotic prescribing should be considered before prescribing antipsychotics in pediatric patients.

Despite the higher total number of psychotropics prescribed, we found that GD patients were readmitted more rapidly than CG peers. The shorter time to readmission seen in the GD group has associated socioeconomic risks, such as disruption to social support, decreased school performance, and increased stigmatization.[31-33] Causes for quicker time to readmission may be reflective of the complexity of treatment for GD patients, limited community resources, and the need for improved discharge processes in this population. Inpatient case management and detailed discharge planning (eg, follow-up care, partial hospitalization, residential care) have decreased psychiatric readmission rates in children and adolescents.[31] Given the risks for poor social outcomes and financial burden to the

TABLE 3: Readmission outcomes for primary and subgroup populations

	Primary Population			TG Subgroup		
	GD Group (n = 255)	CG Group (n = 255)	*P* Value	GAHT (n = 21)	No GAHT (n = 151)	*P* Value
No. of patients readmitted, n (%)	68 (26.7)	60 (23.5)	.414	2 (9.5)	45 (29.8)	.051
No. of patients readmitted within 30 days, n (%)	37 (54.4)	17 (28.3)	.003	1 (50.0)	25 (55.6)	.127
Total No. of readmissions, mean (SD)	1.4 (0.8)	1.5 (0.9)	.993	1.0 (0.6)	1.5 (0.9)	.046
Days to first readmission, median (IQR)	26.5 (8.8–76.0)	48.5 (23.3–106.3)	.037	31.0 (18.0–44.0)	26.0 (7.5–71.5)	.958

CG = cisgender; GAHT = gender-affirming hormone therapy; GD = gender diverse; IQR = interquartile range; TG = transgender.

health system and patients, it is prudent to assess for ways to reduce readmissions.[31-33]

In the TG subgroup, GAHT did not impact psychotropic prescribing; however, those on GAHT had fewer readmissions. One study found an increase in psychotropic prescribing after initiating GAHT.[12] Although the use of GAHT has been associated with improved mental health outcomes and decreased distress, the impact on psychotropic use has not been well defined and should be a focus of further research.[13-16]

Our study is not without limitations. The retrospective design caused several limitations. First, we did not assess the impact of secondary diagnoses on psychotropic prescribing. Studies have consistently shown that TG patients have higher rates of mental health disorders.[1,2,34] One study of TG patients found significantly higher rates of all psychiatric diagnoses evaluated compared with CG controls.[34] In addition to the high prevalence of depression and anxiety, this study found 10% to 11% of TG patients had diagnoses of bipolar, substance use disorder, and attention deficit hyperactivity disorder compared with less than 2% in CG controls. Thus, some of our GD patients may have increased medication use due to additional psychiatric disorders that were not present in the CG group. Another limitation due to the retrospective nature of the study was that we did not collect information on indication for use of medications, and off-label, or nonpsychiatric, uses could not be ruled out. Furthermore, we could not evaluate the impact of guardian consent for medication treatment.

Although our behavioral health facility is one of the largest inpatient centers in the region, it is difficult to account for external psychiatric admissions with the single-center design and may influence readmission outcomes. This study's length of stay was not evaluated because of a specialized, therapy-focused unit within our institution, which may have skewed duration of stay. Moreover, our single-center design yielded low minority race and transfeminine patients, likely reflective of our region of practice and less generalizable. Our small sample of TG patients on GAHT may highlight that access to specialty services in our region is low, and findings may not correlate with larger sample sizes. Lastly, it is important to note statewide differences in GD care and parental consent laws, which we cannot account for in this study, limiting results to areas with differing practices.

Conclusion

GD youth had a higher number of antidepressants and antipsychotics prescribed compared with CG peers with the same primary mental health diagnosis. Because of the overall complexity of mental illness in GD patients, careful and judicious prescribing needs to occur in this vulnerable population. The risks and benefits of adding additional medications must be assessed, especially antipsychotics, for GD patients and further studies are needed to evaluate the proper prescribing of psychotropic medications in GD youth. Furthermore, future studies should investigate underlying causes for shorter times for readmission, and explore ways to reduce readmission rates in this valuable population.

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