Mental Health and Timing of Gender-Affirming Care

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abstract

BACKGROUND: Gender-incongruent (GI) youth have high rates of mental health problems. Although gender-affirming medical care (GAMC) provides psychological benefit, some GI youth present to care at older ages. Whether a relationship exists between age of presentation to GAMC and mental health difficulties warrants study.

METHODS: A cross-sectional chart review of patients presenting to GAMC. Subjects were classified a priori as younger presenting youth (YPY) (<15 years of age at presentation) or older presenting youth (OPY) (≥15 years of age). Self-reported rates of mental health problems and medication use were compared between groups. Binary logistic regression analysis was used to identify determinants of mental health problems. Covariates included pubertal stage at presentation, social transition status, and assigned sex.

RESULTS: Of 300 youth, there were 116 YPY and 184 OPY. After presentation, more OPY than YPY reported a diagnosis of depression (46% vs 30%), had self-harmed (40% vs 28%), had considered suicide (52% vs 40%), had attempted suicide (17% vs 9%), and required psychoactive medications (36% vs 23%), with all $P < .05$. After controlling for covariates, late puberty (Tanner stage 4 or 5) was associated with depressive disorders (odds ratio 5.49; 95% confidence interval [CI]: 1.14–26.32) and anxiety disorders (odds ratio 4.18 [95% CI: 1.22–14.49]), whereas older age remained associated only with psychoactive medication use (odd ratio 1.31 [95% CI: 1.05–1.63]).

CONCLUSIONS: Late pubertal stage and older age are associated with worse mental health among GI youth presenting to GAMC, suggesting that this group may be particularly vulnerable and in need of appropriate care.

WHAT'S KNOWN ON THIS SUBJECT: Mental health problems are prevalent among gender-incongruent youth. Although gender-affirmative treatment provides psychological benefit, some youth present to care later in age and puberty. It is not known if older age at presentation is associated with worse mental health.

WHAT THIS STUDY ADDS: Gender-incongruent youth who present to gender-affirming care later in life have higher rates of psychoactive medication use and mental health problems. We use our findings to suggest that this group is particularly vulnerable and highlight the need for appropriate care.

Gender-incongruent (GI) youth often experience gender dysphoria, the distress resulting from the discordance between birth-assigned and experienced gender.[1] These youth face higher rates of mental health problems (including mood and anxiety disorders, self-harm, suicidal ideation, and suicide attempts)[2–8] than gender-congruent youth.[9,10] GI youth are also more likely to be hospitalized[9] for mental health concerns compared with their gender-congruent peers. Puberty is a vulnerable time for youth with gender dysphoria because distress may intensify with the development of secondary sex characteristics corresponding to the assigned rather than the experienced gender.[11]

Youth with gender dysphoria who receive gender-affirming medical care (GAMC), namely, hormone blockers and/or gender-affirming hormones, experience a decrease in emotional and behavioral problems and an improvement in overall psychological functioning.[12,13] Despite these benefits, reports of GI youth seeking GAMC demonstrate that some youth present to care later in adolescence with more pubertal development.[2–5,14]

It is possible that presentation at earlier ages may be associated with fewer mental health concerns. We are aware of one study in which researchers address this question directly: Holt et al[7] reported that youth referred to a gender clinic at age ≥12 were more likely to have suicidal ideation and attempts, self-harm, and low mood and/or depression than those referred at younger ages. Pubertal stage may be more important than age, but we know of no researchers who have investigated the relationship between pubertal stage at presentation to GAMC and mental health. Because better understanding of the factors associated with poor mental health among GI youth could lead to mitigation strategies, we examined the relationship between timing of presentation to GAMC and rates of mental health problems among 300 GI youth.

METHODS

This study was conducted at the Transgender Youth Clinic (TYC) at The Hospital for Sick Children in Toronto, Canada, an interdisciplinary clinic that provides GAMC to youth with gender dysphoria who are in puberty but <18 years of age. Although psychiatric evaluation is not a prerequisite for assessment or treatment, mental health screening is routine, with involvement of mental health professionals when warranted. As part of a universal health care system, payment is not required to access the TYC; referrals from health care providers are required.

Study Design

Collection and analyses of data were approved by Quality and Risk Management at The Hospital for Sick Children as part of a quality improvement project within our clinic. Data were extracted from hospital records by chart review. Patients with initial TYC visits between October 2013 and June 2016 (cohort 1) or August 2017 and June 2018 (cohort 2) were included. Cohort 1 comprised patients seen in the first 2.5 years after the TYC was established. Some features of this cohort have been described previously.[4] Cohort 2 comprised patients seen after the expansion of clinical service to accommodate increasing referrals. We used two distinct cohorts to account for changes within our clinic as well as changes in characteristics of youth seeking care that may have occurred since the creation of the TYC. Diagnoses of gender dysphoria were made by trained health care providers using *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*, criteria. Youth were excluded if they were not seeking GAMC or if they had previously been started on hormone blockers or gender-affirming hormones.

Data Collection

Unless specified, data were obtained from initial TYC visit documentation. The in-person initial assessment was performed by the member(s) of the interdisciplinary team (including adolescent medicine practitioners, pediatric endocrinologists, and/or allied health providers with expertise in the care of transgender youth) using a standardized template, which prompted questions around gender history and treatment goals, medical history, and past and present mental health status. Youth were first assessed together with their caregiver(s). Subsequently, a confidential HEEADSSS (home environment, education and employment, eating, activities, drugs, sexuality, suicide and depression, and
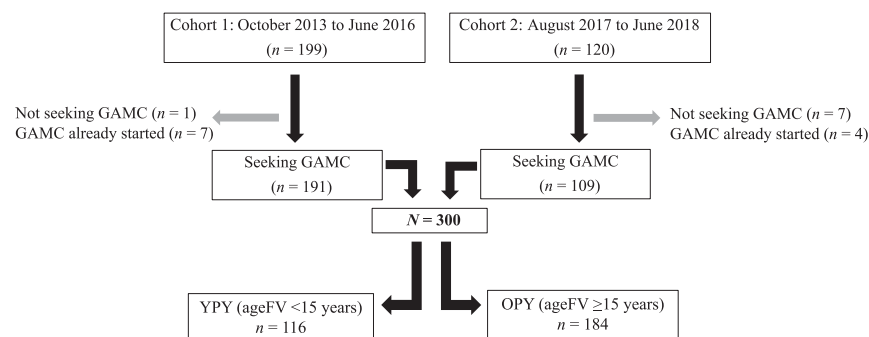

FIGURE 1
Flowchart of subjects included in chart review. In the 2 time periods, 319 youth presented to the TYC, and 300 met inclusion criteria. Youth were clustered on the basis of age at first visit (ageFV).

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safety)[15,16] history was performed with the youth alone, including a mental health screen. Data were collected and managed by using Research Electronic Data Capture tools.[17]

Demographic data including dates of referral and initial visit, age at initial visit, sex assigned at birth, and ethnicity were abstracted.

The following gender history events were recorded from youth and their caregiver(s): (1) age of recognition of gender incongruence, (2) age of coming out, (3) social transition, and (4) age of social transition (the age at which the youth first socially transitioned in at least one real-life environment). If ages were not recorded, birth date was used to estimate ages of gender history events that were described relative to the time of year or school grade. For example, if a youth born in December 2002 reported that an event occurred in the summer of 2013, the age for this event would be estimated at 10 years and 7 months. The age of recognition of gender incongruence was set to 2.5 years when the youth or caregiver(s) reported "always" knowing that the youth's gender identity differed from the assigned gender because children can recognize gender identity by 2 to 3 years of age.[18,19] If data were missing from the initial clinic note, referral documentation was used as a secondary source.

Pubertal Stage

We now only perform pubertal examinations when needed for clinical decision making. However, at the time of visits reviewed here, examinations routinely occurred at the first or, more often, second clinic visit, a few weeks to several months later. For puberty data, initial or second clinic visit notes were the primary source, with referral notes used if necessary. Because menarche typically occurs at Tanner stage 4, this pubertal stage was assigned to postmenarchal youth assigned female at birth (AFAB) without a documented physical examination.[20] For youth assigned male at birth (AMAB), recorded testicular volume was used to determine pubertal stage[21]; if unavailable, pubic hair Tanner stage was used.

Mental Health Problems

Youth or caregiver reports of formal diagnoses of depressive, anxiety, and autism spectrum disorders were extracted from initial visit documentation. Reported active use of psychoactive medication, suicidal ideation at the time of or preceding the TYC visit, and history of self-harm or suicide attempt were also recorded.

Statistical Analyses

Subjects were classified on the basis of age at first TYC visit. Before data analysis, those <15 years of age were classified as younger presenting youth (YPY), whereas those ≥15 years were classified as older presenting youth (OPY). Given the normal ages of pubertal initiation for females (8–13 years) and males (9–14 years), a cutoff age of 15 assures that the majority of OPY have experienced significant pubertal development. Menarche and spermarche often occur at Tanner stage 4. Therefore, youth presenting to the TYC at Tanner stages 1 to 3 were considered pre- or early pubertal, whereas Tanner stages 4 and 5 were used to represent late puberty.

Descriptive statistics were used to analyze data on the basis of age group. Continuous variables were not normally distributed and are reported as medians and interquartile range (IQR), whereas categorical variables are reported as percentages. Demographic characteristics, age of gender history events, and time intervals between events were compared between YPY and OPY by using the Mann–Whitney U test for continuous variables and either Pearson's χ^2 test or Fisher's exact test for categorical variables. Pearson's χ^2 test or Fisher's exact test was used to compare rates of mental health diagnoses between YPY and OPY.

Logistic regression was performed to assess whether age at first visit (as a continuous variable), pubertal stage (pre- or early vs late), date cohort (1

TABLE 1 Demographic Characteristics of All Youth by Age at First Visit

	YPY (n = 116)	OPY (n = 184)	P
Age at first visit, y, median (IQR)	13.9 (12.9–14.5)	16.3 (15.6–16.8)	<.001
Range	10.5–14.9	15.0–17.9	
AFAB, n (%)	87 (75.0)	142 (77.2)	.67
Cohort, n (%)			.03
1	65 (56.0)	126 (68.5)	
2	51 (44.0)	58 (31.5)	
Time from referral to first visit, mo, median (IQR)[a]	3.6 (2.1–5.5)	3.3 (2.3–5.6)	.73
Tanner stage category, n (%)			<.001
Pre or early: 1, 2, or 3[b]	24 (20.7)	2 (1.1)	
Late: 4 or 5	82 (70.7)	166 (90.2)	
Not reported	10 (8.6)	16 (8.7)	
Socially transitioned, n (%)	76 (65.5)	149 (81.0)	.002
Autism spectrum disorder, n (%)	7 (6.0)	11 (6.0)	.98
Ethnicity, n (%)			.91
White	53 (45.7)	94 (51.1)	
Indigenous (First Nations, Inuit, Métis)	4 (3.4)	5 (2.7)	
Other nonwhite	8 (6.9)	17 (9.2)	
>1 ethnicity	9 (7.8)	13 (7.1)	
Unknown and/or not reported	42 (36.2)	55 (29.9)	

Continuous variables were not normally distributed and are presented as median and IQR.
[a] Not recorded for 20 subjects (11 OPY and 9 YPY).
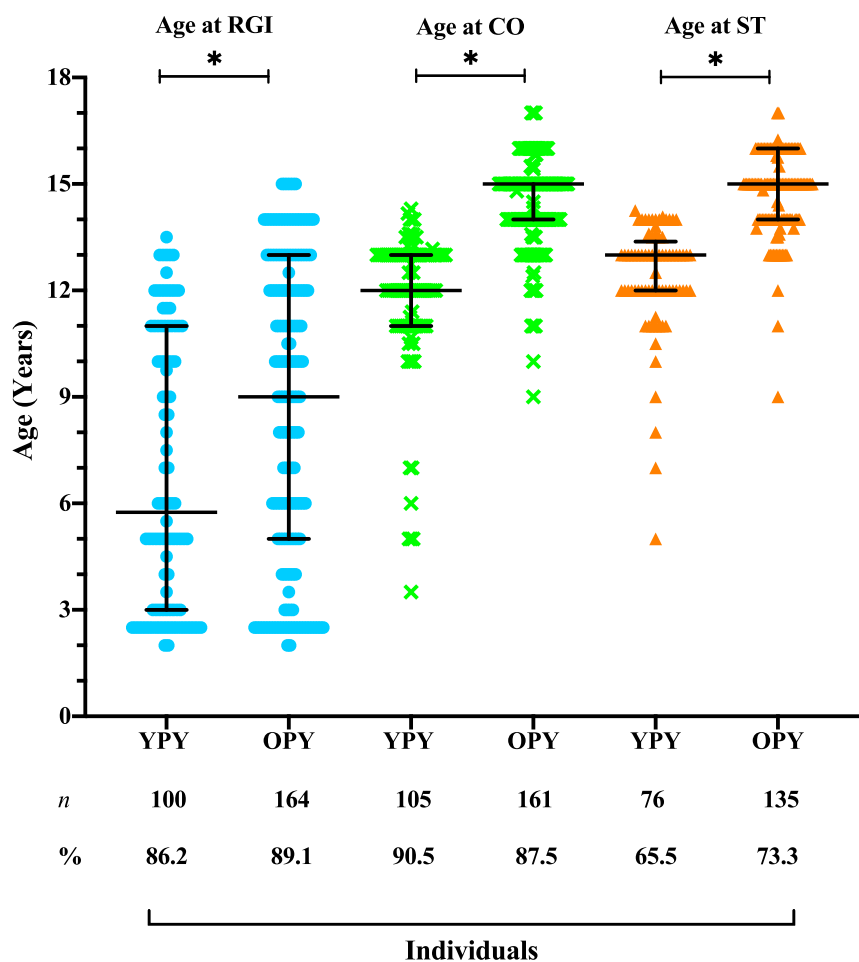[b] Three youth were prepubertal at the time of the first clinic visit.

FIGURE 2
Age at gender history events. Individual data points are presented with the median and IQR, along with the number (*n*) and proportion (%) of youth with available data. * *P* < .001. CO, coming out; RGI, recognition of gender incongruence; ST, social transition.

at a median age of 13.9 years (IQR 12.9–14.5), whereas OPY presented at a median age of 16.3 years (IQR 15.6–16.8). Most patients (274 of 300; 91.3%) had a documented pubertal examination at the first or second clinic visit. More YPY than OPY were in pre- or early puberty, and more OPY than YPY had socially transitioned before the first visit (Table 1). YPY were more likely to be from cohort 2, consistent with a shift over time toward slightly younger ages at presentation to our clinic.[4]

The median age of recognition of gender incongruence was significantly younger among YPY than OPY (5.8 years [IQR 3.0–11.0] vs 9.0 years [IQR 5.0–13.0]; *P* < .001). YPY reported coming out about their gender identity at younger ages (12.0 years [IQR 11.0–13.0] vs 15.0 years [IQR 13.0–15.0]; *P* < .001). Social transition occurred earlier for YPY than for OPY (13.0 years [IQR 12.0–13.4] vs 15.0 years [IQR 14.0–16.0]; *P* < .001; Fig 2).

To investigate whether differences were related to age of recognition of gender incongruence, we assessed the time between this and other variables. YPY and OPY waited a similar amount of time to come out after they recognized their gender incongruence (4.5 years [IQR 1.0–8.0] vs 4.3 years [IQR 1.0–9.0]; *P* = .42). The time from recognition of gender incongruence to first TYC visit was also similar between YPY and OPY (7.4 years [IQR 3.1–10.4] vs 6.8 years [IQR 3.5–11.9]; *P* = .11), as was the time between coming out and the first TYC visit (1.3 years [IQR 0.9–2.0] vs 1.7 years [IQR 1.1–2.3]; *P* = .06; Fig 3).

Mental Health Problems

At the first TYC visit, 78% of youth reported ≥1 mental health problem. Depressive and anxiety disorders were reported by 40.0% and 44.3% of youth, respectively. Approximately one-third (34.7%) of youth had engaged in self-harm, 12.3%

vs 2), and social transition were associated with rates of self-reported mental health problems. These variables were identified a priori. The likelihood ratio test was used to determine if the resulting model was more effective than the null model, with *P* < .05 indicating this was true. The Hosmer-Lemeshow goodness-of-fit test was used to assess how well the model fit the data, with *P* > .05 indicating that the model did not have evidence of poor fit.[22] Spearman correlation was used to determine the relationship between age at first visit and Tanner stage. A variance inflation factor of 5 was used to indicate collinearity between these 2 variables.[23]

Statistical analyses were conducted by using SPSS 25.0 (IBM SPSS Statistics, IBM Corporation).[24] Entries with missing data were excluded from the analyses involving that particular variable.

RESULTS

Patient Population and Timing of Events

There were 319 new patient visits to the TYC over the study time periods (Fig 1). A total of 300 subjects met inclusion criteria, with 116 YPY and 184 OPY. Overall, the median age of presentation was 15.4 years (IQR 14.2–16.4). YPY presented to GAMC
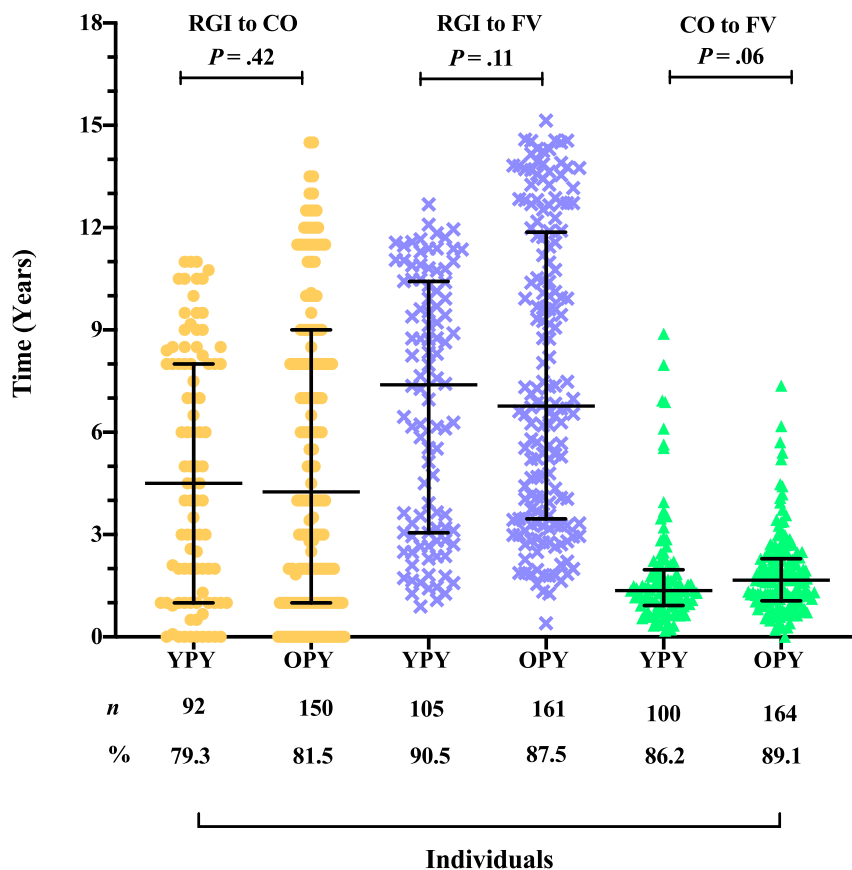
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FIGURE 3
Time intervals between gender history events. Individual data points are presented with median and IQR, along with the number (*n*) and proportion (%) of youth with available data. CO, coming out; FV, first visit; RGI, recognition of gender incongruence.

endorsed current suicidal ideation, 47.3% had considered suicide, and 14.0% had attempted suicide. A total of 31.3% of youth were taking psychoactive medications. To assess the relationship between age of presentation to GAMC and mental health problems, rates were compared between YPY and OPY. OPY reported significantly higher rates of depressive disorders, self-harm, previous suicidal ideation, suicide attempts, and psychoactive medication use (Fig 4).

Factors Associated With Mental Health Problems

For each mental health problem, logistic regression modeling was performed with age at first visit, date cohort, pubertal stage, social transition status, and assigned sex as covariates (Supplemental Table 3). Although Spearman correlation coefficient indicated an association between age at first visit and Tanner stage (r_s = 0.39; $P < .001$), there was no significant multicollinearity (variance inflation factor = 1.0). Conditions for goodness-of-fit testing were not met for the previous suicide attempt and current suicidal ideation models in which the frequencies of these events among early pubertal youth were low. The results of the remaining models are displayed in Supplemental Table 3. With the exception of history of suicidal ideation, the proposed model was more effective at predicting mental health outcomes compared to the null model. Late pubertal youth were 5.49 (95% confidence interval [CI]: 1.14–26.32) times and 4.18 (95% CI:

1.22–14.49) times more likely to report depressive and anxiety disorders, respectively, compared with early pubertal youth. AFAB youth had 3.41 (95% CI: 1.42–8.19) times the odds of reporting self-harm compared with AMAB youth. With every 1-year increase of age at presentation, the odds of psychoactive medication use increased by 1.31 (95% CI: 1.05–1.63; Table 2).

DISCUSSION

As reported by ourselves[4] and others,[2,3,5–8] we found high rates of mental health problems among the transgender youth in our clinic, with 78% reporting at least one mental health issue. To expand on that past literature, we examined the relationship between age at presentation and rates of mental health problems among GI youth presenting for GAMC. We identified several differences between YPY and OPY (Fig 4) and found that the age-based differences in rates of depression and anxiety appear to be accounted for by late pubertal stage, whereas older age at presentation was independently associated with higher rates of psychoactive medication use (Table 2). Our data add to the existing literature, suggesting that distress may be particularly profound among GI youth who present for care at older ages and with more advanced puberty. Moreover, these data point to a complex relationship among mental health, age, and pubertal development because many of the differences between YPY and OPY were no longer significant after controlling for pubertal stage (Supplemental Table 3).

When controlled for pubertal development, we did not identify an association between age at presentation and depressive or anxiety disorders that might explain the higher rate of psychoactive
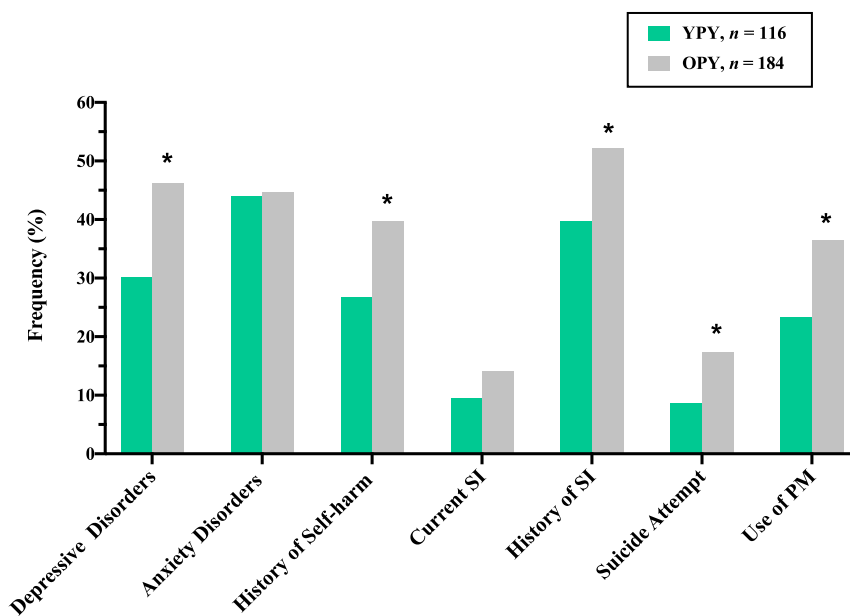
FIGURE 4
Rates of self-reported mental health problems. More OPY than YPY reported a diagnosis of depression (46% vs 30%), had self-harmed (40% vs 28%), had considered suicide (52% vs 40%), had attempted suicide (17% vs 9%), and required psychoactive medications (36% vs 23%). * $P < .05$ for YPY versus OPY. PM, psychoactive medication; SI, suicidal ideation.

medication use among older GI youth. It could be that providers find older youth to be more severely distressed, leading them to initiate treatment with pharmacologic agents. Conversely, providers may be more hesitant to prescribe these medications to younger individuals.

Although the prevalence of pediatric depression increases with age[25] and peaks after the onset of puberty,[26] particularly for AFAB youth, we found that late pubertal GI youth were 5.49 times more likely to report this diagnosis independent of age and assigned sex. Anxiety disorders in the general population are not shown to exhibit a relationship with pubertal development,[27] yet GI youth with more advanced puberty were 4.18 times more likely to report these

diagnoses. To our knowledge, these are the first quantitative data relating pubertal stage to mental health problems among GI youth presenting to care, supporting clinical observations that pubertal development, menses, and erections are distressing to these youth and consistent with the beneficial role of pubertal suppression, even when used as monotherapy without gender-affirming hormones.[13,28]

Although the median age of youth presenting to our clinic is slightly lower than we have described previously,[4] 61% of this cohort were ≥15 years of age, and 83% were in late puberty at the time of presentation, consistent with literature describing clinical populations of GI youth seeking

GAMC.[2,3,5,14] Within this population, it is not clear why YPY presented to care earlier than OPY. In the last decade, the age criteria for GAMC has changed slightly. In 2017, the Endocrine Society stated that initiation of gender-affirming hormones may be appropriate <16 years of age in selected intances,[29] whereas 16 had been the minimum age criterion in their previous guideline.[30] However, the sole criterion for pubertal suppression, the initiation of puberty, is not age-based and has not changed.

OPY and YPY waited a similar amount of time between recognizing their gender incongruence and coming out and between coming out and presenting to GAMC (Fig 3). On average, OPY simply experienced gender history events at older ages (Fig 2). This suggests that youth who recognize their gender incongruence later in life may start their process of gender exploration later and therefore present to care at older ages. Whether there are additional differences between these two groups warrants further study. Our data also suggest that age and pubertal stage at the first visit rather than the duration of transgender identity underlie some of the mental health distress among youth who present to GAMC later in life.

This study has limitations. Through its cross-sectional design, we can identify associations but not cause-and-effect relationships. We captured rates of mental health problems at only 1 point in time and do not know age at diagnosis, leaving open the possibility that our findings could be explained, partly, by OPY having had more time to accrue these diagnoses. Although retrospective data may be incomplete, we mitigated this concern by the use of standardized histories. By using self-report data, bias can be introduced. We attempted to minimize this by considering only reports of formal mental health diagnoses and did not infer diagnoses

TABLE 2 Determinants of Mental Health Problems Among Youth Presenting to GAMC

	B	SE	P	Odds Ratio (95% CI)
Depressive disorders, pubertal stage (late)	1.703	0.800	.03	5.49 (1.14–26.32)
Anxiety disorders, pubertal stage (late)	1.432	0.631	.02	4.18 (1.22–14.49)
History of self-harm, assigned sex (female)	1.227	0.447	.006	3.41 (1.42–8.19)
Psychoactive medication use, age at first visit, y	0.269	0.113	.02	1.31 (1.05–1.63)

Data for all models and covariates can be found in Supplemental Table 3.

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on the basis of descriptions of the youth's emotional state.

Although our study is composed of a large data set of GI youth, the data are derived from chart review and are based on patient, family, and/or caregiver recall. Some youth were unable to recall the timing of various gender history events, and we cannot verify the ages that were reported. Our study included only a small proportion (8.7%) of youth in early puberty and some youth did not have documented pubertal examinations. Study of a larger population of treatment-naïve early pubertal youth, particularly those at ages representing the upper bounds of normal pubertal timing, is needed to support the finding that puberty, rather than age, is more highly related to depressive and anxiety disorders among GI youth.

Finally, the generalizability of our findings may be limited by the demographics of our study population. We recognize that in our study, we only include youth who were able to and wanted to access GAMC at a tertiary center. AFAB youth predominated in our population, but this is consistent with what has been described in other recent clinic-based samples.[2,31,32] Although lower than in some populations,[2,7,14] our reported rate of autism spectrum disorders (6%) is similar to that described by other Canadian[3,31] and Dutch gender clinics.[33] Of youth with reported ethnicities, most (147 of 203; 72%) were white, which is in keeping with the predominantly white participants in Canadian studies of GI youth and adults.[34,35] It is difficult to know whether our findings would apply to clinical settings with more AMAB patients and increased ethnic diversity.

CONCLUSIONS

In our study, we found that older age and later pubertal stage at the time of presentation to GAMC are associated with increased rates of psychoactive medication use and increased rates of mental health problems (depression and anxiety), respectively. These data suggst that GI youth who present to GAMC later in life are a particularly high-risk subset of a vulnerable population. Further study is required to better describe the mental health trajectories of transgender youth and determine if mental health status or age at initiation of GAMC is correlated with psychological well-being in adulthood.

ABBREVIATIONS

AFAB: assigned female at birth
AMAB: assigned male at birth
CI: confidence interval
GAMC: gender-affirming medical care
GI: gender incongruent
IQR: interquartile range
OPY: older presenting youth
TYC: Transgender Youth Clinic
YPY: younger presenting youth

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