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Psychiatric Morbidity Among Adolescents and Young Adults Who Contacted Specialised Gender Identity Services in Finland in 1996–2019: A Register Study

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ABSTRACT

Aim: To examine the prevalence of severe psychiatric morbidity among gender-referred adolescents, focusing on gender differences and outcomes related to medical gender reassignment.

Methods: Finnish nationwide cohort of all under-23-year-old gender-referred individuals between 1996 and 2019 ($n = 2\,083$) and 16 643 matched controls. Cross-tabulations with X^2 statistics and Cox regression were used to analyse the data.

Results: Gender-referred adolescents showed significantly higher psychiatric morbidity than controls both before (45.7% vs. 15.0%) and ≥ 2 years after referral (61.7% vs. 14.6%). Those referred after 2010 had greater psychiatric needs than earlier cohorts, both before (47.9% vs. 15.3%) and ≥ 2 years after (61.3% vs. 14.2%) referral. Among adolescents who underwent medical gender reassignment, psychiatric morbidity increased markedly during follow-up—rising from 9.8% to 60.7% in feminising gender reassignment and from 21.6% to 54.5% in masculinising gender reassignment. After adjusting for prior psychiatric treatment, all gender-referred adolescents had similarly elevated risks of psychiatric morbidity, with hazard ratios approximately three times higher than female controls and five times higher than male controls.

Conclusion: Severe psychiatric morbidity is common among gender-referred adolescents and appears to be more prevalent in those referred after the recent surge in referrals. Psychiatric needs do not subside after medical gender reassignment.

1 | Introduction

Gender dysphoria (GD) involves the distress or impaired functioning that individuals may experience when their gender identity does not match their biological sex [1]. This often leads to a desire to undergo hormonal and surgical treatments known as medical gender reassignment (GR) to align one's physical body with their experienced gender. The twenty-first century has seen a significant increase in the number of adolescents referred to specialised gender identity services (later: Gender-referred adolescents; GIS) for the purpose of considering GR [2, 3]. Medical GR initiated during the developmental

Abbreviations: CI, confidence interval; CRHC, Care Register for Health Care; GD, gender dysphoria; GIS, gender identity services; GR, gender reassignment; HR, hazard ratio; OR, odds ratio; SII, The Social Insurance Institution.

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Summary

- Gender-referred adolescents show high psychiatric morbidity, yet gender differences and mental health trajectories after medical gender reassignment remain poorly understood.
- These adolescents had markedly higher psychiatric morbidity than controls before and after referral, with treatment needs often persisting and even intensifying after medical interventions—on some, they might even have a negative impact.
- Findings emphasise the need for thorough psychiatric assessment and ongoing treatment throughout medical gender reassignment.

years may provide the desired physical results better than treatments initiated in adulthood, and positive psychosocial outcomes, including reduced depression, self-harm, and suicidality, are also expected [4–6].

Gender-referred adolescents exhibit elevated levels of psychopathology, particularly depression and anxiety. A systematic review of papers published by the end of 2020 concluded that among gender-referred adolescents, the prevalence of mental health problems—most commonly depression and anxiety—ranged from 22% to 78% [7]. Subsequent studies [8–12] have confirmed similar prevalences. As far as we know, only two earlier studies have examined secular trends in psychiatric morbidity among gender-referred adolescents. Nyquist et al. observed a slight downward time trend in psychiatric diagnoses per person, and the prevalence of depression decreased from 2000 to 2022 [10]. Arnoldussen et al. found a downward trend in clinically significant externalising symptoms between 2000 to 2016; however, no such trend was observed in total or internalising symptoms [13]. In addition, no population control group was used in either of these studies.

Gender differences in psychiatric morbidity in gender-referred adolescents have not been subjected to systematic analysis [7]. In older studies involving adult transgender subjects, either no differences were found between genders, or transwomen displayed higher rates of psychopathology [14]. A recent study found that gender-referred adolescents with female sex had more psychiatric diagnoses than gender-referred adolescents with male sex [10]. It is known that in general population studies, adolescent girls have more mental health issues than adolescent boys [15, 16].

The bulk of the literature on adolescent GD suffers from two very common shortcomings: A lack of control groups, making it unfeasible to estimate truly excessive morbidity, and small sample sizes that leave room for chance variation. In the only large scale, comparative study, around two thirds of the transgender subjects had a psychiatric diagnosis (8–9-fold prevalence ratio (PR)) and just under 10% had had a psychiatric hospital admission (22–24-fold PR) six months before documented transgender status; lifetime psychiatric diagnoses were observed in 70% (PR 3–4) and psychiatric hospitalisations in 13%–15% (PR 8–10), when compared to cisgender peers [17].

Medical GR is often suggested to be beneficial, even vital, for the mental health of adolescents suffering from GD [4–6], but the evidence supporting subsequent improvements in mental health, quality of life or functioning is very limited [18, 19]. Many of the studies in this field are cross-sectional and unsuitable for assessing developments. The few longitudinal studies have been of low quality and provided inconsistent results. The sample sizes have been small; there usually has been no control group, follow-up periods have been short, and the measures of assessing changes in mental health have varied. Loss to follow-up has often been substantial. A notable exception to this is the study by Hisle-Gorman et al., who, in their register-based follow-up study, discovered that transgender youth presented with greater psychiatric morbidity and greater needs for mental healthcare than their siblings. After medical GR interventions, the overall need for mental healthcare had not decreased, and the need for psychotropic medication had increased across therapeutic classes [20].

Paediatric gender medicine is much debated and polarised, with international and national treatment guidelines drifting in opposite directions [21, 22]. The sex and age distribution among those seeking gender reassignment has changed towards a preponderance of adolescents with female sex [10, 13]. Complex psychiatric needs have been documented among young people seeking gender reassignment [18], but it is not known if these needs reflect an increasing secular trend among youth in general [23, 24] and if those needs differ by gender. Trajectories of psychiatric morbidity among those who undergo medical GR and those who do not are not known [18].

1.1 | Aims of the Study

This nationally representative register study aims to address these gaps. The research questions were:

1. Are there differences in the need for specialist-level psychiatric treatment between gender-referred adolescents and their matched population controls?
2. Is there a difference in the need for specialist-level psychiatric treatment among those referred before 2010 and after 2011, when there has been a tenfold increase in the number of referrals [2, 3]?
3. Can any gender differences be observed in psychiatric morbidity?
4. How do the psychiatric needs develop among those who undergo medical GR and those who do not, and is there any difference between genders in these developments?

2 | Methods

2.1 | Finnish Registers

Each resident of Finland receives an 11-digit personal identification number at birth or upon acquiring Finnish citizenship. This number serves as a unique identifier across various national registers. The Finnish Population Information System contains current personal data on all residents. Since 1994, the National Institute for Health and Welfare has maintained

the Care Register for Health Care (CRHC), which documents healthcare visits by Finnish residents, including diagnoses, procedures, and medical speciality codes. The Social Insurance Institution (SII) of Finland records prescription medication purchases, while the causes of death register maintained by Statistics Finland documents residents' causes and times of death.

2.2 | Study Population

Gender identity assessments potentially leading to medical GR are in Finland centralised nationally to two university hospitals. This study conducted a register-based follow-up of individuals attending these gender identity clinics in Finland in 1996–2019 before reaching the age of 23. The follow-up commenced at the first appointment at the GIS (the index date), and continued until death or June 2022, when the dataset was compiled. We opted to extend the inclusion age to 22 years, mindful that the identity development in young individuals extends beyond the age of legal maturity [25]. In the results that follow, these individuals are called GD subjects for consistency and clarity.

2.3 | Control Group

The Population Information System provided four male and four female controls, matched for birth year and municipality of birth for each gender-referred individual. The index date of the gender-referred person was assigned to all controls.

2.4 | Variables

Birth year and currently registered sex data were extracted from the Population Information System. Sex as registered in the Population Information System will be referred to below as registered sex. This invariably coincided with the subject's biological sex for the controls and those subjects in the GD group who did not undergo medical GR. It is plausible to assume that subjects contacting the GIS were indeed seeking medical GR towards the opposite sex. In analyses exploring gender differences we used the following groups among the GD subjects: "GD, towards female, GR–" = GD subjects who had not undergone medical GR and were registered males; "GD, towards male, GR–" = GD subjects who had not undergone medical GR and were registered females; "GD, towards female, GR+" = GD subjects who had undergone feminising GR; and "GD towards male, GR+" = GD subjects who had undergone masculinising GR.

Index year refers to the year of the subject's first appointment at the GIS.

Need for specialist-level psychiatric treatment before the index contact (yes/no) and thereafter (yes/no) was recorded. Psychiatric treatment, excluding gender identity assessments and appointments with a multi-disciplinary team therein, subsequent to the index contact was defined as continuing two years or more after the index contact, to allow time for the gender identity assessment and potential medical GR initiation. The number of contacts with specialist-level psychiatric treatment was extracted from the CRHC and categorised as follows: None, 1–5, 6–25, 26–100 and 101+. Psychiatric diagnoses were categorised into the ICD-10 main F categories in supplementary analyses.

Medical GR interventions included masculinising/feminising hormonal treatments, chest masculinisation, and/or genital surgery (vaginoplasty/phalloplasty/metoidioplasty). Hormonal GR was recorded if the register of the SII showed that the patient had purchased masculinising/feminising hormones with a special reimbursement code that is available for individuals diagnosed with F64.0 in the nationally centralised GIS when the treatment has continued for a year. Information on surgical GR was obtained from the CRHC.

2.5 | Statistical Analyses

Statistics Finland pseudonymised the data, which were then analysed using IBM SPSS Statistics v.27.0. Basic demographic and treatment-related details were examined through cross-tabulation, $\chi 2$ tests and Fisher's exact test. In comparisons between gender groups, all other groups were pairwise compared first with male and then with female controls. Multivariable analyses were performed using Cox regression models, and hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. Need for specialist-level psychiatric treatment ≥ 2 years after the index contact was used as the dependent variable. The first independent variable was the gender group. In the next step, controlling for possible confounders: Birth year and index year and finally adding the need for specialist-level psychiatric treatment before the index contact. To minimise type 1 errors due to multiple testing and the large dataset, the threshold for statistical significance was set at $p < 0.01$.

3 | Results

A total of 2 083 individuals under the age of 23 sought gender identity assessments, and the matched controls numbered 16 643. The mean (SD); median age of those seeking assessments was 18.5 (2.2); 19. The mean follow-up period was 5.49 years, with a median of 4.93 and a maximum of 25 years. At the time of data collection, 41.3% of the GD subjects (860/2 083) and 50.0% of the controls (8 325/16 643) were registered males. Among the GD subjects, 481 were seeking change towards female, 1 602 towards male, and 38.2% (796) underwent medical GR.

In bivariate analyses, the GD subjects presented with a more common and more intense need for specialist-level psychiatric treatment than the controls (Table 1).

Differences between the groups in need for specialist-level psychiatric treatment, categorised by the time of contacting GIS, are presented in Table 2. Among those with index dates in 1996–2010, differences between the GD subjects and the controls with a history of specialist-level psychiatric treatment prior to index date appeared quite large but did not reach statistical

TABLE 1 | Need for specialist-level psychiatric treatment among the GD subjects and the controls before and ≥2 years after the index date (%, *n*).

	GD subjects (*n* = 2 083)	Controls (*n* = 16 643)	*p*
Specialist-level psychiatric treatment before the index date	45.7 (952)	15.0 (2 493)	< 0.001
Specialist-level psychiatric treatment ≥2 years after the index date	61.7 (1 285)	14.6 (2 424)	< 0.001
Lifetime number of contacts to specialist level psychiatric treatment			< 0.001
None	23.4 (487)	74.0 (12 321)	
1–5	11.0 (230)	8.1 (1 342)	
6–25	16.0 (333)	7.2 (1 200)	
26–100	22.0 (459)	6.4 (1 070)	
≥101	27.6 (574)	4.3 (710)	

Abbreviation: GD = gender dysphoria.

TABLE 2 | History of specialist-level psychiatric treatment among the GD subjects and the controls with index date in 1996–2010 and in 2011–2019 (%, *n*).

	1996–2010			2011–2019		
	GD subjects *n* = 186	Controls *n* = 1 488	*p*	GD subjects *n* = 1 897	Controls *n* = 15155	*p*
Specialist-level psychiatric treatment before the index date	23.7 (44)[a]	11.8 (175)[b]	0.03	47.9 (908)[a]	15.3 (2 318)[b]	< 0.001
Specialist-level psychiatric treatment ≥2 years after the index date	66.1 (123)[c]	17.9 (267)[d]	< 0.001	61.3 (1 162)[c]	14.2 (2 157)[d]	< 0.001

Note: Comparisons within the groups between the earlier and later cohorts.
Abbreviation: GD = gender dysphoria.
[a] $p < 0.001$.
[b] $p < 0.001$.
[c] $p = 0.2$.
[d] $p < 0.001$.

significance (23.7% vs. 11.8%, $p = 0.03$). However, a statistically significant difference was observed in the need for psychiatric treatment ≥2 years after the index date (66.1% vs. 17.9%, respectively, $p < 0.001$). Among those with an index date in 2011–2019, the GD subjects had needed specialist-level psychiatric treatment more frequently both before the index date (47.9% vs. 15.3%, $p < 0.001$) and ≥2 years thereafter (61.3% vs. 14.2%, $p < 0.001$). The proportion of those with a history of specialist-level psychiatric treatment prior to index contact doubled among the GD group from the earlier cohort to the later (Table 2).

3.1 | Psychiatric Treatment Needs Prior to Contacting GIS and in Follow-Up

In the bivariate analyses by gender and GR status it was seen that those GD subjects who did not undergo medical GR had, regardless of gender, needed specialist-level psychiatric treatment more commonly than either the male or the female controls before the index contact (probably due to severe psychiatric morbidity being a contraindication for medical GR), as had also those seeking change towards male who had obtained medical GR. Those seeking change toward female who subsequently underwent medical GR did not differ from either control males or females in terms of need for psychiatric treatment before the index contact (Table 3).

The GD subjects, regardless of gender and GR status, needed specialist-level psychiatric treatment for ≥2 years after the index contact more commonly than controls of either sex. From before the index date to ≥2 years later, considerable increases in the need for psychiatric treatment were seen among those adolescents who had undergone medical GR, particularly among those seeking change towards female, while changes among the controls and the GD subjects who did not undergo medical GR were minor (Table 3).

For details about diagnoses, see Table S1.

3.2 | Multivariable Analyses of Need for Psychiatric Treatment After Gender Identity Assessments

To investigate trajectories after medical GR in psychiatric morbidity, multivariable models accounting for year of birth, index date and psychiatric treatment needs before the index date were run. When no confounding factors were accounted for, those who did not undergo GR, regardless of the desired direction of change, displayed the highest HRs for subsequent specialist-level psychiatric treatment (Tables 4 and 5). Those who had undergone medical GR also presented with an increased risk compared to both the male and the female controls. However, after accounting for all the variables, the differences in HRs between the GR– and GR+ groups levelled out. The adjusted HRs for subsequent need for specialist-level psychiatric treatment when compared to the control males were between 4.7 and 6.1, and compared to the control females, between 3.0 and 3.7. Furthermore, later index year and being born in a later year were predictors of psychiatric treatment after the index date (Tables 4 and 5).

4 | Discussion

In this nationally representative, long-term register-based follow-up study, gender-referred adolescents, regardless of their gender, had significantly more psychiatric morbidity than their matched population controls. Those referred after 2010 displayed noticeably more psychiatric morbidity than those referred earlier. The need for specialist-level psychiatric treatment increased considerably in follow-up among those who underwent medical GR. After controlling for specialist-level psychiatric treatment before contact with the GIS, the risk for

TABLE 3 | Psychiatric treatment contact before the index date and ≥ 2 years after among the control males and females and those seeking medical gender reassignment (GR) stratified by direction of desired change and undergoing medical GR (%, n).

	Control, male $n = 8\,325$	Control, female $n = 8\,318$	GD, towards female, GR– $n = 318$	GD, towards male, GR– $n = 969$	GD, towards female, GR+ $n = 163$	GD, towards male, GR+ $n = 633$
Psychiatric treatment before the index date[a,b]	13.6 (1 132)	16.4 (1 362)	53.1 (169)	65.0 (630)	9.8 (16)	21.6 (137)
Psychiatric treatment ≥ 2 years after the index date[c,d]	11.1 (920)	18.1 (1 504)	59.7 (190)	67.2 (651)	60.7 (99)	54.5 (345)

Abbreviations: GD = gender dysphoria; GR– = did not undergo medical gender reassignment; GR+ = underwent medical gender reassignment.
[a]Comparisons to control males: Control females $p < 0.001$, GD towards female GR– $p < 0.001$, GD towards male GR– $p < 0.001$, GD towards female GR+ $p = 0.2$, GD towards male GR+ $p < 0.001$.
[b]Comparisons to control females: GD towards female GR– $p < 0.001$, GD towards male GR– $p < 0.001$, GD towards female GR+ $p = 0.02$, GD towards male GR+ $p = 0.001$.
[c]Comparisons to control males: Control females $p < 0.001$, GD towards female GR– $p < 0.001$, GD towards male GR– $p < 0.001$, GD towards female GR+ $p < 0.001$, GD towards male GR+ $p < 0.001$.
[d]Comparisons to control females: GD towards female GR– $p < 0.001$, GD towards male GR– $p < 0.001$, GD towards female GR+ $p < 0.001$, GD towards male GR+ $p < 0.001$.

TABLE 4 | Hazard Ratios (HR) (95% CI) for specialist-level psychiatric treatment contact ≥ 2 years after the index date among female controls and the different gender/gender reassignment (GR) groups among the GD subjects with control males as the reference group.

	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Group						
Control males	ref		ref		ref	
Control females	1.7 (1.5 to 1.8)	< 0.001	1.7 (1.6 to 1.9)	< 0.001	1.7 (1.5 to 1.8)	< 0.001
GD, towards female, GR–	8.3 (7.1 to 9.7)	< 0.001	7.7 (6.6 to 9.0)	< 0.001	4.8 (4.1 to 5.6)	< 0.001
GD, towards male, GR–	11.1 (10.1 to 12.3)	< 0.001	8.9 (8.0 to 9.8)	< 0.001	4.7 (4.2 to 5.3)	< 0.001
GD, towards female, GR+	3.9 (3.1 to 4.8)	< 0.001	5.9 (4.8 to 7.3)	< 0.001	6.1 (4.9 to 7.5)	< 0.001
GD, towards male, GR+	4.2 (3.7 to 4.7)	< 0.001	5.3 (4.7 to 6.0)	< 0.001	4.9 (4.4 to 5.6)	< 0.001
Year of birth	—		1.04 (1.03 to 1.06)	< 0.001	1.06 (1.04 to 1.07)	< 0.001
Index year	—		1.6 (1.6 to 1.6)	< 0.001	1.5 (1.5 to 1.6)	< 0.001
Specialist-level psychiatric treatment before index date	—		—		3.1 (2.9 to 3.3)	< 0.001

Abbreviations: CI, confidence interval; GD, gender dysphoria; GR–, did not undergo medical gender reassignment; GR+, underwent medical gender reassignment.

TABLE 5 | Hazard Ratios (HR) (95% CI) for specialist-level psychiatric treatment contact ≥2 years after the index date among the different gender/gender reassignment (GR) groups among the GD subjects, with control females as the reference group.

Group						
Control females	ref		ref		ref	
GD towards female, GR−	5.0 (4.3 to 5.8)	<0.001	4.5 (3.9 to 5.2)	<0.001	3.0 (2.6 to 3.5)	<0.001
GD towards male, GR−	6.8 (6.1 to 7.3)	<0.001	5.2 (4.7 to 5.7)	<0.001	3.0 (2.7 to 3.3)	<0.001
GD towards female, GR+	2.3 (1.9 to 2.8)	<0.001	3.5 (2.9 to 4.3)	<0.001	3.7 (3.0 to 4.5)	<0.001
GD towards male, GR+	2.5 (2.2 to 2.8)	<0.001	3.1 (2.8 to 3.5)	<0.001	3.0 (2.7 to 3.4)	<0.001
Year of birth	—	—	1.05 (1.03 to 1.06)	<0.001	1.06 (1.04 to 1.07)	<0.001
Index year	—	—	1.7 (1.6 to 1.7)	<0.001	1.7 (1.6 to 1.7)	<0.001
Specialist-level psychiatric treatment before index date	—	—	—	—	2.8 (2.6 to 3.0)	<0.001

Abbreviations: CI, confidence interval; GD; gender dysphoria; GR−, did not undergo medical gender reassignment; GR+, underwent medical gender reassignment.

severe psychiatric morbidity in follow-up was similar among all the gender-referred adolescents, regardless of desired direction of change and GR status. The novel contributions of the present study comprise a direct comparison to a matched population and an analysis of gender differences in mental health outcomes in a large, nationally representative data set with a long follow-up.

4.1 | Differences in Morbidity Between Gender-Referred Adolescents and Their Population Controls

In the bivariate analyses, the gender-referred adolescents had three times more psychiatric morbidity before the index date than their matched population controls. This aligns with earlier research [20]. In the follow-up, subsequent to contacting the GIS, their need for specialist-level psychiatric treatment was nearly 1.5-fold compared to that before their first visit to the GIS. In contrast, the need for treatment among the controls remained almost unchanged in follow-up. Additionally, the specialised psychiatric treatment had typically been more intensive among the gender-referred adolescents, indicating either long-standing psychiatric morbidity and/or particularly severe symptoms.

4.2 | Secular Trends in Morbidity

From 1996 to 2010, the need for psychiatric treatment before contacting the GIS did not differ statistically significantly between the gender-referred adolescents and the controls. However, from 2011 to 2019, half of the gender-referred adolescents had already required specialist-level psychiatric treatment before their contact with the GIS—a figure that had doubled compared to those seeking evaluations earlier. No such change was observed among the controls. This suggests that increasingly, adolescents with severe psychiatric morbidity are referred to GIS. The change is hardly attributable to improved recognition of mental disorders, as no similar rise was observed in the control group. Minority stress theory [26] posits that mental disorders in transgender identifying people largely arise from actual and internalised prejudice. With the opening up of society with regard to sexual and gender minorities, a decrease in psychiatric morbidity might have been expected in the later GD cohorts, although reduced stigma may also increase treatment seeking. The notable increase in those contacting the GIS and the increased psychiatric morbidity among them since the 2010s may also suggest that, for some, mental health challenges may manifest as concerns related to gender identity [18].

4.3 | Gender Differences

Among the gender-referred adolescents, the greatest need for specialist-level psychiatric treatment before contact with the GIS was seen among those seeking change towards male, but gender differences evened out in the follow-up. Among the controls, lifetime prevalences of depression and anxiety disorders were higher among the gender-referred adolescents with female than male sex. Factors related to sex may shape psychiatric morbidity more than identity, although this topic remains underresearched [7].

4.4 | Development of Psychiatric Needs According to Medical GR

When prior psychiatric morbidity was controlled for, the gender-referred adolescents had a 5- to 6-fold increased need for specialist-level psychiatric treatment two years or more after the index date compared to the male controls, and 3- to 4-fold greater risk compared to the female controls, regardless of the desired direction of change and GR status. This does not support the suggested improvement in mental health after medical GR initiated during developmental years [4–6], and in light of the present findings, severe psychiatric disorders do not appear primarily attributable to GD [20, 27]. Psychiatric disorders require their due treatment regardless of a young person's gender identity [22].

Actually, considerable increases in need for psychiatric treatment were seen among those adolescents who had undergone medical GR, particularly among those seeking change toward female. Oestrogen has been found to potentially cause depressive

symptoms in both cisgender women [28] and transwomen [29], which may partly explain the increases in psychiatric needs among those who underwent feminising GR. Masculinising hormones may temporarily improve mood, and testosterone-related bodily changes—typically emerging within a few months [29]—could be expected to alleviate GD and subsequently psychiatric treatment needs. However, psychiatric treatment needs were also markedly increased among those who obtained masculinising GR. Subsequent morbidity burden may also arise from treatments not meeting the expectations placed on them.

4.5 | Strengths and Limitations

This study has several strengths, including a large, nationally representative sample, a three-decade inclusion period that allowed exploring secular trends, the use of matched population controls and a long follow-up period. The register datasets used are comprehensive, with no loss of data during follow-up because reporting is mandatory for health authorities, and patients may not opt out. Specialist-level psychiatric treatment is only available based on accepted referrals and indicates severe mental disorders. National guidelines ensure a consistent threshold across the country. The Finnish school system regularly screens students for possible mental health disorders. As such, both the gender-referred and their controls have been assessed many times during their lifetime. This reduces the risk that undiagnosed psychiatric morbidities in the controls, or better screening in the GD group, would confound the findings. The index date for most of the subjects was in the 2010s, when the change in the demography of the patients had already been observed [27]. Consequently, the findings should be generalisable to gender-referred youth in the mid 2020s.

Our methodological choices followed common practice by first comparing case–control prevalences with chi-square tests, as these proportions offer readers an essential contextual understanding. For multivariable analyses, Cox regression was preferred over logistic models to account for substantial variation in follow-up times across three decades, while municipality was excluded as a covariate due to its large number, its role only in matching, and its limited analytic utility. Additional Cox models incorporating matching-based strata produced substantively unchanged results but could not estimate the index year because of collinearity. Therefore, our original analytical approach remains methodologically justified and consistent with previous publications using this dataset [e.g., 27].

A limitation of this study is that more detailed information on patients' reasons for using the psychiatric services could not be analysed. It is also of note that the overrepresentation of prior psychiatric treatment in those who did not proceed to treatment probably reflects the fact that severe psychiatric morbidity may be a contraindication for medical GR. In addition, controlling for socioeconomic background, which is known to associate with psychiatric morbidity [30], would have improved the analysis. Regarding adolescents, parental socioeconomical status would be of interest. Future research should pursue to include variables illustrating this in comparable analyses. Lastly, more nuanced subgroup analyses, such as whether there were specific subgroups of adolescents benefiting from early medical GR or were at risk of poor mental health outcomes, were beyond the scope of this study. These will be explored in the authors' future studies.

4.6 | Clinical Implications

Regardless of gender, adolescents suffering from GD present with excessive psychiatric morbidity. Subsequent to medical GR, psychiatric treatment needs appear to increase. It should be noted that in some individuals, medical GR appears to be linked to deterioration in mental health. Possible mechanisms and vulnerable subgroups should be explored in future studies. The effects of medical GR and the expectations of the patient must be addressed before commencing the treatment. The considerable severe psychiatric morbidity prior to contacting the GIS, and its increase over time, suggest that for some of these adolescents, GD may be secondary to other mental health challenges. This underscores the need to thoroughly assess and appropriately treat mental disorders among those seeking GR before and after undergoing irreversible medical treatments. Psychiatric needs must be adequately met.

Author Contributions

Sami-Matti Ruuska: writing – original draft (lead), formal analysis (equal), conceptualization (equal). **Katinka Tuisku:** writing – review and editing (supporting), methodology (supporting), conceptualization (supporting). **Timo Holttinen:** methodology (lead), writing – review and editing (supporting), data curation (supporting). **Riittakerttu Kaltiala:** writing – review and editing (lead), data curation (lead), funding acquisition (lead), conceptualization (equal), formal analysis (equal), supervision (lead).

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Ethics Statement

Approval for the study was granted by the Ethics Committee of Tampere University Hospital (ETL R20040R), Findata (THL/5188/14.02.00/2020), and Statistics Finland (TK/1016/07.03.00/2020). In accordance with Articles 6e and 9i and j of the Regulation (EU) 2016/679 of the European Parliament and of the Council, individual informed consent of each registrar was not required.

Conflicts of Interest

S.-M.R.: Research funding from Siun säätiö and Psykiatrian Tutkimussäätiö. R.K.: Research funding: Wihuri foundation, Suomen kulttuurirahasto, Tampere University Hospital Research fund, Finnish state research funding instrument and the Foundation for paediatric research. Honoraria for lectures and/or travel expenses covered by Tallinn Children's Hospital, Denmark Southern Region, Finnish Society for Adolescent Psychiatry, EFCAP, Finnish Medical Society Duodecim, Society for Evidence Based Gender Medicine, Finnish Society for Child Psychiatry, Finnish Psychiatric Association, CAN-SG, Finnish Society for Paediatrics, Skepsis, Prison and probation services Finland, Helsinki University Hospital, National Advisory Board for Ethics and

Social and Health Care (ETENE), Pohjois-Savo Wellbeing County, Etelä-Pohjanmaa Wellbeing county, Observatoire la Petite Siréne, Royal College of Psychiatrists, Amsterdam Centre for Family Law, Lundbeck, Biocodex. Board and committee memberships: ETENE, member; The Cass Review, member of advisory board; EFCAP Finland, chairperson.

Data Availability Statement

The data that support the findings of this study are available from Findata. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from https://findata.fi with the permission of Findata.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Table S1:** Lifetime prevalence of the most common psychiatric diagnoses (classified to main ICD-10 categories) by gender among the GD subjects and the matched controls (% (n)). A diagnosis was coded as present if it had been recorded as either the primary or the first or second additional diagnosis.