Desire for genetically related children among transgender and gender-diverse patients seeking gender-affirming hormones

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Objective: To assess predictors of desire for genetically related children among a national cohort of reproductive-age transgender and gender-diverse patients aged 18 to 44 years initiating gender-affirming hormone therapy for the first time.
Design: Cross-sectional study.
Setting: National telehealth clinic.
Patients: A cohort of patients from 33 US states initiating gender-affirming hormone therapy. A total of 10,270 unique transgender and gender-diverse patients—aged 18 to 44 years (median age 24 years), with no prior use of gender-affirming hormone therapy—completed clinical intake forms between September 1, 2020, and January 1, 2022.
Intervention(s): Patient sex assigned at birth, insurance status, age, and geographic location.
Main Outcome Measure(s): Self-reported desire for children using own genetic material.
Result(s): Transgender and gender-diverse patients seeking gender-affirming medical treatments who are open to having genetically related children are an important population to identify and appropriately counsel. Over one quarter of the study population reported being interested in or unsure about having genetically related children, with 17.8% reporting yes and 8.4% unsure. Male-sex-assigned-at-birth patients had 1.37 (95% confidence interval: 1.25, 1.41) times higher odds of being open to having genetically related children compared with female-sex-assigned-at-birth patients. Those with private insurance had 1.13 (95% confidence interval: 1.02, 1.37) times higher odds of being open to having genetically related children compared with those without insurance.
Conclusion(s): These findings represent the largest source of self-reported data on the desire for genetically related children among reproductive-age adult transgender and gender-diverse patients seeking gender-affirming hormones. Guidelines recommend that providers offer fertility-related counseling. These results indicate that transgender and gender-diverse patients, particularly male-sex-assigned-at-birth individuals and patients with private insurance, could benefit from counseling regarding the impacts of gender-affirming hormone therapy and gender-affirming surgeries on fertility. (Fertil Steril Rep® 2023;4:224–30. ©2023 by American Society for Reproductive Medicine.)
Key Words: Telehealth, fertility, parenthood, testosterone, estrogen

In the United States (US), an estimated 1.27 to 1.4 million adults aged 18 years and older identify as transgender and gender diverse (TGD) (1, 2). Estimates vary, but between 2% and 12% of adolescents and young adults identify with a gender identity other than cisgender. Adults aged 18–34 years are 4 times more likely to identify as TGD than those older than 34 years (3). Gender-affirming hormone therapy (GAHT, e.g., using estrogen or testosterone) is a critical part of medical care for some TGD individuals. An estimated 80%–95% of adult TGD Americans desire GAHT (2), with similar needs reported among adolescents and young adults aged <18 years (3, 4).

Gender-affirming hormone therapy is heterogeneous, and different patients will use different hormonal

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medications depending on their embodiment goals. Each hormone therapy has its own profile regarding its impact on fertility; fertility is specific to the gonads of an individual and the medications used. Patients on feminizing GAHT who use estrogens will generally experience a decrease in fertility (5). Although a few studies have shown success in patients producing sperm after discontinuation of estrogen therapy, current guidelines still recommend fertility preservation (FP) before initiation of estrogen (6).

Patients on testosterone GAHT appear to have more options with regard to fertility. A number of recent studies have described successful ovulation induction and pregnancies after discontinuation of testosterone (7, 8) with ovulatory parameters similar or slightly lower in individuals previously treated with testosterone than age-related peers (9, 10). Despite this, as clinicians cannot guarantee no impact of testosterone on fertility, patients are still counseled that the only way to assure no impact of testosterone is FP in advance of GAHT initiation.

Pediatric patients, both those with ovaries and testes, treated with gonadotropin-releasing hormone (GnRH) agonists (i.e., puberty "blockers") who choose to subsequently initiate GAHT in adolescence have impaired fertility because of the arrest of gamete development; few options currently exist for FP in patients treated with GnRH agonists who then begin GAHT (11). Given the risk of fertility impairment because of some gender-affirming therapies, the UCSF Center of Excellence for Transgender Health (12), the World Professional Association for Transgender Health (13), the Endocrine Society (14), the American Society for Reproductive Medicine (15), and the American College of Obstetrics and Gynecology (16) all have established guidelines for counseling patients initiating gender-affirming medical treatment, including GAHT, about potential fertility impact, limitations on future reproductive options, and options for FP.

A limited body of research indicates that many TGD individuals do desire genetically related children; however, existing studies of desire for genetically related children in TGD patients have relied on relatively small cohorts (10, 17–20). Clinical and community-based survey research on desire for genetically related parenthood and other family planning goals has also been conducted for TGD populations (10, 17). One of the largest population-based surveys of US adults found that, among 187 TGD individuals without children, 21% desired children in the future (21); 24% of the total sample considered fertility important. A survey of 409 TGD Australians found that a third of respondents considered their fertility to be important; however, most of these subjects reported a lack of information on FP (22). In a convenience study of 50 transgender men, 54% of the population expressed the desire to have genetically related children, and 22% already had genetically related children (23).

Fewer studies have assessed fertility desires in TGD children and adolescents (18, 24), including those treated with GnRH agonists. Surveys with small samples of TGD youth indicate that 36%–56% express a desire for children, either genetically related children or adoption children (18, 25, 26). Existing data have also been used to interrogate the factors that influence patients' fertility desires and paths to parenthood. Small studies have shown that cost, medical insurance coverage, and existing family structures all play a role (27, 28).

Because the number of TGD youth and young adults seeking gender-affirming medical care continues to grow and care delivery evolves (29, 30), it is increasingly important that providers identify and support patients with TGD interested in parenthood. Understanding the prevalence and determinants of fertility desire among patients with TGD initiating GAHT for the first time provides insight into a key clinical interaction that could include counseling on fertility impact and patient goals.

This study presents data from one of the largest national clinical cohorts of patients with TGD aged 18–44 years initiating GAHT for the first time. Our primary aim is to evaluate the proportion of patients who are interested in having genetically related children. Our secondary aim is to investigate factors related to patients with TGD's desire to have genetically related children. Given the clear financial barriers to accessing care, our hypothesis was that patients presenting for GAHT who reported a desire for genetically related children would be more likely to be privately insured, wealthier, and younger than the overall sample.

MATERIALS AND METHODS

Data and Study Population

Data were drawn from the electronic health records of patients using Plume, the first telehealth service providing GAHT to patients in 33 states across the US. Plume's GAHT services are self-pay, subscription-based, and available to adults aged ≥ 18 years [available on Notes for further descriptions of Plume services and locations]. Data were collected before a provider visit to initiate GAHT for the first time using a secure, HIPAA-compliant app (Spruce Health, San Francisco, CA).

Patients were included if they completed intake between September 2020 and December 2021 (n = 15,103). Patients were excluded if they were not within the age range of interest (18–44 years) (n = 1,013), were intersex or had unknown sex assigned at birth (SAB) (n = 111), had previously used gender-affirming hormones and/or undergone gonadectomy (n = 3,643), or had missing data for the question on fertility desire (n = 66). The final sample included 10,270 unique patients.

Outcome Variable

Patient self-reported responses to the question on the intake form "Do you desire to have children with your own genetic material?" were recorded as yes, no, or unsure. For logistic regression models only, patients were assigned to 2 categories: 1 = yes or unsure; and 0 = no. Patients who answered yes or were unsure were considered together as being open to having genetically related children because they represent the population that could potentially benefit from fertility counseling.

Predictors Variables

Demographics included age at the date of intake, insurance status (uninsured, private, Medicaid, or unknown), and SAB (male or female). Health behavior variables included current

smoker, defined as answering in the affirmative to "Do you currently smoke or otherwise use tobacco?," and major depressive disorder, defined as scoring 3–6 on the PHQ-2 self-assessment (31). Gender-affirmation variables included: had a previous gender-affirming surgery of any kind (breast augmentation, orchiectomy, vaginoplasty, mastectomy, hysterectomy, oophorectomy, vaginectomy, scrotoplasty, metoidioplasty, or phalloplasty); wants a gender-affirming surgery of any kind (breast augmentation, orchiectomy, vaginoplasty, mastectomy, hysterectomy, oophorectomy, vaginectomy, scrotoplasty, metoidioplasty, or phalloplasty) someday; and length of time out as current gender.

Statistical Analyses

First, we compared differences in demographics, health behaviors, and gender-affirmation variables by SAB. Chi-square tests were used for categorical variables, and *t*-tests were used for continuous variables. Next, as fertility potential and family-building experiences change across the lifespan, we estimated the proportion of female and male SAB patients across age groups stratified by fertility and family-building potential (18–25, 26–34, and 35–44) who reported being interested in having genetically related children, did not want genetically related children, or were unsure at the time of intake.

Next, we estimated the association between demographic, health behavior, and gender-affirmation characteristics and the desire for genetically related children using a logistic regression model. We used pairwise deletion for missing data. All data were analyzed using Python 3 and R in April of 2022. The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) cohort reporting guidelines were used in preparing this manuscript. This study was reviewed and approved by Oregon Health Sciences University IRB No. 00024232 and Western Copernicus Group IRB (IRB00000533).

RESULTS

Table 1 shows differences in patient characteristics by SAB. Among the 10,270 TGD patients, 54% (n = 5,534) identified as male-sex-assigned-at-birth (MSAB). The median age of the population was 24 years. Nearly a third (32%) of the population had no insurance. Almost half (44%) of the population resided in the south. Almost a third of the population had depression and were current tobacco users. Half of the population identified with their current gender for >2 years, and only 6% have received gender-affirming surgery. Female-sex-assigned-at-birth patients were younger, had a slightly higher rate of insurance, a higher rate of tobacco use, and reported a higher rate of desire for gender-affirming surgeries.

TABLE 1

Characteristics of patients with TGD aged 18–44 years seeking first-time GAHT.

Demographics	Overall (n = 10,270)	FSAB (n = 4,736)	MSAB (n = 5,534)	*P*-value[a]
Age, y (median, IQR)	24.0 (20.0, 28.0)	23.0 (20.0,27.0)	24.0 (21.0,30.0)	<.001
Insurance				
Medicaid	1,046 (10.3)	547 (11.7)	499 (9.2)	<.001
None	3,193 (31.5)	1,374 (29.4)	1,819 (33.4)	
Private	4,456 (44.0)	2,101 (44.9)	2,355 (43.2)	
Unknown	1,434 (14.2)	655 (14.0)	779 (14.3)	
Region[b]				
Midwest	1,609 (15.7)	638 (13.5)	971 (17.6)	<.001
North	1,685 (16.5)	858 (18.2)	827 (15.0)	
South	4,526 (44.3)	2,121 (45.0)	2,405 (43.7)	
West	2,396 (23.5)	1,097 (23.3)	1,299 (23.6)	
Health behaviors				
Current depression[c]	2,972 (29.0)	1,275 (27.0)	1,697 (30.7)	
Current tobacco use[d]	2,896 (28.2)	1,387 (29.3)	1,509 (27.3)	.024
Gender-affirmation characteristics				
Previous surgery	623 (6.1)	235 (5.0)	388 (7.0)	<.001
Desire surgery in the future				
No	480 (4.7)	178 (3.8)	302 (5.5)	<.001
Unsure	2,931 (28.5)	781 (16.5)	2,150 (38.9)	
Yes	6,859 (66.8)	3,777 (79.8)	3,082 (55.7)	
Length of time out as current gender				
<6 mo	1,352 (13.2)	404 (8.5)	948 (17.1)	<.001
6 mo to 2 y	3,364 (32.8)	1,403 (29.6)	1,961 (35.4)	
>2 y	5,554 (54.1)	2,929 (61.8)	2,625 (47.4)	

FSAB = female-sex-assigned-at-birth; GAHT = gender-affirming hormone therapy; IQR = interquartile range; MSAB = male-sex-assigned-at-birth; TGD = transgender and gender diverse.
[a] Tests differences by sex-assigned-at-birth. Chi-square tests were used for categorical variables and *t*-tests were used for continuous variables.
[b] 54 patients had missing data for state of residence.
[c] 11 patients had missing data for depression.
[d] 8 patients had missing data for tobacco use.

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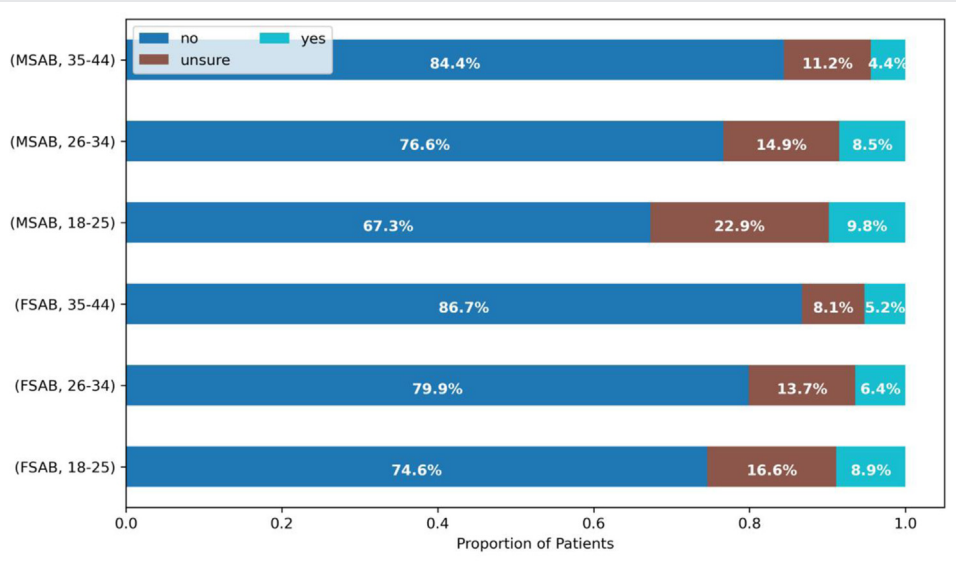
FIGURE 1



Desire for genetically related children among transgender and gender diverse patients by age group and sex at birth. FSAB = female-sex-assigned-at-birth; MSAB = male-sex-assigned-at-birth.

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Figure 1 shows the age-specific prevalence of the outcome variable. Female-sex-assigned-at-birth patients across all age categories had a higher prevalence of not wanting children with their own genetic material. Among MSAB patients aged 18–25 years, 23% were unsure, and 10% wanted genetically related children, compared with 15% and 9% of those aged 26–34 years and 11% and 4% of those aged 35–44 years (Figure 1). Among female-sex-assigned-at-birth (FSAB) patients aged 18–25 years, 17% were unsure, and 9% wanted genetically related children, compared with 14% and 6% of those aged 26–34 years and 8% and 5% of those aged 35–44 years.

Table 2 shows results from the logistic regression model estimating the association between openness to having a child with one's own genetic material (response of "yes" or "unsure") and demographic variables. Male sex assigned at birth patients had 1.37 (95% confidence interval [CI]: 1.25, 1.41) times higher odds of reporting desire for genetically related children or being unsure about the desire for genetically related children at the time of intake compared with FSAB patients. Compared with those 35–44 years old, the odds of reporting desire for genetically related children or being unsure at the time of intake were 1.44 (95% CIs: 1.24, 1.67) times higher among those 18–25 years old and 0.42 (95% CIs: 0.36, 0.48) times lower among those 26–34 years old. Compared with those without insurance, the odds of reporting a desire for genetically related children or being unsure at the time of intake were 1.13 (95% CIs: 1.02, 1.37) times higher among those with private insurance. Compared with those in the southern region, the odds of reporting a desire for genetically related children were 1.24 (95% CIs: 1.10, 1.39) times higher in the west, 1.22 (95% CIs: 1.07, 1.40) times higher in the north, and similar in the Midwest region.

DISCUSSION

In this study of reproductive-age TGD adults seeking GAHT, over a quarter of the total sample reported desire for genetically related children or reported being unsure about the desire for genetically related children at the time of intake. To our knowledge, this is the largest sample of TGD adults reporting current desire for genetically related children when initiating GAHT. In our cohort, only a fraction of patients presenting for GAHT reported desire for genetically related children or were unsure, including patients who are in the dominant family-building years of the mid-twenties to thirties. Although this may reflect previously determined parenthood desires, patients who have already built their families or are interested in other paths to parenthood, it is notable that there was relative stability across age ranges regarding fertility desire, suggesting patients at different phases of their reproductive lives had similar perspectives. Previous research in TGD adolescents indicates that the desire and need of TGD patients for GAHT in the short term outweighs the potential fertility impact; this is particularly pronounced for FSAB patients (18, 26).

General attitudes in the US may also impact patients with TGD's desire for genetically related children. A population-based online survey of adults aged 18–75 years found 76% of respondents agreed that TGD Americans should be given options for genetically related parenthood, and 60% agreed

TABLE 2

Association between being open to having genetically related children and demographic variables.

Variable	Odds ratio	95% confidence interval		*P*-value
Sex-at-birth—male (reference: female)	1.37	1.25	1.51	<.001
Age group				
18–25 y	1.44	1.24	1.67	<.001
26–34 y	0.58	0.52	0.64	<.001
35–44 y	-			
Insurance type				
Private insurance	1.13	1.02	1.27	0.031
Medicaid	1.18	0.99	1.40	0.061
Unknown	1.28	1.09	1.49	<.001
Uninsured	-			
Region				
West	1.24	1.10	1.39	<.001
North	1.22	1.07	1.40	<.001
Midwest	0.99	0.86	1.15	0.979
South	-			

Kyweluk. Fertility desire among TGD patients. Fertil Steril Rep 2023.

FP should be offered to patients before initiating GAHT or other potentially fertility-compromising treatments (32). Qualitative research, including in-depth interviews, has explored parenthood and family formation desires and found patients with TGD have diverse preferences with respect to genetically related children, including coparenting arrangements, use of partner(s) as gestational carriers, and use of gametes from partner(s) or donor(s) (17, 19, 20, 24).

Our sample showed differences in the reported desire for genetically related children on the basis of insurance status and US region. Patients with private insurance were more likely to report desire for, or being unsure about the desire for, genetically related children than those without insurance. Insurance and/or socioeconomic status, as well as geographic differences impacting access to gender-affirming medical care and specialist reproductive endocrinology and infertility care, may influence observed differences in desire for genetically related children in patients from the west and north of the US. For example, the literature suggests that geographic and financial limitations on access to FP specialists and high costs for gamete retrieval and storage may be significant barriers to FP (26–28, 33). This likely contributes to the reported low utilization of FP by patients with TGD, including those treated in multidisciplinary care settings with access to counseling and referral to fertility medical services. Insurance mandates in several US states extending FP coverage to patients with GD pursuing GAHT are recent; their impact on patients with TGD decision-making has yet to be understood (28). Similarly, gestational surrogacy has only recently become a component of mainstream assisted reproductive technologies (ARTs) (34).

Practice guidelines recommend that health professionals provide information on fertility risks from gender-affirming medical interventions as well as a briefing on FP options before initiating GAHT (22, 23). Previous research indicates that providers in relevant specialties have reasonable levels of knowledge related to FP and ART but are not always comfortable providing fertility-related information to gender-diverse patients and lack formal training (27). Evolving research on the impact of GAHT on fertility—and on the necessity of discontinuing GAHT during fertility treatments—and the lack of research on the short-term vs. long-term impacts of hormone treatment on fertility can complicate patient education and counseling (7, 8, 35). Gender-affirming medical care that could impact fertility, including evolving surgical interventions for TGD patients—for example, FSAB patients retaining ovaries and pursuing phalloplasty—is also evolving (36). Suitable values-based assessments and educational tools for patients are needed to facilitate informed consent and discussions between patients with TGD and providers and have been explored in adolescents and young adults.

Strengths of this current study include the large sample size of patients with TGD and geographic diversity across the US, including several states where the availability of gender-affirming care providers is limited (37). Data were drawn from patients initiating GAHT using self-pay telehealth services; this may contribute to selection bias in this sample. Additionally, no information was available about patients' current partnership status, whether they already had genetically related children, adopted children, or were parenting children of a partner, and other details on family planning and desires. Our study team recognizes that genetically related family building is only one path to parenthood and that our data cannot be used to make assumptions about the broader parenting intentions of this population (24, 38). Further, adult patients who had been treated with puberty blockers during adolescence and were initiating GAHT may have different reported fertility desires than those who had not been treated with puberty blockers, although the proportion of these patients was likely small because only adult patients initiating GAHT for the first time were included in the present analysis and most adolescents would have typically initiated GAHT before the age of 18 years. Fertility preservation interest and

access were not assessed; patient's reported desire for genetically related children may be dictated by the expectation of logistical and/or financial access to FP, particularly given low reported rates of FP utilization in patients with TGD (26).

CONCLUSIONS

As the first large study to assess the desire for genetically related children in patients with TGD, we showed diverse desires across anatomies and age groups. Although access to ART and expansion of parenting options continue to influence parenting landscapes for patients with TGD, ours is the first study to show the range of fertility desire across a large sample of reproductive-age adults. Results indicate that many patients desire genetically related children or are unsure; patient desires should not be assumed, and the full range of family-building options should still be offered to all patients, regardless of SAB, age, gender identity, socioeconomic or insurance status, or existing parenthood status. Additional population-level data on transgender healthcare experiences and patient desires around fertility and family planning will have implications for both clinical practice and policy. Further investigation into the impacts of GAHT and other gender-affirming medical care on fertility, as well as up-to-date knowledge among providers on evolving fertility-related care guidelines and research on fertility outcomes for patients using GAHT, are necessary to provide evidence-led, high-quality, and timely counseling to TGD patients. Counseling on family-building goals and FP is a shared responsibility across primary care providers, specialists, including reproductive endocrinology and infertility specialists and obstetrics and gynecology providers, and providers in any setting who provide reproductive and sexual healthcare and/or gender-affirming medical care.

NOTES

As of December 2021, services were available in 33 US states (Arizona, Alabama, Arkansas, California, Colorado, Florida, Georgia, Iowa, Kentucky, Louisiana, Maine, Maryland Massachusetts, Michigan, Minnesota, Missouri, Nebraska, Nevada, New Jersey, New York, North Carolina, Illinois, Ohio, Oklahoma, Oregon, Pennsylvania, Texas, Tennessee, Vermont, Virginia, Utah Washington, and Wyoming). Because testosterone is a Schedule III controlled substance, Plume does not prescribe testosterone in 5 of these states (Minnesota, Utah, Arkansas, Louisiana, and Ohio) because these states' medical boards require an in-person clinical visit before prescribing. Clinicians provide services to patients in the state(s) where they are licensed.

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