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Continuation of Gender-affirming Hormones Among Transgender Adolescents and Adults FREE

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Abstract

Introduction

Concerns about future regret and treatment discontinuation have led to restricted access to gender-affirming medical treatment for transgender and gender-diverse (TGD) minors in some jurisdictions. However, these concerns are merely speculative because few studies have examined gender-affirming hormone continuation rates among TGD individuals.

Methods

We performed a secondary analysis of 2009 to 2018 medical and pharmacy records from the US Military Healthcare System. We identified TGD patients who were children and spouses of active-duty, retired, or deceased military members using International Classification of Diseases-9/10 codes. We assessed initiation and continuation of gender-affirming hormones using pharmacy records. Kaplan-Meier and Cox proportional hazard analyses estimated continuation rates.

Results

The study sample included 627 transmasculine and 325 transfeminine individuals with an average age of 19.2 ± 5.3 years. The 4-year gender-affirming hormone continuation rate was 70.2% (95% CI, 63.9-76.5). Transfeminine individuals had a higher continuation rate than transmasculine individuals 81.0%

(72.0%-90.0%) vs 64.4% (56.0%-72.8%). People who started hormones as minors had higher continuation rate than people who started as adults 74.4% (66.0%-82.8%) vs 64.4% (56.0%-72.8%). Continuation was not associated with household income or family member type. In Cox regression, both transmasculine gender identity (hazard ratio, 2.40; 95% CI, 1.50-3.86) and starting hormones as an adult (hazard ratio, 1.69; 95% CI, 1.14-2.52) were independently associated with increased discontinuation rates.

Discussion

Our results suggest that >70% of TGD individuals who start gender-affirming hormones will continue use beyond 4 years, with higher continuation rates in transfeminine individuals. Patients who start hormones, with their parents' assistance, before age 18 years have higher continuation rates than adults.

Keywords: transgender gender dysphoria, sex-hormones, treatment, adolescent, adult

Issue Section: Clinical Research Article

Approximately 1 in 250 adults or almost 1 million adults in the United States identify as transgender (1). The frequency of adults, and especially younger adults, reporting a gender-diverse identity has increased over time (1). Some persons who identify as transgender or gender-diverse (TGD) will seek treatment with gender-affirming hormones to align their bodies more closely with their gender identity (2). Medical treatment of people who identify as transgender improves body satisfaction, quality of life, and mental health (2, 3). However, many of these treatments are not entirely reversible (4).

Some adolescents or adults who take gender-affirming hormones subsequently elect to stop treatment (5, 6). Most adults who stop gender-affirming hormones report doing so for reasons unrelated to a change in gender identity, such as pressure from family, difficulty obtaining employment, or discrimination (7). Also, discontinuation of

gender-affirming hormones does not necessarily represent a failure in treatment or initial decision-making. Some TGD adolescents and adults who start and then discontinue gender-affirming hormones experience use of hormones as an important part of consolidating their gender identity and experience no regret over the use of hormones despite some permanent effects (5, 7, 8). However, a portion of TGD individuals who pursue gender-affirming medical or surgical affirmation do express regret over the permanent effects of treatment (5, 9, 10). In a metanalysis of 7928 TGD individuals who had gender confirmation surgery, 1% expressed regret after surgery (9). The most prevalent reason for regret was psychosocial circumstances, particularly from a lack of social support or negative reactions from family and employers (9). Concerns about future regret after medical or surgical affirmation and the capacity of adolescents to provide informed assent for this treatment, with the assistance of their families, have led legislators and members of the judiciary in some locations to attempt to limit access to these interventions for youths (11-14). For example, in the United States, 16 states do not provide coverage for gender-affirming medical care through public insurance for those with incomes below the federal poverty line (Medicaid). Two states have outlawed gender-affirming care for minors, another state has taken administrative action to classify gender-affirming medical care for minors as child abuse, and 20 state legislatures are considering laws to make some or all aspects of gender-affirming medical care for minors illegal during the 2022 legislative session (13, 14). In the United Kingdom, a court ruled that gonadotropin-releasing hormone analogues could not be administered to transgender patients younger than age 16 years without obtaining a court order and suggested that older TGD adolescents should be required to obtain a court order before starting gender-affirming hormones (12).

Clinical guidelines for medical affirmation of persons who identify as TGD suggest that the rate of "de-transition" among postpubertal adolescents and adults is rare, but few studies have assessed the actual rate of treatment discontinuation (6, 7, 10). In a cross-sectional study of a self-selected sample of 27 715 TGD adults in the United States, 61.9% reported a history of social affirmation (ie,

changing name, pronouns, appearance), 44.8% reported medical affirmation with hormones, and 19.5% reported surgical affirmation (7). A history of stopping affirmation and reverting to living in their sex assigned at birth for at least a little while was more common among people who only engaged in social affirmation (30.8%) than among people who had started medical (9.1%) or surgical (6.9%) affirmation (7). Among TGD adults who stopped affirmation, 82.5% reported at least 1 external factor, such as pressure from family and community or difficulty with employers as a reason to stop and 15.9% reported at least 1 internal factor, such as psychological distress and uncertainty or fluctuation in gender identity as a reason to stop. Only 5% of people who stopped affirmation reported stopping because they realized that changing gender was no longer desired. At the time of the survey, 68% of people who had discontinued affirmation had subsequently restarted (7). In a 1-year chart review of 174 adults treated at a national gender clinic in the United Kingdom, 12 (6.9%) patients discontinued medical affirmation during a 1-year period. Of these 12 patients, 4 later reengaged in gender-affirming care (6). At the Center of Expertise on Gender Dysphoria, a specialized gender clinic that provides > 95% of all gender-affirming medical and surgical care in the Netherlands, > 75% of TGD adults who started gender-affirming hormones between 1972 and 2014 had completed 1.5 years of gender-affirming hormones and met criteria for gonadectomy by the end of 2015 (10). However, this study did not assess hormone continuation rates directly.

Prior studies of treatment discontinuation rates among TGD adults undergoing medical affirmation have been limited to small samples of patients from specialized gender clinics who stopped coming in for appointments or a cross-sectional study of self-reported de-transition rates among adults who continue to identify as TGD and obtained hormonal therapy both in and outside the health care system (6, 7, 15). These studies found low levels of treatment discontinuation. The discontinuation that did occur was frequently temporary and unrelated to a change in gender identity. However, none of these studies have examined discontinuation rates among minors or assessed objective measures of medication continuation. Therefore, in the current study, we assessed the rate of treatment

discontinuation after starting gender-affirming hormones among TGD adolescents and adults and identified demographic groups at higher risk of discontinuation of gender-affirming hormones. We hypothesized that gender-affirming hormone continuation rates will not differ between individuals who start hormones before or after reaching the age of legal majority.

Methods

This study is a secondary analysis of US Military Healthcare System's (MHS) medical and pharmacy billing records from October 2009 to September 2018 for family members of active-duty service members. Data were extracted from the Military Healthcare Data Repository, which includes insurance billing records of all inpatient and outpatient care and outpatient prescriptions provided to individuals enrolled in the military's health care benefit (TRICARE) both domestically and abroad at military and civilian treatment facilities.

We used the following inclusion criteria for our study:

- The patient was a child or spouse of an active duty, retired, or deceased servicemember at the time of the initial TGD-related diagnosis
- Patient had 2 or more medical encounters for a TGD-related diagnosis on different days (International Classification of Diseases [ICD] codes: ICD-9 302.6, 302.85 302.50, 302.51, 302.52, 302.53, and ICD-10 F64.0, F64.1, F64.2, F64.8, F64.9, Z87.890)
- Patient received an initial prescription for gender-affirming hormones between 30 days before the date of their first TGD-related medical encounter and 90 days after their date of his or her last TGD-related medical encounter
- Patient received at least 2 prescriptions for gender-affirming hormones.

We excluded active-duty servicemembers and military retirees from our analysis because servicemembers are required to obtain

permission from the military service to transition while on active duty (16) and follow rules governing gender affirmation and use of gender-affirming hormones. We felt this would make them a distinctly different population from their family members and it would be inappropriate to combine them.

Use of ICD 9/10 codes to identify TGD individuals is a validated methodology. In a previous study, these codes were well-matched with clinical text notes in identification of TGD individuals (17, 18). We required patients to have 2 or more encounters with an associated TGD diagnosis to limit false-positive identifications.

We used medical and pharmacy records to identify TGD individuals who started gender-affirming hormones. We identified a TGD individual's sex assigned at birth using the sex recorded at the first encounter, for any reason, in our dataset. Then, we used pharmacy billing records to identify prescriptions and days supplied of gender-affirming hormones for both initial prescriptions and refills. We defined gender-affirming hormone prescriptions as prescriptions for testosterone issued to individuals coded as female at their first encounter and prescriptions for estrogens issued to individuals coded as male at their first encounter. We attempted to limit our sample to patients using gender-affirming hormones by requiring patients to obtain at least 2 prescriptions for gender-affirming hormones and obtain the initial prescription for gender-affirming hormones between 30 days before the date of their first TGD-related medical encounter and 90 days after their date of their last TGD-related medical encounter.

We collected patient age at the initial TGD-related encounter, age at the time of the first prescription for gender-affirming hormones, family role (spouse vs offspring), determined if the patient started gender-affirming hormones before or after gender-affirming health care became an officially covered military benefit for family members on September 1, 2016, and military rank of the insurance sponsor (16). We used military rank (enlisted vs officer) of the patient's insurance sponsor at the time of the last medical encounter in our dataset as a proxy for family income. Officers are required to have a 4-year college degree before military service, whereas enlisted servicemembers are

only required to have a high school degree or equivalent. Officers also have a higher average base pay than enlisted servicemembers. In 2019, the average base salary for servicemembers with 10 years of military service was $48 864 for enlisted servicemembers and $86 832 for officers (19).

We used Kaplan-Meier analyses to estimate the rate of discontinuation of gender-affirming hormones after starting treatment (20). We identified patients as discontinuing their gender-affirming hormones if they failed to obtain another prescription for gender-affirming hormones more than 90 days after completing their most recent prescription. Patients were censored from further analysis if they were no longer obtaining health care in the MHS (reached the date of their most recent medical encounter in the database).

We used the log-rank test to assess the influence of sex assigned at birth, age at initiation of gender-affirming hormones (< 18 years vs 18 years of age and older), family income (officer vs enlisted insurance sponsor), family role (spouse vs offspring), and if the patient started gender-affirming hormones before or after gender-affirming care became an official TRICARE benefit on September 1, 2016 (16). We limited our analysis of the influence of official insurance coverage to the first 22 months after starting gender-affirming hormones because we only had 22 months of data after the change occurred. We also used Cox proportional hazard analysis to determine the independent influence of our demographic factors on discontinuation rates. This study was institutional review board-approved as a secondary analysis of preexisting records. Statistical significance was defined as $P < 0.05$.

Results

Of the 952 individuals in our study, 66% were assigned female at birth, 61% were ≥ 18 years old, 71% had an enlisted insurance sponsor, and 90% were children of active duty, retired, or deceased servicemembers (Table 1, Fig. 1). Patients who discontinued obtaining refills of gender-affirming hormones continued to obtain medical

care in the MHS for an average of 324 days (SD, 274; range, 91-1602) after they completed their final prescription for gender-affirming hormones (Table 1). The number of patients initiating gender-affirming hormones increased during the study period, and 58% of patients had their first appointment for transgender-related care during the last 22 months of our study (September 2016-June 2018), after gender-affirming care was included as an officially covered TRICARE benefit for family members (14) (Table 1 and Fig. 2).

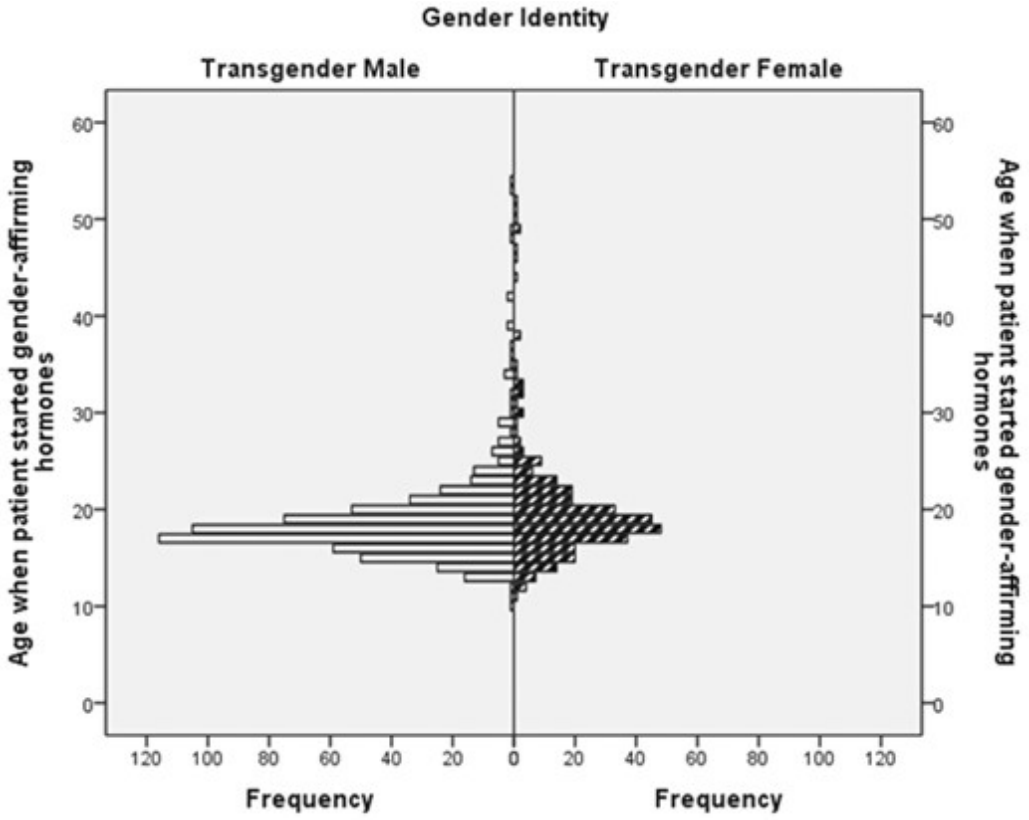
Table 1. Sample demographics (n = 952)

Demographic group	**%**
Gender identity	
Transfeminine	34.1
Transmasculine	65.9
Age at Initiation of Gender-Affirming Hormones	
<18 years old	39.1
≥18 years old	60.9
Insurance sponsor rank	
Enlisted (high school or some college)	70.6
Officer (college education and beyond)	29.4
Family member type	
Dependent child	90.1
Spouse	9.9
Started gender-affirming hormones before or after approval of gender-affirming care as an official TRICARE benefit	
Before approval (October 2009-August 2016)	42
After approval (September 2016-June 2018)	58.0

	Mean ± SD (range)
Days between stopping gender-affirming hormones and last visit	324 ± 274 (91-1602)

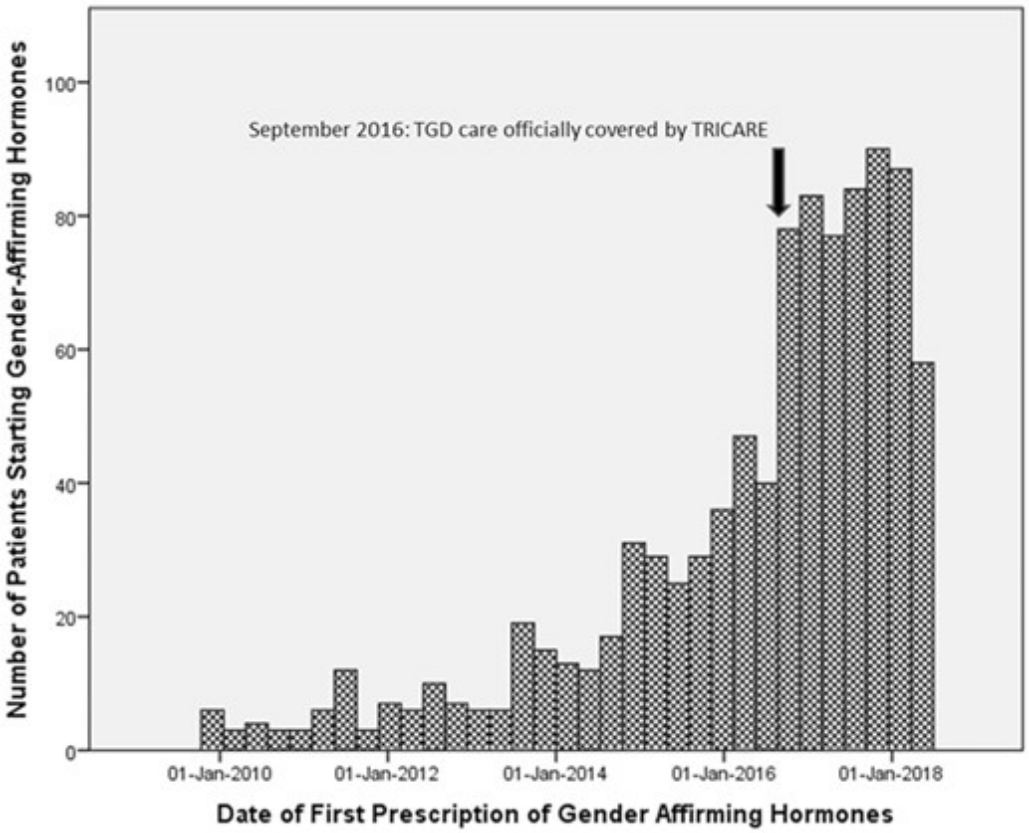
Gender-affirming medical care became an authorized TRICARE benefit for dependents on September 1, 2016.

Figure 1.



Age at initiation of gender-affirming hormones by sex assigned at birth.

Figure 2.

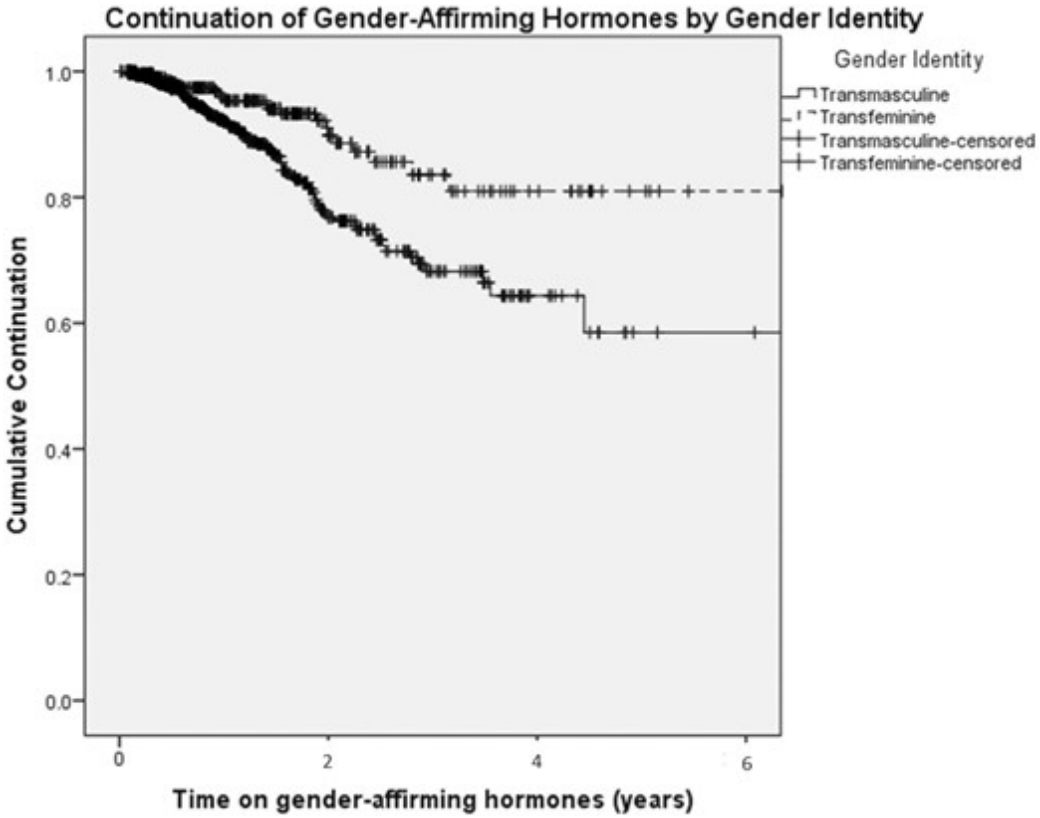


Incidence of gender-affirming hormone initiation over time.

In our sample, 70.2% (95% CI, 63.9-76.5) of patients who started medical affirmation continued to fill prescriptions for gender-affirming hormone for at least 4 years (Fig. 1). Transfeminine individuals were more likely to continue obtaining gender-affirming hormones in the MHS than transmasculine individuals. The 4-year continuation rate for transfeminine individuals was 81.0% (95% CI, 72.0-90.0) vs 64.4% (95% CI, 56.0-72.8) for transmasculine individuals (log-rank test χ^2, 11.860) (Fig. 3). Patients who were younger than 18 years of age when starting hormones were less likely to discontinue use than patients who were 18 years of age and older. The 4-year continuation rate among people who started treatment under 18 years of age was 74.4% (95% CI, 66.0-82.8) and the rate among people who were ≥ 18 years was 64.4% (95% CI, 56.0-72.8) (log-rank test χ^2, 4.461) (Fig. 4). Family income (enlisted vs officer insurance sponsor; log-rank test χ^2, 0.013) and family member type (spouse vs child; log-rank test χ^2, 1.002) had no influence on continuation rates. Starting hormones before or after official

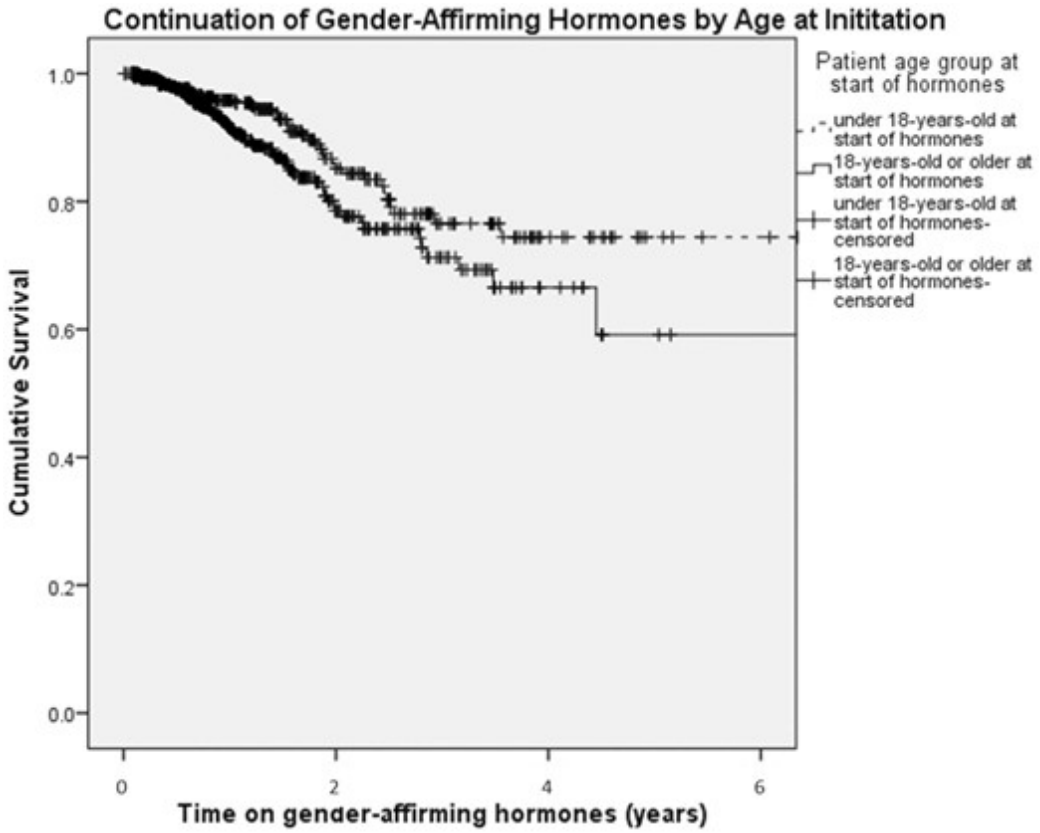
coverage of gender-affirming medical care by TRICARE on September 1, 2016, also had no influence on continuation rates (log-rank test χ^2, 0.728).

Figure 3.



Continuation of gender-affirming hormones by gender identity.

Figure 4.



Continuation of gender-affirming hormones by age at initiation.

In a Cox regression model containing assigned gender and age at initiation of hormones, transmasculine individuals were more than twice as likely to stop obtaining hormones in the MHS compared with transfeminine individuals (hazard ratio 2.40; 95% CI, 1.50-3.86) and people who started hormones after turning 18 years of age were more likely to stop obtaining gender-affirming hormones compared with people who started hormones before age 18 years (hazard ratio, 1.69; 95% CI, 1.14-2.52) (Table 2).

Table 2. Multivariate regression: independent association of age and gender identity on discontinuation of gender-affirming hormones

Demographic factor	Risk of discontinuing of gender-affirming hormones
Gender identity	Hazard ratio (95% CI)
Transfeminine	Reference

Transmasculine	2.40 (1.50-3.86)
Age at initiation of gender-affirming hormones	
<18 years old	Reference
≥18 years old	1.69 (1.14-2.52)

Discussion

Our study documented higher gender-affirming hormone continuation rates among transfeminine individuals and by patients who started hormones before reaching the age of legal majority in a population with universal insurance and access to low or no-cost medical and pharmaceutical care. Family socioeconomic status, family member type, and the official status of gender-affirming care as a TRICARE-covered benefit at the time the patient began taking gender-affirming hormones had no influence on continuation of gender-affirming hormones.

We noted a higher hormone continuation rate among TGD individuals who were younger than 18 years old at the time of first use of gender-affirming hormones compared with those who were aged 18 years and older when starting hormones. This has not been documented in previous studies.

The patients who started before turning 18 years would require parental consent for this treatment, whereas those aged 18 years and older do not. Parents who consent to use of gender-affirming hormones likely have a higher level of support for their child's gender affirmation on average than parents who do not. Parental support plays an important role in the mental health of TGD youth (21). A prior study of adults found that lack of family support for a TGD individual's gender was associated with a history of discontinuing social or medical gender affirmation (7). Higher parental support may explain the higher continuation rate among patients who start gender-affirming hormones as minors compared with people who start as adults.

Regardless of the reason for the higher hormone continuation rate among TGD youth, this finding provides support for the idea that TGD individuals below the age of legal majority, with the assistance of their parents or legal guardians and health care providers, can provide meaningful informed assent for gender-affirming hormones and do not appear to be at a higher risk of future discontinuation of gender-affirming hormones because of their young age alone.

There was a higher gender-affirming hormone continuation rate among transfeminine individuals compared with transmasculine individuals in our study. This has not been observed in previous studies. The reasons for this difference cannot be determined using the data from this study. If confirmed in future studies, this would suggest a need to ensure routine screening of transmasculine patients for osteoporosis risk after oophorectomy, especially if this procedure occurs at a younger age.

As in a previous study, there was an increase in the number of patients presenting for gender-affirming care over time (10, 22). However, unlike previous studies, the coverage status of gender-affirming care in our study changed over time. We noted a large increase in patients presenting for care after designation of gender-affirming care as a covered benefit in the MHS.

This leads to a concern that patients and providers who were engaging in gender-affirming care in the MHS before it was officially sanctioned were different than the patients and providers who did not start engaging in gender-affirming care in the MHS until after it was officially sanctioned. However, we did not see a difference in continuation rates between these 2 groups.

The large number of adolescents in our study, the longitudinal data for TGD individuals in a naturalistic and varied clinical setting, use of objective measures of ongoing hormone use, and comparison of gender-affirming hormone use among adolescents and adults are unique strengths of our study, but there are several limitations that must be noted.

We only collected information on medication refills obtained using a single insurance plan. If patients elected to pay out of pocket for

hormones, accessed hormones through nonmedical channels, or used a different insurance plan to pay for treatment before and/or after obtaining gender-affirming hormones using TRICARE insurance, we did not capture this information. This means that our findings are likely an underestimate continuation rates among transgender patients.

We attempted to address our concern about overestimating discontinuation rates by only recording cessations among patients who stopped obtaining prescriptions for gender-affirming hormones while continuing to receive medical care using TRICARE insurance for more than 90 days. We would miscategorize patients as terminations if patients elected to obtain their gender-affirming medications using alternative payment options while continuing to receive other medical care using TRICARE.

However, the medication copay for generic medications purchased using TRICARE is quite low at $0 to $3 per prescription when compared with other private insurance programs in the United States. For example, a transgender woman using TRICARE insurance would pay a total of $0 to $72 for a 1-year supply of estrogen and spironolactone. For transgender women with private insurance in the United States, the out-of-pocket expenses for gender-affirming medications would be $230 per year and $500 per year for transgender men with insurance (23). This cost difference makes it less likely that a patient would continue to use TRICARE for medical care but elect to use a different insurer to obtain gender-affirming hormones.

This study was limited by reliance on accuracy of billing data and lack of patient-level data. We cannot know why patients in our study stopped obtaining refills of gender-affirming hormones using their TRICARE insurance. Many factors inform an individual patient's desire or ability to continue obtaining refills of gender-affirming hormones including gender identity, treatment intentions, difficulty finding a provider who offers gender-affirming care, satisfaction with treatment outcomes, or social context.

In a previous study, only 16% of TGD individuals who stopped gender-affirming hormones cited a change in gender identity or

mental health concerns as a reason to discontinue social or medical gender affirmation (7). Many of the individuals who reported stopping gender-affirming hormones reported subsequently restarting treatment or the intention to restart treatment (7).

The lack of patient level detail in our study makes it impossible to predict individual patient outcomes with our findings. However, our findings can still be useful to inform policy makers or legislators when assessing the risk of transgender care for minors.

A related limitation is our reliance on the gender marker at the first medical encounter as a proxy for sex assigned at birth. It is possible that this information is wrong or reflects a change in gender marker that occurred before the beginning of our study interval. We attempted to address this concern using our inclusion criteria. For example, with our inclusion criteria, we would incorrectly include a cis-male patient who was assigned male at birth, changed the sex recorded in the electronic medical record to female, received a transgender-related diagnosis at 2 different medical encounters, and then elected to fill 2 prescriptions for testosterone during the same time period he had the 2 transgender-related medical encounters. This combination would likely be a rare event and, if present, have a minimal impact on the findings of the study.

Before September 2016, gender-affirming care was not an officially covered health care benefit under TRICARE (16). Patients may have had trouble finding a TRICARE-approved clinician who would prescribe hormones or a pharmacy that would fill the prescription in their area, especially in cases where they initiated care in 1 location and then they or their family moved. However, we did not see a difference in continuation rates between patients who started hormones before or after gender-affirming care becoming an officially covered benefit.

Determining if these differences in continuation rates exist in other groups of TGD individuals and determining if there are differences in reasons for discontinuation by gender identity or age is an important topic for future studies. Future prospective studies should investigate the rate of hormone discontinuation between transfeminine and transmasculine individuals to determine whether the same pattern of

discontinuation is observed. The reasons for discontinuing treatment and whether patients anticipate restarting treatment at a future date would also be important to assess. Finally, it would be useful to prospectively assess the number of TGD individuals who experience regret after starting gender-affirming hormones and if there are any associated factors that can be used to identify patients at a higher risk of regret. This would assist clinicians in providing nuanced counseling regarding treatment options to TGD individuals before starting hormones.

Conclusion

In our study, transmasculine individuals were more likely to discontinue use of gender-affirming hormones during the first 4 years of use than transfeminine individuals. We also found that individuals who start gender-affirming hormones before reaching the age of legal majority are less likely to subsequently discontinue use when compared with individuals who start hormones after becoming a legal adult. If replicated in future studies, the improved continuation rate among patients who are not legal adults at the time of treatment should provide some reassurance to those concerned about the ability of minors to provide informed assent to use of gender-affirming hormones. A higher continuation rate among minors could also be used to inform the actions of legislators and judges who wish to prohibit gender-affirming treatment for minors to protect them from the consequences of health care decisions they make with the assistance of their parents and health care providers.

Abbreviations

ICD International Classification of Diseases

MHS Military Healthcare System

TGD transgender and gender-diverse

Acknowledgments

The contents of this article are solely the responsibility of the authors and do not necessarily represent the official views of the Uniformed Services University, the US Air Force, the US Navy, the US Department of Defense, or the US Government.

Disclosures

The authors report no competing interests.

Data Availability

A deidentified copy of the dataset for this study is available from the authors on reasonable request

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