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# Low Fertility Preservation Utilization Among Transgender Youth

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#### ABSTRACT

**Purpose:** Research demonstrates a negative psychosocial impact of infertility among otherwise healthy adults, and distress among adolescents facing the prospect of future infertility due to various medical conditions and treatments that impair reproductive health. Guidelines state that providers should counsel transgender youth about potential infertility and fertility preservation (FP) options prior to initiation of hormone therapy. The purpose of this study was to examine the rates of fertility counseling and utilization of FP among a cohort of adolescents with gender dysphoria seen at a large gender clinic.

**Methods:** An Institutional Review Board—approved retrospective review of electronic medical records was conducted of all patients with ICD-9/10 codes for gender dysphoria referred to Pediatric Endocrinology for hormone therapy (puberty suppression and/or cross-sex hormones) from January 2014 to August 2016.

**Results:** Seventy-eight patients met inclusion criteria. Five children were prepubertal, no hormone therapy was considered, and they were therefore excluded. Of the remaining 73 patients, 72 had documented fertility counseling prior to initiation of hormone therapy and 2 subjects attempted FP; 45% of subjects mentioned a desire or plan to adopt, and 21% said they had never wanted to have children.

**Conclusions:** Utilization rates of FP are low among transgender adolescents. More research is needed to understand parenthood goals among transgender youth at different ages and developmental stages and to explore the impact of gender dysphoria on decision-making about FP and parenthood. Discussions about infertility risk, FP, and other family building options should be prioritized in this vulnerable adolescent population.

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# IMPLICATIONS AND CONTRIBUTION

About 98.6% of transgender adolescents (n = 72) at a large pediatric academic center were counseled about infertility risk due to hormone treatment yet only two attempted fertility preservation. Parenthood goals need to be explored among transgender youth at different ages/developmental stages, to optimize care and prevent potential regret about missed opportunities.

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Approximately 6.7 million women and 3.3—4.7 million men in the United States experience fertility impairment [1], which has been shown to negatively impact quality of life and psychosocial well-being [2,3]. Although the majority of research regarding fertility in pediatrics has been conducted in oncology, a significant subset of fertility problems may result from other

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pediatric medical conditions and/or therapies prescribed in childhood/adolescence as well, including cross-sex hormone therapy for transgender youth. In this context, there is an emerging need for pediatric providers to initiate discussions about infertility risk and fertility preservation (FP) options with these at-risk or high-risk youth and their families [4]. Established FP methods exist for postpubertal males (sperm cryopreservation) and postmenarchal females (oocyte and embryo cryopreservation), with experimental options available for younger children (e.g., testicular and ovarian tissue cryopreservation) [5,6]. Several groups, including the American Academy of Pediatrics, American Society for Reproductive Medicine, and American Society of Clinical Oncology, have published guidelines urging providers to counsel patients about fertility risks and refer to reproductive specialists to discuss FP options prior to initiation of treatment [6-8].

Long-term follow-up studies show childhood cancer survivors express distress about potential infertility due to cancer treatment and regret about missed opportunities for FP [9-11], leading to initiatives designed to improve access to FP for newly diagnosed cancer patients [12]. As guidelines have recently been updated to expand fertility counseling beyond cancer [6,13,14], one area of particular emphasis has been on youth with gender dysphoria because these individuals often experience discrimination, limited access to medical services, and psychosocial difficulties [15,16]. Gender dysphoria is a condition in which an individual experiences distress due to discordance between the gender assigned at birth and the gender with which he or she identifies; many of these individuals identify as transgender. Mental health conditions including depression, anxiety, posttraumatic stress disorder, self-harm, and suicidal ideations/attempts are commonly seen in transgender youth [15,17]. Hormone therapy is used to help alleviate gender dysphoria and allow transgender youth to achieve physical changes consistent with their affirmed gender, with puberty blockers initiated in early puberty, and then cross-sex hormone therapy (testosterone or estrogen) in later puberty [18]. Long-standing exposure to these hormones may impact both spermatogenesis and oocyte production and may be followed by surgery to remove reproductive organs; thus, the Endocrine Society, World Professional Association for Transgender Health, and American Society for Reproductive Medicine guidelines emphasize the importance of counseling about infertility risk and offering FP prior to therapy [7,18-20].

Despite emerging literature about family planning among transgender individuals, little is known about fertility-related attitudes and parenthood goals among transgender youth or adults [21]. Two survey studies were conducted among transgender adults in Belgium, in which both transgender males and females expressed a desire for biological children and many stated that they would have considered FP had it been offered [22,23]. However, other smaller studies suggest that transgender adults and others in the sexual and gender minority community are less likely to envision biological parenthood [24,25]. Notably, there have been no studies among transgender youth with regard to attitudes toward fertility, parenthood, and FP. With puberty blockers often prescribed at the onset of puberty, as early as 8–11 years of age, and an increasing number of clinical programs offering cross-sex hormone therapy at 13-14 years of age [26], it remains unclear if and how transgender youth consider future parenthood and whether or not they choose to utilize FP technologies prior to hormone therapy. The goal of this study was to

assess FP utilization/consideration among transgender youth prior to starting hormone therapy at a large pediatric academic center.

#### Methods

An Institutional Review Board—approved retrospective review of electronic medical records was conducted at a single large pediatric academic center, of all patients with ICD-9/10 codes for gender dysphoria referred to Pediatric Endocrinology for hormone therapy (puberty suppression and/or cross-sex hormones), from January 2014 (when a structured gender management program was established) to August 2016. Because of the nature of the study, informed consent was waived. A standardized abstraction form was used by a trained investigator and physician to collect the following information from documentation in the patients' electronic medical records: age and Tanner stage at the Endocrinology visit where hormone therapy was discussed, gender assigned at birth, affirmed gender, initiation of hormone therapy (GnRH analogue and/or cross-sex hormone), documentation of fertility counseling including whether FP had been offered and pursued, reasons for declining FP (if available), mental health morbidities, and information about legal guardians/adoptive status. When abstracting information, the study team reviewed all clinical encounters and medication orders in each patient's chart.

## Fertility counseling practices

All patients were diagnosed with gender dysphoria by a child psychiatrist and subsequently referred to one of two pediatric endocrinologists specializing in care of transgender youth. During each new patient visit, the pediatric endocrinologist and a social worker met with the patient and family to review risks/ benefits of hormone therapy and provide comprehensive fertility counseling, including discussions about potential risk of infertility due to hormone therapy, a review of established FP options including sperm banking or oocyte preservation, and an estimated cost of these options (including the fact that procedures may not be covered by insurance). For pubertal transgender females, a referral to the local sperm bank was offered for collection of a semen sample via masturbation. In cases where an adolescent expressed interest in FP but discomfort with masturbation, testicular sperm extraction was also offered. Postmenarchal transgender males were offered a referral to a reproductive endocrinologist at a nearby practice to discuss oocyte preservation in more detail. All youth were informed that pursuing FP after beginning puberty blockers or cross-sex hormone therapy would require cessation of hormone therapy and may require further progression of natal puberty. At the end of the visit, a summary of information was provided in writing (treatment consent forms to be signed by patients and parents). If within the next 2-4 weeks, the adolescent declined FP and wished to start hormone therapy, the appropriate treatment was prescribed, and signed treatment consent forms were scanned into the medical record.

# Data analyses

Data analyses were performed using SPSS version 21.0 (IBM Corp, 2012). Descriptive statistics were used to summarize characteristics of the study sample, documentation of fertility counseling prior to treatment (yes vs. no), and utilization of FP (yes vs. no). Pearson's chi-square test and Fisher's exact test were used to

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assess for differences with regard to reasons for declining FP, based on gender, history of mental health diagnoses, and adoptive status.

#### Results

# Sample characteristics

Seventy-eight subjects met the inclusion criteria, all of whom had been diagnosed with gender dysphoria by a child psychiatrist with subsequent referral to Pediatric Endocrinology for hormone therapy. Five children were prepubertal based on the pediatric endocrinologist's examination, so no hormone therapy was considered, resulting in a sample of 73 subjects for the analysis (50 transgender males and 23 transgender females). Median age at first Endocrinology visit was 15.2 years (range 9–18 years). Median age at which puberty blockers and cross-sex hormone therapy were prescribed was 15.0 (range 9–18 years) and 16.0 (range 14–18 years), respectively.

# Fertility preservation utilization

A treatment plan was determined based on age and pubertal stage of the patient according to Endocrine Society guidelines [18], though many adolescents were ultimately started on cross-sex hormones without prior pubertal suppression due to lack of insurance coverage for GnRH analogues. Seventy-two of 73 subjects (98.6%) had documented fertility counseling provided by the pediatric endocrinologist prior to initiation of any therapy; 91% of transgender females had progressed beyond Tanner stage 2 and were offered an opportunity to bank sperm; 96% of transgender males were postmenarchal and were offered a referral to a reproductive endocrinologist at a nearby fertility practice.

Twenty-seven subjects (Tanner 2–5) had a GnRH analogue prescribed for pubertal suppression. In one case, although the patient had gender dysphoria on presentation, the primary indication for treatment was actually precocious puberty; in this case, there was no documented fertility counseling prior to treatment. The indication for treatment was gender dysphoria in the other 26 cases, all of these records contained documentation of the potential for infertility in the event that the patient was to progress directly to cross-sex hormones. Forty subjects had cross-sex hormones (testosterone or estrogen) prescribed (all Tanner 4–5), and in all cases, there was documentation of the potential for infertility after beginning cross-sex hormone therapy. In the remaining cases, no medication had yet been prescribed.

Of the entire group where fertility counseling was documented (N=72), two subjects opted to attempt FP (both transgender females): one produced a sample with low volume and no viable sperm (age 13 years, testes 10 mL) and the other produced a sample with viable sperm that was banked (age 15 years, testes 15–20 mL). The other 70 patients declined to consider FP interventions.

## Reasons for refusal

At least one reason for declining FP was documented in 74% of subjects who were offered fertility counseling; 45.2% of subjects mentioned that they were considering/planning to adopt (38.1% of transgender females; 50% of transgender males, p=.256); 21.9% stated "I never want to have children" or "I have never wanted to have children" (38.1% of transgender females; 16% of transgender males, p=.045); 8.2% reported that FP would be too

expensive (4.8% of transgender females; 10% of transgender males, p=.422); 1.4% reported that masturbating to produce a semen sample would be too uncomfortable; 1.4% reported that they were unwilling to undergo FP due to concern about potentially delaying hormone treatment.

## Mental health morbidities and adoptive status

Of the youth in our sample, 92.3% had one or more of the following psychiatric diagnoses (past or current): major depressive disorder, bipolar, generalized anxiety disorder, social anxiety, and/or post-traumatic stress disorder (Nahata L, Quinn GP, Caltabellotta NM, Tishelman AC, unpublished data, October 2016). No differences in reasons for FP refusal were noted between those with or without documented mental health conditions. Out of 73 subjects, 15 were noted to have been adopted or living in foster care (20.5%). There was no association between adoptive status and reasons for FP refusal, that is, the percentage of subjects who mentioned they wanted to adopt did not differ by adoptive status (p = .196).

#### Discussion

This study shows low FP utilization rates in transgender youth seeking hormone therapy. Of 72 patients, only 2 patients (both transgender females) attempted FP. This is despite the fact that all of the patients for whom hormone therapy was prescribed for gender dysphoria were told about the risk of infertility and offered options for FP/referral to a fertility specialist, as per recommendations from various organizations and recent literature [18–20,26]. Of note, in prior adult studies, 51% of transgender females would have considered sperm banking if it had been offered [22]; 54% of transgender men reported a desire for children, and 37.5% would have considered freezing germ cells had it been offered [23]. At that same center, 15% of transgender women seen in 2011 reportedly chose to store their sperm [27]. This discrepancy between our findings and these studies raises a question as to whether these transgender youth may change their perspectives about FP later in life, particularly after transitioning to their affirmed gender. Alternatively, our study sample may be more similar to the cohorts from the smaller studies showing that transgender adults and others in the sexual and gender minority community have less desire for biological children than adults outside of this community [24].

Although single case reports/series of FP in transgender youth have been published [14], the majority of information about FP in pediatrics has been obtained in other patient populations, such as adolescent and young adult (AYA) cancer survivors. Surveys, semi-structured interviews, and focus groups have shown that both male and female AYA cancer survivors report a desire for biological children and express disappointment, anger, and regret about missed opportunities for FP prior to starting cancer therapy [10,11]. Even studies done at the time of cancer diagnosis show that AYA rank fertility as a priority [9]. However, FP remains underutilized, with  $\sim$  25% of pubertal males newly diagnosed with cancer in the United States opting to bank sperm [28], and often lower cryopreservation rates reported among female cohorts [29]. Although research has shown that the development of structured programs and informational brochures has helped increase referral rates and patient satisfaction with regard to fertility [30], barriers such as cost/lack of insurance coverage for FP, inadequate provider knowledge, severe illness, fear of recurrence and early mortality, and inadequate time to complete FP procedures are all ongoing problems in children and AYA with cancer [31].

Transgender youth and AYA have self-reported some of these same barriers as well (such as cost), but given the significantly lower FP rates in this transgender cohort compared to FP rates in AYA with cancer, other factors such as dysphoria about one's body and/or mental health morbidities may contribute to lower rates of FP utilization among transgender youth. Notably, nearly one-fourth of the subjects with a documented reason for declining FP stated that they "never wanted to have children." This was noted more frequently in those identifying as female, which is interesting and a topic for further investigation. Despite the fact that youth in general may have difficulty envisioning future parenthood, it is uncommon to see reports of adolescents in other populations commenting that they know they "do not ever want to have children." In fact, a study about perceptions of fertility among healthy, cisgender, and teen girls (in a similar age range to our cohort) showed they already had strong thoughts about having children in their future [32]. This discrepancy raises questions about differences between transgender and cisgender youth with regard to parenthood desires.

A number of hypotheses for the low FP utilization rates in transgender youth can and should be prioritized for future research. These may include the impact on decision-making of the mental health morbidities reported in our cohort and in other studies, such as low self-esteem, depression, self-harm, and suicidality [16,33]. All of these factors can be linked to a sense of a foreshortened future and hopelessness regarding potential for adult happiness and family satisfaction. In addition, many transgender youth experience family disruption and outright rejection, which could also impact desire for parenthood [34,35]. Notably, transgender youth experience body dysphoria at high rates and often report a strong desire to undergo medical interventions to alter or remove body parts inconsistent with their affirmed gender [36] and may therefore be reluctant to engage in any thoughts or actions that involve sex and genderassociated internal or external anatomy. Some transgender adolescents may feel pressured by societal expectations of what a family unit should encompass and thus discount the idea of being a mother or father [21]. Finally, some youth presenting in gender clinics may feel an urgency to obtain hormonal intervention to reduce gender dysphoria, and these feelings may override other considerations.

According to the World Professional Association for Transgender Health guidelines, one of the roles of the treating mental health practitioner is to assess whether mental health comorbidities are interfering with an individual's ability to make treatment decisions, including those related to hormone therapy and FP [19]. In these situations, it is imperative that the multidisciplinary team (e.g., endocrinologist, psychologist/psychiatrist, social worker, and/or therapist) work together to ensure that optimal care is provided and that the patient and family are fully informed about long-term risks of medical treatment and all potential options prior to initiating therapy. In some cases, it may be important to directly assess whether mental health factors may be detrimentally impacting decision-making and even check back with patients about fertility preferences soon after hormonal treatment is initiated, when gender dysphoria and related mental health risks may be reduced, and discussions about FP preferences can be revisited.

Almost half of the subjects mentioned a desire or plan to adopt. However, the reasons for adoption preference versus a

desire for biological children were not elaborated and therefore not available in the medical record. Transgender youth may have difficulty envisioning having a biological child with anatomy/gametes with which they do not identify. This concern was reported in the previous adult transgender surveys, though many of those respondents said they would still like to have biological children, raising a question about a potential shift in the perceived pros/cons in these different age groups [22,23]. Limited available data suggest adoption is more common for transgender youth populations than for the general population [37]; it could be plausible that those who have been adopted themselves may view adoption as a more palatable or positive parenthood option than youth who are raised with biological parents (thus leading to lower desire to participate in FP), but our data did not show any association. Given that cost is often mentioned as a barrier to FP (though less so in this study), discussions about cost and logistics of adoption should routinely occur as well. Some youth and families may not be fully informed and/or have realistic expectations of the adoption process, and there have been cases of transgender persons experiencing difficulty when attempting to adopt [21,38]. There may be other factors explaining this preference for adoption, and this should be a high priority topic for future research.

Another factor that was mentioned, though much less frequently, was the physical discomfort among natal males, with masturbating for a semen sample. Providers should become educated in order to counsel patients and families about other options for FP, such as testicular sperm extraction or electroejaculation stimulation [39]. Although our center does not offer electroejaculation, testicular sperm extraction is an option, though was not chosen by any of the patients/families in this study. Finally, although this was only provided as a reason for declining once in this study (in a patient who had already completed puberty), some transgender youth may feel that attempting FP will delay initiation of hormone therapy. It is important to emphasize that FP may require only 24–48 hours for a transgender female and 1–2 weeks for a transgender male. Again, it may be valuable to check back in with youth and family soon after the initiation of hormonal interventions, as perspectives may alter when the urgency to receive intervention subsides. Situations in which a child is just starting puberty may present significant challenges, however, since more time would be needed in order to be a candidate for established FP options.

This study was done at a single institution, limiting the generalizability of our findings. Additionally, its retrospective nature limited our ability to obtain more details about the decision-making process about FP, such as the parents' perspectives or other perceived benefits/barriers to FP, or information such as sexual orientation of subjects which could impact family-building decisions. Additionally, we could not determine whether mental health diagnoses were past or current/active. Despite these limitations, to our knowledge, this is the first study in which FP utilization has been examined among transgender youth and emphasizes the need for prospective studies in this area. Although many of the patients in this study were not treated with GnRH analogues at the early stages of puberty due to lack of insurance coverage and/or seeking care at a later age. this may change over time and as a consequence, children and families may be faced with decisions about FP at even earlier ages/developmental stages.

In conclusion, although recent editorials and guidelines make statements that transgender adults have the same desire for L. Nahata et al. / Journal of Adolescent Health xxx (2017) 1-5

biological children as cisgender adults [20], there is little evidence to support this assertion, and the available data are mixed [22–24,33]. More research is needed to examine parenthood goals among transgender youth and adults, to understand whether attitudes regarding fertility and parenthood persist or change as individuals get older and transition to their affirmed gender. Perceived benefits and barriers to FP should be explored, in addition to assessing factors impacting decisions to pursue FP, including the role of providers, caregivers, and romantic partners, and the potential association with psychosocial comorbidities.

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