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REVIEW ARTICLE

Reproductive health in transgender and gender diverse individuals: A narrative review to guide clinical care and international guidelines

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ABSTRACT

Background: Hormonal treatments and surgical interventions practiced with the aim to affirm gender identity in transgender and gender diverse patients may impact their future reproductive ability, family building, and family planning options. Whereas it is recommended by international guidelines to discuss the potential risks of infertility and to present fertility preservation (FP) options to transgender individuals and their families prior to initiating any of these treatments, many barriers still remain. Further, transgender and gender diverse individuals often experience barriers to accessing contraception, abortion, pre-conception care, and comprehensive perinatal care.

Aims: In this review we summarize the current literature on reproductive healthcare issues reported in transgender people including fertility issues, fertility preservation (FP), contraception, pregnancy and lactation and perinatal health.

Methods: A narrative literature search of major databases (Pubmed, Medline, PsycInfo, Google Scholar, Web of Science) was conducted. Given the paucity and heterogeneity of studies, summative review tactics were not available. The literature was critically reviewed by international experts in the field with focus on the impact of gender-affirming medical interventions on future fertility, current FP options and reproductive health issues in transgender people.

Results: The current literature supports that transgender and gender diverse individuals may wish to have genetically related children in the future, rendering the issue of FP relevant to this patient group. The cryopreservation of mature gametes is an efficacious option for FP for post-pubertal adolescents and adults. It is recommended to discuss these options at time of planning for gender-affirming hormonal therapy (GAHT) or engaging with other gender-affirming procedures that can limit future fertility. Discontinuation of GAHT may allow individuals to undergo FP later, but data are limited and there is the concern of symptoms and consequences of stopping GAHT. For pre-pubertal and early pubertal children, FP options are limited to the cryopreservation of gonadal tissue. At present the tissue can become functional only after re-transplantation, which might be undesirable by transgender individuals in the future. Preconception counseling, prenatal surveillance, perinatal support, contraceptive, and pregnancy termination related healthcare need to be meaningfully adapted for this patient population, and many knowledge gaps remain.

Discussion: Specialized FP reproductive healthcare for transgender and gender diverse individuals is in early evolution. Research should be conducted to examine effects of medical interventions on fertility, timing of FP, gamete preservation and outcome of the fertility treatments. Strategies to inform and educate transgender and gender diverse patients can lead to optimization of reproductive care and counseling and decision making of FP for this population.

KEYWORDS
Abortion; cryopreservation; fertility preservation; gender-affirming hormone therapy; infertility; oocytes; pregnancy; sperm; transgender

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Introduction

Gender affirming hormone treatments and surgical interventions provided to transgender and gender diverse people to align their bodies with their gender identity may limit or alter future reproductive options to varying degrees. It is therefore highly recommended to discuss the risk of infertility inherent to these interventions, as clearly stated in the current guidelines for gender-affirming medical treatment from the World Professional Association for Transgender Health (WPATH) (Coleman et al., 2012) and the Endocrine Society (Hembree et al., 2017). For individuals facing treatments that can affect their fertility potential several options for fertility preservation (FP) have been developed. The most used and available at nearly all reproductive medicine clinics worldwide include the cryopreservation of embryos, oocytes, and sperm, which can be offered to adult patients. These methods may be also applicable to post-pubertal adolescents (Nahata et al., 2019; Rodriguez-Wallberg et al., 2019a). Research protocols for ovarian and testicular tissue cryopreservation have also been developed at some centers and these methods can be also applied in children (Borgström et al., 2020; Nahata et al., 2019; Rodriguez-Wallberg et al., 2019a, 2019b).

Most of the reported data on FP in young patients and children have been provided by programs developed for patients with cancer undergoing gonadotoxic therapies, but the number of indications to preserve fertility have rapidly increased over the years, including also benign diseases and genetic conditions (Rodriguez-Wallberg et al., 2019a). The use of embryos, mature oocytes and sperm have all proven to be efficacious when used in assisted reproductive treatments (ART). Recently, the cryopreservation of mature (postpubertal) ovarian tissue has also become a straightforward technique and is no longer considered experimental (Practice Committee of the American Society for Reproductive Medicine, 2019). However, the future use in several patient populations is quite challenging and thus is still considered experimental in some settings. Indeed, future re-transplantation of gonadal tissue aiming at obtaining fully functional gametes is the standard utilization of the cryopreserved tissue. Additional methods that are also suitable for patients that cannot be recipients of the ovarian tissue transplant, due to risk of reintroducing malignant cells in case of cancer, or because the transplant is undesirable, such as the use of laboratory methods for culture of gametes aiming at *in vitro* maturing gamete cells up to maturation, are under development (Practice Committee of the American Society for Reproductive Medicine, 2019; Telfer & Andersen, 2021; Wyns et al., 2020).

In the case of prepubertal children, although no longer technically experimental, gonadal tissue cryopreservation remains a difficult decision to make. This is owing to the fact that the true capacity for the residing ovarian primordial follicles to mature to their full capacity after transplantation has not been shown (Anderson et al., 2020; Practice Committee of the American Society for Reproductive Medicine, 2019) nor has the ability to obtain mature sperm from spermatogonia preserved in pre-pubertal cryopreserved testicular tissue been demonstrated in humans (Borgström et al., 2020; Goossens et al., 2020).

Given the clinical complexities outlined above, and financial considerations related to fertility preservation which are currently evolving in many parts of the world (Kawwass et al., 2021), it is challenging for many transgender and gender diverse individuals to make fertility preservation decisions (Rodriguez-Wallberg, 2020). At the same time, it is important to note that transgender and gender diverse people may reproduce while previously or even currently using gender affirming hormonal therapy (GAHT), and this may be a desired or undesired outcome. As many transgender and gender diverse people retain their gonads, the possibility to either become pregnant (if they have a uterus, ovaries and tubes) and of contributing to a pregnancy (if they have penis, testes, and sperm) regardless of past and in some cases current use of GAHT, has to be discussed with all individuals. However, these discussions not always take place as in general, healthcare in gynecology and obstetrics may often not be well prepared to provide the multidisciplinary care tailored to transgender and gender diverse individuals (Falck et al., 2021; Hahn et al., 2019; Hoffkling et al., 2017; Johansson et al., 2020; Rodriguez-Wallberg, 2020).

The goal of this review is to provide a comprehensive description of the current knowledge

on reproductive issues in transgender and gender diverse people including fertility counseling and fertility preservation, pregnancy, perinatal issues and lactation, contraception, and abortion care.

Methods

A literature search of major databases (Pubmed, Medline, PsycInfo, Google Scholar, Web of Science) was conducted using search terms pertaining to the population of interest (e.g., transgender, gender diverse, nonbinary) and reproductive health topics (e.g., fertility, contraception, pregnancy, and abortion). No date restrictions were utilized. Although summative analytics were considered, the heterogeneity of data sources, populations, treatments, and variables made summative techniques unfeasible. The literature was critically revised by experts in the field with focus on the impact of gender-affirming medical interventions on future fertility and options for fertility preservation for transgender people. This expert group is part of the working committee on World Professional Association for Transgender Health (WPATH) Standards of Care (SOC) 8 Committee and the review was part of the WPATH SOC8 Committee work. Regarding terminology use we use transgender and gender diverse throughout to describe people whose current gender identity differs from that commonly associated with their sex assigned at birth. At times we use terms such as transgender men, transgender women, and/or non-binary among others if that is how original research was described. We use the terminology sex assigned at birth to describe the anatomic and physiological constellations most prevalent with females and males of the human species while recognizing individuals who have differences of sex development or are intersex may not be completely captured in this terminology, but detailed handling of their reproductive health needs is outside of the scope of this review.

Results

Infertility and family building aiming at achieving genetically related children in transgender people

Infertility is an acknowledged cause of psychosocial distress. Several causes of distress have been related to infertility, such as the development of gonadal dysfunction due to underlying medical conditions or gonadotoxic therapies (Armuand et al., 2014). Fertility treatment using donor gametes are available worldwide, however, studies among transgender and gender diverse individuals regarding parenthood goals indicate a preference for genetically related children, although the results provided are conflicting. Some studies indicate that transgender and gender diverse individuals might be less likely to desire genetically related children, or children at all, compared to cisgender individuals (Defreyne et al., 2020; Russell et al., 2016; von Doussa et al., 2015). However, a substantial proportion of available studies support that many transgender and gender diverse individuals wish to have genetically related children, regret missed opportunities for FP and may be willing to delay or interrupt GAHT to undergo procedures aimed at FP or to conceive (Armuand et al., 2017; Auer et al., 2018; Chen et al., 2018; De Sutter et al., 2002; Defreyne et al., 2020; Light et al., 2014; Tornello & Bos, 2017; Vyas et al., 2021; Wierckx et al., 2012a, 2012b).

Impact of medical and surgical gender-affirming interventions on future fertility

Individuals assigned female at birth

GAHT may negatively impact future reproductive capacity. There are various approaches to GAHT. In young adolescents, the use of Gonadotropin-Releasing Hormone agonists (GnRHa) has been reported for pubertal suppression or to prevent further pubertal progression in post-pubertal individuals, as well as to induce menstrual suppression (Bangalore Krishna et al., 2019). The treatment with GnRHa is usually transitory and it impacts the maturation of gametes as long as the treatment is continued, without causing permanent damage to the gonads, as demonstrated by follow-up of children receiving treatment with GnRHa (Feuillan et al., 1999; Heger et al., 1999; Tanaka et al., 2005). Thus, puberty development, follicle development and oocyte maturation including menstrual cycles would be expected to resume after stopping the medication (Bangalore Krishna et al., 2019).

Testosterone administration in transgender men with the goal of inducing masculinizing characteristics also has effects on reproductive function (Moravek et al., 2020). However, the effects are also thought to be transitory and restoration of ovarian function with oocyte maturation has been reported in observational studies after testosterone interruption among transgender and gender diverse people who reported long-standing exogenous testosterone administration previously and achieved natural conception thereafter (Light et al., 2014; Moseson et al., 2021b). A retrospective study of FP by oocyte cryopreservation showed no differences in the numbers of oocytes retrieved or their maturity between transgender men and age- and BMI-matched cisgender women (Adeleye et al., 2019). There are few studies reporting on live birth rates using assisted reproductive techniques including in vitro fertilization (IVF) and comparing transgender men to cisgender women. In a recent study of transgender men who underwent hormonal ovarian stimulation to either carry a pregnancy or to use their oocytes to be carried by their cisgender women partners, the live birth rate was comparable to that of cisgender women. Sixty-one percent of the transgender men reported prior testosterone exposure (Leung et al., 2019). In all such cases testosterone was discontinued and ovarian stimulation was initiated after either the start of menses or when testosterone levels reached the natal female range. Two additional observational studies (Light et al., 2014; Moseson et al., 2021b) reported on pregnancies among community-dwelling transgender and gender expansive individuals who had used testosterone prior. Light et al. did not specifically address whether testosterone use was continued into pregnancy but did note that 68% of prior testosterone users stopped taking testosterone to become pregnancy and 20% of prior testosterone users were still amenorrheic from testosterone at the initiation of pregnancy. Moseson et al. directly inquired about testosterone use during and immediately prior to pregnancy. They surveyed 1,694 transgender and gender expansive people in the United States and found that 3.5% ($n = 15$) of the total pregnancies ($n = 433$) occurred after initiating testosterone and 0.9% ($n = 4$) occurred while participants were taking testosterone. Overall, results seem reassuring that testosterone impact on the reproductive organs and function is reversible. Nevertheless, data from prospective studies evaluating the effect of long-term GAHT on fertility are lacking (i.e., if GAHT started in adolescence), as well as data from individuals treated with GnRHa in early puberty that thereafter received testosterone therapy. It is important to consider the fact that the required hormonal stimulation and the examinations and invasive procedures needed for cryopreserving oocytes (e.g., pelvic examinations, vaginal ultrasonography for monitoring of follicle growth, and transvaginal oocyte pick-up) may be challenging for transgender men and lead to increasing gender dysphoria in these patients (Armuand et al., 2017; Rodriguez-Wallberg, 2022).

Surgical interventions among transgender and gender diverse people assigned female at birth will have obvious implications for gestational and reproductive capacity. If a hysterectomy is pursued, ovaries can be retained for the future possibility of a genetically related child with pregnancy carriage by another individual (Rodriguez-Wallberg, 2020). Alternatively, if the ovaries are removed, there may also be the option for concurrent ovarian tissue cryopreservation at the time of oophorectomy. Although this procedure is no longer considered experimental in adults, many transgender and gender diverse people assigned female at birth may be reluctant to the idea of re-transplant the ovarian tissue in the future, which is the current established method to regain fertility in cisgender women, and they may desire instead to undergo procedures for *in vitro* growth and maturation of primordial follicles, which are still at investigational stages (McLaughlin et al., 2018). Studies evaluating oocyte function have shown that oocyte cumulus complexes isolated from ovaries of transgender men under testosterone treatment at time of oophorectomy can be matured *in vitro* to developing normal metaphase II meiotic spindle structure, however their developmental capacity is substandard (De Roo et al., 2017; Lierman et al., 2017; 2021). The data thus suggest that for transgender and gender diverse people assigned female at birth FP should therefore be performed before initiating or after cessation of GAHT (Rodriguez-Wallberg, 2022).

Individuals assigned male at birth

It has been demonstrated that the continuous treatment with GnRHa inhibits spermatogenesis. However, the data suggest that discontinuation of treatment allows resumption of spermatogenesis in postpubertal individuals. In children treated using GnRHa for precocious puberty, follow-up studies indicate also resumption of puberty and spermatogenesis after discontinuation of the treatment (Bertelloni et al., 2000; Tanaka et al., 2005). The recovery of mature sperm requires at least 3 months or longer (Bertelloni et al., 2000). However, the psychological burden of re-exposure to testosterone with appurtenant masculinization should be considered for transgender women.

Anti-androgens and estrogens impair sperm production (de Nie et al., 2020; Jindarak et al., 2018; Kent et al., 2018). However, these effects seem to be transitory and spermatogenesis might resume even after discontinuation of prolonged treatment with anti-androgens and estrogens, but data are limited (Adeleye et al., 2019; Alford et al., 2020; Schneider et al., 2017). In a previous study testicular volume was found to be clinically diminished after GAHT including estradiol with or without spironolactone, finasteride or progesterone for a duration of at least 6 months and up to 20 years (Matoso et al., 2018).

Semen quality in transgender and gender diverse people assigned male at birth may also be negatively affected by specific behavioral factors such as a low frequency of masturbation, wearing the genitals tight against the body or bringing the testicles into the inguinal canal ('tucking') (Jung & Schuppe, 2007; Mieusset et al., 1985, 1987). A recent prospective study of transgender women providing sperm samples for FP in Sweden indicated a higher proportion of sperm abnormalities in sperm of transgender women, even if they had not undergone previous gender-affirming hormone therapy (Rodriguez-Wallberg et al., 2021a, 2021b).

Fertility preservation options for transgender and gender diverse individuals

Cryopreservation of mature gametes

Cryopreservation of sperm and oocytes are FP techniques with proven efficacy through the use of the gametes in assisted reproductive technology treatments (Rodriguez-Wallberg et al., 2019a, 2019b). As mature gametes can be achieved naturally or after hormonal stimulation in adults and post-pubertal individuals, these methods can be offered to pubertal, late pubertal, and adults, preferably before GAHT treatment has been initiated or after interruption of GAHT (Chen et al., 2017; De Roo et al., 2016; Martinez et al., 2017; Nahata et al., 2017, 2018; Wierckx et al., 2012a, 2012b). Cryopreservation of embryos can be offered to adult (post-pubertal) transgender and gender diverse individuals with an available partner(s) or identified donor source. The future use of cryopreserved gametes is also dependent on the gametes and reproductive organs of future partner(s) (De Roo et al., 2017).

Semen parameters may be compromised when FP is performed after initiation of GAHT. If GAHT is discontinued, semen parameters may become comparable with those of transgender and gender diverse persons who had never used GAHT medication, according to a recent study with a mean discontinuation period of 4.4 months (Adeleye et al., 2019). However, sperm of transgender women has been reported with higher frequency of anomalies, even if the individuals have not had GAHT previously, which might be associated to the behavioral factors, as discussed above (Rodriguez-Wallberg et al., 2021a, 2021b).

In transgender men, response to ovarian stimulation, with oocyte yields and vitrified and their subsequent use on ART treatments seem to be comparable with those obtained in cisgender women (Adeleye et al., 2019; Leung et al., 2019; Maxwell et al., 2017). The recent European guideline on female FP from the European Society of Human Reproduction and Embryology, ESHRE, included recommendations for transgender individuals, where a stimulation protocol using letrozole alongside gonadotropins has been proposed as a Good Clinical Practice recommendation to reduce systemic estrogen during hormonal stimulation and increasing compliance with this treatment (Anderson et al., 2020; Armuand et al., 2017).

Although these are established FP methods, few pubertal, late pubertal or adult transgender and gender diverse persons undergo FP, and

many experience challenges while undergoing FP interventions. Not only is the cost of these methods a barrier, but these processes are often physically uncomfortable and many express concerns about postponing the transitioning process (Chen et al., 2017; De Sutter et al., 2002; Nahata et al., 2017; Wierckx et al., 2012a, 2012b). Especially for people assigned female at birth, the invasiveness of endovaginal ultrasound to monitoring follicle development during hormonal ovarian stimulation and the oocyte retrieval procedures have been cited as a barrier (Armuand et al., 2017; Chen et al., 2017). There is also the concern that young adults who are transitioning might not have a clear vision on parenting and therefore decline the opportunity to use FP while at adult age, they might have different opinions on parenthood (Hudson et al., 2018). As gender dysphoria diminishes while going through transitioning, this could have an influence on the decision process concerning FP (Nahata et al., 2017). Discussing FP options should therefore be performed and repeated at different stages during transition (Hudson et al., 2018; Nahata et al., 2018).

Cryopreservation of gonadal tissue

For pre-pubertal and early pubertal children, FP options are limited to the storage of gonadal tissue. Although this option is possible for transgender and gender diverse children as it is for cisgender children (for example undergoing gonadotoxic therapies), there is no literature that we were able to find, describing the utilization of this approach among transgender and gender diverse populations. To recover fertility, the tissue needs to be re-transplanted, which has currently resulted in over 130 live births in cisgender women worldwide (Donnez & Dolmans, 2015; Jadoul et al., 2017). Among those who have undergone ovarian tissue re-implantation, most conceived naturally without using of additional methods for assisted reproduction, such as in vitro fertilization, and the large majority of cases used ovarian tissue that was cryopreserved at adult age. At present, only three reports of live-births from re-transplantation of ovarian tissue during early pubertal adolescents have been published. The cases described reflect a similar success of using tissue retrieved from adolescents to that of tissue cryopreserved at adult age (Demeestere et al., 2015; Matthews et al., 2018; Rodriguez-Wallberg et al., 2021b).

Re-transplantation of ovarian tissue might be undesirable in transgender and gender diverse people, due to the potentially undesirable effects of estrogen secretion when the transplanted tissue resumes hormonal function. Also dysphoria toward these organs may make this possibility unrealistic or unwanted (Rodriguez-Wallberg, 2020). Laboratory methods aimed at culture and maturation of oocytes would be the ideal future application for stored ovarian tissue of transgender people, but this technique is still under development in basic research settings (Ladanyi et al., 2017; Rodriguez-Wallberg & Oktay, 2010).

In pre-pubertal people assigned male at birth, testicular tissue biopsies obtained for FP in pre-pubertal boys have been documented as a low risk procedure (Ming et al., 2018) and although some authors have described this as a theoretical option in transgender and gender diverse people (De Roo et al., 2016; Martinez et al., 2017; Nahata et al., 2018), there are no reports of in literature describing the clinical or investigational utilization of this FP option in these populations. Moreover, the clinical application of auto-transplantation of testicular tissue still has yet to be proven in humans and in-vitro maturation techniques are still basic research. Thus, FP specialists for pre-pubertal people assigned male at birth consider this technique experimental (Picton et al., 2015). It is therefore advisable to discuss the possibility of storing gonadal tissue prior to any transition surgery, however the absence of currently established methods for the use of this tissue must be clearly addressed.

Reported use of fertility preservation in transgender and gender diverse individuals and fertility perspectives

The current consensus that infertility is not a prerequisite of gender transition (Ethics Committee of the American Society for Reproductive Medicine, 2015; Meyer et al., 2002)

has allowed transgender and gender diverse patients to achieve genetically-related parenthood. Further, achieving family building goals is supported by the positive advances in social attitudes, advances in reproductive medicine and gender affirming healthcare. However, current research indicates that the majority of transgender or non-binary people might not want to undertake FP (Riggs & Bartholomaeus, 2018). Counseling provided to individuals requesting GAHT that potentially hamper fertility may thus also include also information and support on alternative options such as fostering, adoption, and co-parenting among others (Bartholomaeus & Riggs, 2020). The experience of transgender people who have been offered this complete type of discussion and a chance to elect to undergo procedures for FP has been reported overall as positive (Armuand et al., 2017; De Sutter et al., 2002; James-Abra et al., 2015). The need for appropriate training of healthcare providers is critical (Armuand et al., 2020).

A large study conducted in Australia including a cohort of 409 adult transgender and non-binary individuals from 18 years of age and older reported positive patients' experiences of FP when healthcare personnel acted professionally and knowledgeably during provision of affirming and caring services. The patients also described in that study the negative experiences associated with healthcare professionals that acted mainly as gatekeepers of fertility preservation (Bartholomaeus & Riggs, 2020). This study clearly indicates the sensitive role of healthcare providers, as they may act as facilitators and being encouraging, or creating barriers through discouragement about FP. The authors of the study also discussed the WPATH SOC7 guidelines published in 2011 (The World Professional Association for Transgender Health, 2011), which encourage FP briefly and generally, but without specific detailed guidance.

Little is known about fertility-related perspectives among youth transgender and gender diverse people. Two studies recently conducted in the United States (cumulative age range 9-21 years) showed that <5% opted for FP (Chen et al., 2017; Nahata et al., 2017). Reasons for declining FP included preference for adoption and/or no desire to be a parent (Nahata et al., 2017). Similarly, none of the transgender youth (12–18 years of age) surveyed in a Canadian study had attempted FP (Chiniara et al., 2019). In a survey among 25 transgender youth (13–19 years of age) and their parents, none had preserved fertility and 92% reported learning about GAHT-related fertility risks online (Strang et al., 2018). Although many of these youth endorsed a desire to have a child, few (24%) expressed desire to have their own genetically-related child, yet many acknowledged that their feelings about having a biological child might change in the future (Strang et al., 2018). Another survey study (N = 156, M = 16 years) showed that only 53% of transgender youth who had talked to their health-care providers about GAHT had discussed the impact of hormones on fertility. Sixty-one percent of these respondents were interested in learning more about their fertility and family building options (Chen et al., 2018). Notably, recent studies in the Netherlands and Israel have shown higher FP rates, with ~40% of transgender female adolescents attempting FP (Brik et al., 2019; Segev-Becker et al., 2020). Additionally, parents' recommendations have been shown to have a significant influence on FP rates in cisgender adolescent and young males with cancer (Klosky et al., 2017). These findings can help inform best practices for fertility counseling and FP referrals for transgender and gender diverse individuals.

In contrast to these studies in youth, some studies of transgender and gender diverse adults show a desire to have children which is comparable to the rates of the cisgender population (De Sutter et al., 2002; Defreyne et al., 2020; Wierckx et al., 2012a, 2012b). In the past, transgender and gender diverse individuals who undertook a medical transition were often confronted with the loss of fertility, due to hormonal and surgical interventions, or the specific prerequisite to become sterile before legal sex change recognition (Payne & Erbenius, 2018). This common prerequisite, previously considered essential to a 'successful transition' by a number of clinicians, is no longer the rule, and despite persisting in some countries, it has been removed by law in several countries during recent years (Payne & Erbenius, 2018).

Barriers to fertility preservation

Consistent with literature in other populations at risk for iatrogenic infertility (e.g., adolescents and young adults with cancer), barriers to FP have been reported including cost, time constraints due to the urgency to start a needed treatment, inability of very young patients to make future-oriented decisions, and low level of knowledge in the health care providers (Armuand et al., 2017; Baram et al., 2019; Defreyne et al., 2020; Nahata et al., 2012; Tishelman et al., 2019). Costs of FP vary widely around the world, with many recent changes to insurance coverage and policies (Sax et al., 2020). While the legislative push to increase coverage is promising, many gaps remain (Sax et al., 2020), highlighting the need for more advocacy to ensure reproductive justice (Kawwass et al., 2021). Beyond financial barriers, FP processes are particularly difficult for many transgender patients, as the intrinsic connection of these processes with their sex assigned at birth may worsen the gender dysphoria (Armuand et al., 2017; Baram et al., 2019). A multidisciplinary team needs to be established including both medical and mental health providers in close collaboration with gender-affirming specialists and the reproductive medicine team to overcome some of these barriers.

Attitudes toward parenthood and preconception and prenatal counseling

In addition to addressing fertility issues, efforts should also be made to ensure equitable and high-quality care for all forms of family planning, thus the full reproductive continuum should be covered. This includes pregnancy care and delivery, postpartum and perinatal care, as well as provision of contraceptive options to prevent further unplanned pregnancies, and pregnancy termination services (Bonnington et al., 2020; Cipres et al., 2017; Krempasky et al., 2020; Light et al., 2018; Moseson et al., 2021c). Transgender men and gender diverse people who wish to become pregnant should receive standard of care preconception and prenatal counseling, and should receive also counseling about breast/chest feeding within environments supportive to people with diverse gender identities and experiences (MacDonald et al., 2016; Martinez et al., 2020; Obedin-Maliver & Makadon, 2016).

Pregnancy counseling/perinatal outcomes

The paucity of evidence regarding prenatal care and pregnancy among transgender and gender diverse people is profound. Most transgender men and gender diverse people assigned female at birth can conceive and carry a pregnancy even after long-term testosterone use since most appear to retain their natal reproductive organs (Ellis et al., 2015; Light et al., 2014; Moseson et al., 2021c). Desires for future children are common: 54% of transgender men in a large clinic in Belgium wanted children (Wierckx et al., 2012a, 2012b). Among a more recent US based survey a quarter of transgender men reported fears of not getting pregnant and over a quarter desired children (Light et al., 2018). The largest study we are aware of thus far was conducted in the US with 1,694 transgender and gender expansive community-dwelling individuals assigned female or intersex at birth in the US found that 12% had ever been pregnant, 11% desired future pregnancy, and 16% were uncertain desires for future pregnancy. (Moseson et al., 2021b) Although this was not a population-based study, this group reported an overall past pregnancy rate of 16.8/1,000 per year among transgender and gender expansive people capable of pregnancy. Despite the negative fertility impacts of gender affirming processes and procedures as above, with developments in ART, there are increasing opportunities for transgender and gender diverse people to accomplish family planning goals (De Roo et al., 2017; Ellis et al., 2015; Maxwell et al., 2017). To address these issues Martinez et al. (2020) and Hoffkling et al. suggest providing high-quality preconception and perinatal care while urging providers and systems to understand and address issues specific to transgender pregnancy and reproductive concerns (Hoffkling et al., 2017; Martinez et al., 2020). Some unique considerations for transgender and gender diverse people include: cessation and resumption of affirming hormones, genital/body dysphoria and impact on pregnancy and delivery mode,

social support, lactation, varyingly referred to as breast or chest feeding, and at times unique legal challenges from less-commonly encountered family constellations.

The effects of exogenous or supraphysiologic testosterone on the developing embryo have not been systematically documented in the context of gender-affirming hormone use, but have been demonstrated as teratogenic to fetal sexual and reproductive anatomy in other settings. Therefore, until better evidence is provided, testosterone or other masculinizing hormone therapy should be discontinued prior to and through any pregnancy. However, optimal wash-out period prior to pregnancy to avoid teratogenic effects is unknown. Additionally the optimal timing in terms of pregnant person and neonatal health for testosterone administration after pregnancy is unknown. Since stopping gender affirming hormones may cause distress and exacerbate dysphoria in transgender men, GAHT management and the methods and timing of cessation should be arrived at in a patient-centered approach, ideally prior to conception.

The conception, birth, and post-partum experiences of transgender and gender diverse people are scantily described but suggest that these time periods may be filled with distress. Psychological isolation and depression have been reported in addition to dysphoria related to body changes including the gravid uterus, body shape, and chest changes (Charter et al., 2018; Ellis et al., 2015; Hoffkling et al., 2017; Obedin-Maliver & Makadon, 2016). However, not all reports are negative with some reporting positive experiences around realizing parenting goals and utilizing natal organs (Light et al., 2014; Hempel, 2016). This leaves important questions about the origins of reported distress in other papers as perhaps related to interactions with medical systems that are discriminatory and unprepared to support transgender and gender diverse people (Hahn et al., 2019; Hoffkling et al., 2017; Moseson et al., 2020b; Snowden et al., 2018). As a result, ensuring adequate and perhaps expanded support systems such as including mental health providers during the preconception, peripartum, and postpartum periods may be beneficial. Prenatal care consistent with the local standard of care is recommended, but how gender diversity and or gender dysphoria may influence or call for modifications to that standard of care is unknown. Furthermore, it is unclear how the social, mental, and physiological experiences of being transgender and gender diverse may influence the desires, risk factors, and health outcomes for birth people and their offspring related (Stroumsa et al., 2019). Small case series do not demonstrate any adverse physical or psychosocial differences compared to infants born of presumably cisgender women, however population-based studies are warranted (Brandt et al., 2019; Chiland et al., 2013; Light et al., 2014). There is a critical need for longitudinal studies to evaluate pregnancy processes and outcomes among transgender and gender diverse people with specific consideration of neonatal and pediatric growth, development, and psychosocial outcomes.

As the reality of uterine transplant has been realized for cisgender women, development of protocols and procedures to facilitate pregnancy via uterine transplantation for transgender women and gender diverse people assigned male at birth on the basis of having Absolute Uterine Factor Infertility (AUFI) (Jones et al., 2019). There is historical precedent here as the first known uterine transplant was performed in a transgender woman, Lili Elbe in 1931, which unfortunately resulted in rejection, infection, and her untimely demise. In the contemporary age, uterine transplantation has resulted in more than 23 live births, successfully accomplished in multiple countries (Jones et al., 2019). While there are important clinical complexities in transgender individuals (e.g. anatomical considerations with regard to pelvic structure and vasculature) (Jones et al., 2019), research shows strong interest in uterine transplantation among many transgender women (Jones et al., 2021). Health care systems that provide transplantation must therefore consider equitable access for transgender women and other gender diverse people born without a uterus as they do for cisgender women. It is important to acknowledge, however, that uterine transplantation is currently highly experimental, with significant risks, and uterine transplant programs are available at limited institutions with IRB protocols (Jahromi et al., 2021).

Lactation or chest/breast feeding

Lactation or chest/breast feeding among transgender and gender diverse people assigned female, has been reported in a few small studies and reports. Those studies report that the majority who chose to chest/breast feed postpartum seemed successful (MacDonald et al., 2016; Wolfe-Roubatis & Spatz, 2015). Contributors to success included: preconception counseling, experienced lactation support, and less comprehensive gender-affirming chest reconstruction if any. Because small amount of exogenous testosterone can pass into human, and there is unquantified risk on neonate/child development following testosterone exposure through human milk, testosterone-based is contraindicated during lactation (Glaser et al., 2009). Owing to residual glandular tissue even after chest reconstruction, some transgender and gender diverse people who carry a pregnancy may experience undesired chest growth and therefore should be informed about this potential and supported in lactation suppression if desired (MacDonald et al., 2016).

Information is limited regarded lactation potential and outcomes in transgender and gender diverse people assigned male at birth, however many people do express the desire to chest/breast feed. Though a number of lay press articles and reports describe lactation among transgender women, to our knowledge, there are only two published case reports of transgender women successfully describing induction lactation and infant feeding through a combination of estrogen, progesterone, domperidone, and breast pumping. Future research should examine the nutritional and immunological profile of chest/breast milk to fill this gap and in the interim, patients need to be informed about risks and benefits of this approach to infant feeding (Reisman & Goldstein, 2018; Wamboldt et al., 2021).

Contraception

Since many transgender individuals may retain reproductive organs and thus reproductive ability, and pregnancy can occur even years after initiation of GAHT, unplanned pregnancies may occur (James et al., 2016; Light et al., 2014; Moseson et al., 2021c). Documentation of pregnancies among transgender and gender diverse people, after initiation of testosterone use and while still amenorrheic from testosterone use (Light et al., 2014) or while actively taking testosterone during pregnancy (Moseson et al., 2021b) have been reported. Even though these studies were not designed to document the impact of testosterone on ovulation, they are a proof of principle that pregnancy can and does occur, for at least some people, while on exogenous testosterone. Therefore, we can confidently surmise that suppression of ovulation is not complete even with administration of exogenous testosterone, and therefore testosterone is not a reliable contraceptive. Consequently, full-spectrum, intentional, and gender-affirming family planning counseling including contraception and abortion is needed. The provision of this care is well within the scope of sexual and reproductive health care providers but limited by health care provider training and preparedness (Fix et al., 2020; Klein et al., 2018; Obedin-Maliver, 2015; Stroumsa & Wu, 2018; Unger, 2015). Although evidence about pregnancy and pregnancy avoidance among transgender and gender diverse individuals is limited, our few available studies suggest individuals may not be using any, or the most effective, forms of contraception (Cipres et al., 2017; Light et al., 2018; Sevelius, 2009). One often reported consideration by both patients and providers is the falsely held belief that testosterone is a form of contraception (Abern & Maguire, 2018; Ingraham et al., 2018; Jones et al., 2017; Light et al., 2018). However, given the incomplete suppression of the hypothalamic-pituitary-adrenal axis it provides, testosterone should not be considered contraception (Krempasky et al., 2020) as evidenced by the fact that pregnancies have occurred despite amenorrhea from GAHT with testosterone (Light et al., 2014).

Contraceptive methods used by transgender men and gender diverse people assigned female at birth use are varied (Abern & Maguire, 2018; Bentsianov et al., 2018; Bonnington et al., 2020; Chrisler et al., 2016; Cipres et al., 2017; Jones et al., 2017; Krempasky et al., 2020; Light et al., 2018; Sevelius, 2009). As with all people, indications for contraceptive use may be: pregnancy

prevention, menstrual suppression, abnormal bleeding, or other medical and gynecological indications (Bonnington et al., 2020; Chrisler et al., 2016; Krempasky et al., 2020; Schwartz et al., 2019). Research gaps regarding contraception, its use, and unmet needs for these populations are global, thereby limiting provider counseling and education. To our knowledge, there are no studies on population-based fertility rates among transgender and gender diverse individuals who were female sex assigned at birth, nor about how exogenous testosterone impacts their fertility and fecundity. Furthermore, to our knowledge there are no studies that examine how the contraceptive efficacy or safety profile of hormonal contraceptive methods (e.g., combined estrogen and progestin hormonal contraceptives, progestin only based contraceptives) or non-hormonal and barrier contraceptive methods (e.g., internal and external condoms, non-hormonal intrauterine devices, diaphragms, sponges, etc.) may be modified by use of exogenous androgens (e.g., testosterone). Lastly, although a few studies considering contraceptive choices and experiences have been published, gaps remain to effecting optimal contraceptive care delivery and provision for transgender and gender diverse people (Bentsianov et al., 2018; Bonnington et al., 2020; Fix et al., 2020; Francis et al., 2018; Ingraham et al., 2018; Jones et al., 2017; Krempasky et al., 2020; Moseson, Lunn, et al., 2020a). Despite these research gaps, for any individual patient, if there are no other medical contraindications to any specific method of birth control all contraceptive options should be made available to patients and contraceptive choice should result from patient preferences, goals, and comorbid medical conditions.

Transgender and gender diverse individuals who preserve their penis and testicles may engage in sexual activity with individuals who have a uterus, ovaries, and tubes of any gender. As discussed above, people who have testes and a penis can present with active sperm in semen samples even during GAHT (Adeleye et al., 2019; Jindarak et al., 2018; Kent et al., 2018). Therefore, individuals who retain their penis and testicles may intentionally or unintentionally contribute to a pregnancy, and thus contraception also needs to be considered if a pregnancy is to be avoided between a person with a uterus, ovaries, and tubes and those who have a penis and testicles, if they are engaging in penis-in-vagina sex, irrespective of the use of gender affirming hormones among either partner. Contraceptive methods for sperm-producing partner are currently limited to barriers methods (i.e., external condoms, internal condoms) and sterilization, or gender affirming surgery (e.g., orchiectomy, that also results in sterilization). Contraceptive counseling that considers the sexual behavior and the plausibility of fecundation including information on reproductive capacity of sperm production, follicle development and oocyte maturation is recommended.

Pregnancy termination services

As unplanned pregnancies and abortions occur and have been reported among transgender and gender diverse individuals (Abern & Maguire, 2018; Jones et al., 2020; Light et al., 2014; 2018; Moseson et al., 2021c), planning for and providing these services is necessary. Critical gaps remain however in describing and understanding the population-based epidemiology of abortion needs, provision, and experiences among transgender and gender diverse individuals (Fix et al., 2020; Moseson, Lunn, et al., 2020a; Moseson et al., 2021c).

A recent analysis by Jones et al. of the Guttmacher Institute's 2017 Abortion Provider Census survey, the most comprehensive accounting of abortion provision services in the U.S., estimated that in 2017 non-hospital facilities provided at least several hundred abortions (weighted estimates $n = 462–530$) to transgender and non-binary patients. The authors acknowledge that this estimate is likely lower than actual incidence but hope it serves to bolster the continued efforts to expand gender-inclusive pregnancy termination services (Jones et al., 2020). Another survey study performed in 2018 by Light et al. at this time directed at transgender men directly and focused on family planning and contraceptive use, found 32 of the 183 respondents had 60 pregnancies with 12% ($n = 7$) ending in abortion (Light et al., 2018). They further found 71% of those abortions occurred in people who had

previously used testosterone, though numbers were small overall (Light et al., 2018). Another recent survey by Moseson *et al.* reported on experiences of 1,694 transgender and gender expansive individuals (Moseson et al., 2021b). Among the 1,694 individuals, 12% of the sample (210 people) reported a total 433 pregnancies. This study reported that 21% of the pregnancies ($n = 92$) ended in abortion. For the most recent abortions, 61% occurred at </= 9 weeks of gestation and 61% were performed surgically although respondents 3:1 preferred a medical abortion to surgical abortion citing this methodology as less invasive and more private. A different analysis from the same researchers found that nearly 1 in 5 transgender and gender expansive individuals assigned female or intersex at birth who had been pregnant attempted a self-managed abortion (Moseson et al., 2021a), which is almost 3 times higher than the most liberal estimates of 1 in 15 cited for cisgender women. Although self-managed abortion with standardized abortion regimens can be safe, some methodologies can be quite harmful, and the high numbers reported in this study warrant attention of differential access to pregnancy termination services for transgender and gender diverse people.

Overall, though data are limited, we see that pregnancy termination occurs and services are needed across the gender spectrum. Further, pregnancy termination statistics and experiences differ than those found among cisgender women, calling for clinical and investigational input on these topics to serve these communities. Therefore, since many transgender and gender diverse people retain an anatomic capacity for pregnancy, and pregnancies may not always be planned or desired, ensuring safe, equitable, and accessible gender affirming pregnancy termination services is an important part of comprehensive health care.

Conclusion

The goal of this review was to highlight current considerations regarding FP and other salient aspects of reproductive health care related to pregnancy and perinatal care for transgender and gender diverse individuals, given recent advances in FP methods and the evolving landscape of financial considerations. Limitations of this manuscript were related to design (use of a narrative review rather than a systematic review) and scope (e.g., sexual function/dysfunction was not included given that there have been other recent reviews published on this topic) (Mattawanon et al., 2021).

We found that despite an expanding body of literature highlighting the need for comprehensive reproductive care for transgender and gender diverse individuals, these services are often inadequate or unavailable. Counseling on family building, including discussions about known and unknown infertility risk and FP options, should occur prior to any medical interventions that may impair reproductive capacity, and continue across the care continuum. Contraception, abortion, preconception counseling and perinatal support, should also be routinely provided.

Evidence-based strategies are needed to improve care delivery and FP decision making for this population. Specifically, more research needs to be conducted in transgender and gender diverse people about the effects of GAHT on gonadal function and health of offspring; feasibility of procedures such as uterine transplantation; and family building perspectives at different ages and developmental stages. Finally, structural, and legislative advocacy efforts are needed to ensure equitable access to FP and other aspects of reproductive health care.

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