REVIEW



An Update on Contraception for Transgender, Non-binary, and Gender-expansive Individuals

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Accepted: 12 April 2023 / Published online: 19 May 2023 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2023

Abstract

Purpose of Review The goal of this review is to summarize the current understanding of how exogenous testosterone and estrogen affects fertility in transgender, non-binary, and gender-expansive (TGE) individuals, and what contraceptive options are available for this population.

Recent Findings Recent studies have shown conflicting findings with regards to the effects of exogenous testosterone on ovulation and the endometrium; however, the overarching conclusion continues to be that it cannot be viewed as a contraceptive. Survey studies conducted in the past 5 years have repeatedly shown disparities in the rates of contraceptive use among TGE individuals compared to their cisgendered peers, with condoms being the most commonly used contraceptive among this population, followed by the pill and long-acting reversible contraceptives. Studies on the effects of exogenous estrogen use on testicular structure and spermatogenesis have shown findings suggestive of reduced fertility; however, no long-term data is available and further investigation is needed. Contraceptives need to be recommended for these individuals to avoid unintended pregnancies due to incomplete suppression of spermatogenesis. Data shows condoms are the first-line option. Summary Despite the need for healthcare providers to discuss contraception with TGE individuals, research and guidance on this topic remains limited. Advancements have been made in understanding how exogenous testosterone or estrogen taken as part of gender-affirming hormone therapy (GAHT) can affect fertility, but there remain significant gaps in knowledge beyond the understanding that these therapies are not sufficient to prevent pregnancy and contraception is required to avoid unintended pregnancies. There remain disparities in contraceptive use among TGE individuals, and between TGE individuals and their cisgendered peers. This literature review will focus primarily on new publications related to the contraceptive needs and options for the TGE community to help inform healthcare providers of specific considerations for their TGE patients. By creating a trusting, gender-inclusive environment, reproductive healthcare providers can engage in shared decision-making

Keywords Contraception · Transgender · Reproductive health · Family planning

with TGE patients to select the most appropriate contraceptive for each specific patient.

Introduction

Recent evidence suggests that the proportion of transgender and gender-diverse individuals in the general population ranges from 0.02-0.1% based on health systems-focused

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studies and 0.3-4.5% based on survey studies, with numbers being even higher among children and adolescents (2.5-8.4%) [1]. Many societies, including The American Academy of Pediatrics and The Society for Family Planning, have highlighted the need for healthcare providers to discuss contraception with transgender, non-binary, and gender-expansive (TGE) individuals [2, 3••]. This literature review will focus primarily on new publications related to the contraceptive needs and options for the TGE community. It is important to note that this is a dynamic—and still under researched—field, leaving many questions left unanswered. Most of the recommendations to date, including those made in this review, are extrapolated from research conducted on cisgendered individuals and expert opinion.

A broad range of lived experiences exist for TGE individuals. Not all TGE individuals opt to initiate gender-affirming hormone treatment (GAHT). For those individuals who do pursue GAHT, the treatment is often customized to individualized goals and to maintain good cardiovascular and bone health while attempting to avoid supra-physiologic levels [4, 5]. Transmasculine individuals (individuals assigned female sex at birth with a male gender identity) may opt to take exogenous testosterone to affirm their gender. Transfeminine individuals (assigned male sex at birth with a female gender identity) may take a combination of testosterone-blocking medication, estrogen, and/or progesterone to affirm their gender identity.

Identifying as TGE does not divulge any information about one's sexual attraction, practices, and anatomy of partners. Contraception concerns generally are specific to those who are engaging in sexual practices that could lead to pregnancy—specifically, penetrative vaginal intercourse between someone with a uterus, fallopian tubes, and ovaries, and someone with sperm. Asking open-ended questions about what specific t sexual behaviors they engage in, the anatomy of their partner(s), and what fertility goals they may or may not have, can best guide patient-centered conversations regarding contraceptive needs and options [6]. Even if a patient is not currently engaging in behaviors that can lead to pregnancy, it is still imperative that all prescribers of GAHT remind their patients regarding the risk of unplanned pregnancies [7].

Known Exogenous Testosterone Effects on Fertility in Transmasculine Individuals

Some TGE individuals pursue GAHT in the form of exogenous testosterone, most commonly taken in a transdermal formulation or in short- or long-acting injectable formulations with enanthate and cypionate or undecanoate [8]. While this treatment can induce amenorrhea, it does not necessarily suppress ovulation, and evidence indicates that unplanned pregnancies have occurred in those currently or formerly taking exogenous testosterone as GAHT [7, 9]. These studies are limited by their design, and large epidemiologic studies controlling for the dose and schedule of testosterone use have not yet been performed. Therefore, the actual risk of unplanned pregnancy for TGE individuals currently using testosterone for GAHT is unknown [10].

Exogenous testosterone has a negative feedback effect on the hypothalamic-pituitary–gonadal axis that reduces follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels. These levels are not reduced to those of pre-pubertal individuals and tend to fluctuate, which could result in breakthrough ovulation. This mechanism explains findings of ovarian follicles in different stages of development in individuals taking testosterone for GAHT [11, 12]. Additionally, incomplete suppression of estradiol by exogenous testosterone use has been shown, which could also result in residual ovarian activity [13, 14].

Data on the direct effects of exogenous testosterone on the ovaries is unclear. While a 2015 study showed that testosterone use along with a gonadotropin-releasing hormone (GnRH) agonist and aromatase inhibitor over 16 weeks significantly reduced anti-Mullerian hormone (AMH) levels, a 2020 data report on testosterone use showed no significant changes in AMH levels over 12 weeks [15, 16]. The same report also showed transient rises in ovulation markers shortly after testosterone use began, suggesting that ovulatory cycles were initially continuing despite this therapy. After a year of testosterone use, ovarian tissue analysis in a 2017 study showed that 70% of follicles were primordial and fewer than 1% were secondary follicles, indicating that follicular arrest had occurred [16].

Finally, the data on the effects of testosterone use on the endometrium is similarly conflicting. A 2009 study reported testosterone use resulting in atrophy of the endometrium, and subsequent studies have shown a proliferative effect on the endometrium with long-term treatment, potentially from aromatase conversion of testosterone to estrogen in the periphery [17, 18]. The current best evidence supports that people taking testosterone for GAHT may have atrophic or proliferative endometrium [19].

Given these scientific underpinnings, it is clear that while exogenous testosterone use has effects on ovulatory function and the endometrium that can lead to amenorrhea and reduced fertility, this does not necessarily mean that anovulation has occurred and therefore exogenous testosterone cannot be viewed as a contraceptive. It is therefore important that TGE individuals on testosterone for GAHT with a uterus and ovaries be counseled about their risk for pregnancy and its potential teratogenic effects if taken during pregnancy [20].

Contraceptives in Transmasculine Individuals Taking Testosterone for GAHT

Current rates of contraceptive use among transmasculine identifying individuals has been reported to be between 20 and 38% [21, 22]. A growing body of literature does show disparities between contraceptive access and use in TGE individuals and their cisgender peers [23•, 24]. Barriers that contribute to these disparities include insurance coverage, access to knowledgeable and gender-affirming clinics and clinicians, and misconceptions by both individuals and providers regarding the need for contraception and the risk of unplanned pregnancy [25]. A recent survey showed that a third of TGE adolescents denied that they were offered, or were unsure of being offered, pregnancy prevention options by a physician [26].

The disparities in contraceptive use by TGE individuals stems in part from reproductive health providers being reluctant to discuss options with these patients [27]. A 2015 survey of gynecologists by Unger found that 80% had not received residency training on transgender care and only 29% felt comfortable with providing reproductive care to transmasculine patients [28]. This discomfort in discussing contraception with TGE individuals is due in part to limited research in the area. A 2019 scoping review found that of almost 700 articles on TGE healthcare needs, only 14% focused on sexual health, with most studies focusing more specifically on HIV and sexually transmitted infection (STI) prevention [29]. A 2020 study by Forsberg and Eliason suggested that more education specific to TGE healthcare needs to be included in medical school and residency training, which would improve provider comfort, and recommended that professional and institution-wide pregnancy prevention care guidelines be updated to include all genders [27]. It also promoted the use of a handout by the Reproductive Health Access Project entitled "Birth control across the gender spectrum" and suggested that more genderinclusive reproductive health educational materials be created to improve health literacy [27].

Surveys have shown that the use of condoms is the most common contraceptive method in this population (49.3%), followed by the pill (33.9%) and long-acting reversible contraceptives (10.6%) [30, 9]. A 2019 study by Stark et al. showed that those individuals identifying as transmasculine who were also students, did not have a partner, or had socially transitioned their gender, were less likely to feel comfortable using contraceptive methods that they identified as being traditionally given to cisgender women [22].

It is important to note that no data currently exists showing testosterone use to be a contraindication for any form of contraceptives, and that there is no data indicating that concurrent use of testosterone with hormonal contraceptives has negative effects [31]. Therefore, there is no reason to exclude any contraceptive option from an individual taking testosterone for gender-affirming hormone therapy based on concerns about contraindications alone. However, debate currently exists about whether concurrent use of estrogencontaining hormonal contraceptives by individuals using exogenous testosterone could increase the risk of venous thromboembolism (VTE). Concern for this possibility stems from reports of VTEs in individuals taking testosterone for reasons other than GAHT [32-34], and the fact that combined hormonal contraceptives are known to increase the risk for VTEs among cisgender women [35]. Given these concerns, it is reasonable to discuss this possible concern with patients who are interested in estrogen-containing products and are also on testosterone for GAHT, and potentially even to counsel against the use of estrogen-containing contraceptives by individuals who might also have other increased VTE risk factors, such as being over the age of 35, obesity, or having a personal history of smoking [35].

More research is needed in this area before any definitive recommendations can be made.

With all contraceptive options being potentially viable for TGE individuals, a clinician should consider and counsel on the risks and benefits of each unique method to make patientcentered decisions on which method to use. One should consider general eligibility recommendations for the use of hormonal contraceptives, as well as specific concerns for TGE individuals [36, 37]. Examples of these recommendations can be found in previous literature showing that methods with daily or weekly actions might be less preferable to a patient if they view it as a reminder of their gender incongruence. Hormonal contraceptives that contain estrogen might be perceived as countering the masculinizing effects of testosterone use and/or cause breast tenderness, thereby making these contraceptives less desirable as well [38, 39]. Anecdotal reports of TGE individuals who take estrogen-containing products developing glandular breast tissue after top surgery exist [3]. Options that require gynecological procedures, like insertion and removal of an intrauterine device, may also cause increased distress as a reminder of gender incongruency [40]. However, some newer publications highlight that these assumptions regarding contraceptive preference in the TGE population are not true for all individuals [41].

With these considerations in mind, here is a review of current contraceptive options and some specific considerations for TGE individuals:

Surgical Sterilization

While some patients might pursue tubal ligation/salpingectomy for the purpose of contraception, others will have undergone this procedure as part of a desired genderaffirming surgery, and others still will have been required to undergo these surgeries to access gender-affirming therapy, depending on their country [3]. While this procedure is highly effective at preventing pregnancy, the removal of tubes alone will not affect current bleeding patterns and requires office visits before and after the surgery that might include pelvic examinations and/or ultrasounds. Given that surgical sterilization is considered to be a permanent procedure, the patient must be absolutely sure that they are not interested in spontaneous future pregnancies.

Subdermal Implant

In addition to being the most effective method of birth control in cisgender women, benefits for the TGE population include that no pelvic procedure is required, it is easily concealed, it is a progestin-only option. Additionally, it is currently approved by the FDA for 3 years of use before needing to be replaced, and current evidence suggests extended use of up to 5 years is reasonable. While it is hypothesized that etonogestrel implants could help to achieve amenorrhea in individuals taking exogenous testosterone, the actual incidence of this phenomenon is not yet known [42]. Potential downsides to this method include that an office visit is required for placement, it might be palpable and potentially visible in muscular or thin individuals (which could potentially increase gender dysphoria), and it can sometimes lead to irregular bleeding patterns [3].

Copper Intrauterine Devices (Cu IUDs)

These intrauterine devices might be preferable to some TGE individuals given the lack of hormones. However, cu IUDs do require a pelvic procedure for placement and can cause cramping and spotting possible after placement and/or increased menstrual bleeding, which may make it less desirable. Other considerations to take into account include possible vaginal atrophy in TGE individuals on long-term testosterone, which can increase patient discomfort during and after placement. Options to increase patient comfort include prescribing a 2-week pre-treatment with vaginal estrogen prior to placement to ease the atrophy, and offering to have the patient place the speculum themselves (at least insert it themselves) during the pelvic procedure [3].

While there have been some concerns that long-term gender-affirming testosterone use could cause increased risk of uterine perforation during placement, studies have shown that there are no obvious myometrial changes due to its use and therefore no increased risk of perforation [3]. One study found that TGE IUD users reported higher rates of abdominal and pelvic pain when compared with cisgender users; however, rates of early removal were similar in both groups [43].

Levonorgestrel Intrauterine Devices (LNG IUDs)

This contraceptive brings the benefit of being a progestin-only option that is effective; however, like the Cu IUD, it requires a pelvic procedure for placement. Despite this, a 2022 study found that the rate of uptake for LNG IUDs has steadily increased over the past 10 years in the TGE population, from 0.3% in 2009 to 2.3% in 2019 [44•]. Like with Cu IUDs, LNG IUDs can also cause cramping and irregular bleeding after placement, although they are known to cause less overall bleeding over time than the copper devices.

Depot Medroxyprogesterone Acetate (DMPA)

This method has the benefit of being progestin-only and very effective, though it does require injections every 3 months, which may contribute to it being one of the least commonly

used methods in this population [9], but the rates are increasing [44•]. It is now possible for patients to administer DMPA via subcutaneous self-injection at home, which might be preferable for patients who would like to limit interactions with the healthcare system [3].

Additional considerations for DMPA include that it is irreversible in the short term once injected, can cause weight gain in some individuals which might be especially harmful for patients already experiencing weight gain due to testosterone therapy, and can cause changes to lipoprotein profiles which may exacerbate lipid changes due to testosterone therapy [3].

Pills/Patch/Ring

Although daily contraceptive pills can cause increased gender dysphoria for some, this option presents a relatively affordable and effective method of birth control that does not require a pelvic procedure. While cyclic use of estrogencontaining products like oral contraceptive pills, the transdermal patch, and the vaginal ring causes a menstrual-like bleeding pattern, their use in a continuous fashion can lower (or even stop) the total number of days of bleeding. There are no data on the effects of continuous pill, patch, or ring use on the bleeding patterns in TGE individuals; however, expert clinical experience suggests that their continuous use for TGE patients, who are already amenorrheic on testosterone therapy, does not likely increase bleeding [3]. Some providers do have concerns about continuous use of the patch causing increasing blood levels of ethinyl estradiol over time, which theoretically can increase risk for VTE, and so instead opt for 12 continuous weeks followed by a pill-, patch-, or ring-free week to allow the body to reset [45].

Patch-specific considerations for this population include looking similar to gender-affirming testosterone patches, which may help to prevent gender dysphoria, but that they can cause skin irritation or discoloration for people with darker skin pigmentation, and may be less effective for patients weighing more than 90 kg [3]. Ring-specific considerations include that it requires placement and removal of the ring from the vagina, as well as increased vaginal wetness and leukorrhea, which can increase gender dysphoria for some, but may be beneficial for patients with vaginal atrophy due to extended testosterone use [3].

Progesterone-only pills are preferred by some TGE individuals over combined hormonal pills given the aforementioned concerns about estrogen use and potentially improved amenorrheic rates in this population, but these pills have a higher failure rate due to being more dependent on compliance.

Known Exogenous Estrogen Effects on Fertility on Transfeminine Individuals

Some gender-nonconforming individuals undertake GAHT in the form of GnRH agonists or antiandrogens to reduce male phenotypic characteristics with or without exogenous estrogen to induce female secondary sexual characteristics [46]. Ethinyl estradiol was previously the choice of estrogen implementation for this population, though clinicians now typically prescribe oral or transdermal estradiol instead due to concerns for thrombotic and cardiovascular side effects [47]. This treatment can result in erectile dysfunction for some. Taking irregular or low doses of GnRH agonists or antiandrogens or estrogen-only therapy may enable erectile ability.

Contraceptive studies in cisgendered men have shown that FSH and LH suppression can interrupt spermatogenesis and that it can take 3–7 months after these hormonal levels have risen to reverse this effect [48]. However, studies performed on TGE individuals taking estrogen supplementation have shown inconsistent effects on spermatogenesis after gender-affirming hormonal therapy discontinuation [49]. A 2015 study by Meriggiola and Gava did find testicular changes after prolonged estrogen exposure, but no long-term data has been collected about the effects of estrogen on testicular structure or restoration of function after its discontinuation [46].

Despite long-term data not being available, some studies have shown abnormal Leydig cells and seminiferous tubules with resulting reduction of spermatogenesis after estrogen therapy, and other studies have shown no effects on Leydig cells or spermatogenesis [50]. Still other studies have shown not only reductions in Leydig cells and seminiferous tubules, but also reduction of germ cells and fatty degeneration of testicular connective tissue after estrogen therapy [51, 52]. The former of these studies furthermore showed normal spermatogenesis in only 11% of patients taking estrogen, though measurements were taken only 4 weeks after discontinuation of therapy. The lack of consensus on effects of estrogen therapy on testicular structure and spermatogenesis demonstrates the need to further investigate effects during and after discontinuation of therapy.

Contraceptives in Transfeminine Individuals Taking Estrogen for GAHT

Given that most studies report incomplete suppression of spermatogenesis in individuals taking estrogen for genderaffirming hormonal therapy, it is important that sperm banking is discussed prior to initiation of GAHT, and that contraceptive options are discussed with these patients before and during GAHT. Condoms can be used for both contraception and STI prevention. However, hormonal treatments affecting penile erection can impact condom fit and theoretically reduce the likelihood that it stays correctly placed. Vasectomy can also be considered, as it does not affect the feminization process, though individuals must be appropriately counseled about its intended permanence [53].

Discussion

Based on current research, gender-affirming hormonal treatment is not an effective contraception option for TGE patients. Thus, it is key that reproductive healthcare providers offer patient-centered family planning services to these individuals as there can be additional medical, social, and psychological factors at play for TGE patients that should be addressed when clinicians are providing contraception counseling. Due to the lack of data on the utilization of contraception in TGE individuals, and therefore the difficulty with providing evidencebased care when counseling this population, it is even more important that a shared decision-making model be used to determine how patient preferences and values might influence contraception choices. Each TGE individual will have very divergent life experiences and views of how contraception can impact their gender identities.

In addition to emphasizing shared decision-making when discussing contraceptive choices with TGE patients, it is also important that providers create a gender-inclusive environment for their patients. A 2015 survey study found that 23% of TGE individuals avoided engaging with the healthcare system due to concerns about potential mistreatment, and 33% had negative healthcare experiences in the past [54]. Given that many contraceptive options require further engagement with the healthcare system in order to receive the medication or undergo procedures, it is imperative that providers establish trusting environments with their patients. This can include the removal of binary gender identifiers on intake forms; asking all patients about pronouns and names on a regular basis; avoiding gendered greetings; utilizing gender-neutral language on documentation, bathroom labels, and the name of the clinic itself; displaying educational materials relevant to TGE patients; and establishing and enforcing non-discrimination policies that protect the TGE population [55, 3].

Conclusion

Once a trusting environment is established, providers can have frank conversations with TGE patients regarding what is known about contraceptive care for this population. Until there is more published data about the efficacy, effectiveness, and acceptability of contraceptive methods for TGE individuals, data from studies on cisgender individuals can be extrapolated and survey data from this population can be utilized to guide care. By combining this data with values- and goals-based conversations with their patients, providers can best support their TGE patients with making patient-centered decisions regarding contraception.

Compliance with Ethical Standards

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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