

**REVIEW ARTICLE** 

# **Reproductive aspects of transgenders**

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# Abstract

**Objectives:** The reproductive function of transgender (trans) men and women may be compromised after the implementation of gender-affirming therapy (GAT) and gender-affirming surgeries (GAS). Trans men recover their reproductive capacity months after discontinuing testosterone; however, estrogen therapy can permanently compromise the reproductive function of trans women. The aim of the present study was to discuss the reproductive aspects of transgender people, especially those who seek GAT and/or GAS to adapt their bodies to the gender with which they identify. **Methods:** original articles, case series, case reports, and review articles published in English and indexed in the PubMed, Google Scholar, and Embase databases were taken into consideration. Two authors selected the articles to be included, and a third author judged when there was disagreement between the former two. **Results:** Our search retrieved 1,628 articles. After removing duplicates, 1,426 titles were screened, 112 were considered potential, and 63 were included in this review. **Conclusions:** there are changes in the gonads of trans people caused by estrogen and androgen that can promote infertility in this population, perhaps temporarily or not. Thus, it is necessary to carry out reproductive counseling for this population before starting GAHT and during all medical follow-ups, especially with individuals who will undergo GAS.

Keywords: Infertility; Reproduction; Reproductive Rights; Reproductive Techniques; Transgender Persons

# Introduction

Gender identity is defined as a person's sense of being male, female, or other.<sup>1</sup> Cisgender (cis) refers to a person who identifies, expresses themself, and behaves in a way that is congruent with the gender assigned to them at birth. Transgender (trans), on the other hand, refers to a spectrum of people who identify, express themselves, and behave differently regarding their birth-assigned sex.<sup>1</sup> Gender incongruence (GI) is part of this spectrum, and, according to the ICD-11, GI during adolescence and adulthood "is characterized by a marked and persistent incongruence between an individual's experienced gender and their assigned sex, which often leads to a desire to 'transition' in order to live and be accepted as a person of the experienced gender through hormone treatment, surgery, or other healthcare services to make the individual's body align, as much as desired and to the extent possible, with the experienced gender".<sup>2</sup> According to the ICD-11, the diagnosis cannot be assigned prior to the onset of puberty.<sup>2</sup> Gender-affirming hormone therapy (GAHT), is required for the management of trans individuals to align their characteristics with their gender identity, which can promote well-being and may improve quality of life in this population.<sup>3</sup> This condition may be associated with changes in mental health due to the frequent intra-familial and social problems these individuals face during the transition process, often not being accepted by family members and the social environment, such as at school, at work, and in health institutions.<sup>4,5</sup>

The prevalence of trans people varies geographically on account of the cultural specificities of each country or the invisibility of this population to its peers. In a study involving 2,730 American children aged between 6 and 8 years, 1.3%

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did not identify as male or female.<sup>6</sup> In the general population, the prevalence of people who self-classify themselves as transgender is 6.8 (4.6–9.1)/100,000 inhabitants.<sup>7</sup> In a population-based study carried out in 2018, 0.69% (1,090,200) of 158,000,000 Brazilians self-declared themselves as trans and non-binary men or women,<sup>8</sup> and the perception of the trans condition occurred more so during childhood and adolescence.<sup>5</sup> An estimated 1.4 million self-declared transgender adults currently live in the United States.<sup>9</sup> The proportion of trans women is higher than trans men, even during childhood. In a cohort of Canadian children with trans characteristics who were followed up between 1976 and 2011, the ratio of trans females to males was 4.5:1, which is more than double compared to Netherlands group, whose ratio was 2:1.<sup>10</sup>

The diagnosis of GI is clinical and, according to the ICD-11, this condition is characterized by a marked and persistent incongruence between the experienced gender and the sex assigned to the individual at birth.<sup>2</sup> Clinical findings include, among others, the discomfort of the person with their body and the desire to free themselves from their bodily characteristics that cause dissatisfaction, culminating in changes in mental health. In fact, this population is more exposed to prejudice, discrimination, difficulty in self-acceptance, depression, and a greater risk of ideation or even suicide attempts.<sup>11</sup> Therefore, the promotion of health in people with GI must involve the work of a multidisciplinary team composed of doctors, psychologists, and social workers, among others.

Medical assistance in the phenotypic transition process of the trans person involves the management of GAHT, with estrogen associated or not with antiandrogens for the trans woman and testosterone (T) for the trans man. Surgical procedures called gender affirmation surgeries (GAS) are often necessary and range from minor cosmetic procedures to genitalia reconstruction, including neovaginoplasty, breast augmentation surgery, masculinizing mastoplasty, and phalloplasty, among others.<sup>12</sup> Both GAHT and GAS can permanently compromise the reproductive potential of trans men and women.<sup>12</sup>

The present narrative review aimed to verify the current state of knowledge on reproductive possibilities and fertility preservation strategies for transgender people who seek medical services to undergo GAHT followed or not by GAS.

#### **Methods**

A comprehensive and nonsystematic literature review was performed, focusing on reproductive options and fertility preservation in transgender people. Given the relative paucity of literature in this subject area, all study designs were considered for data acquisition. Thus, original articles, case series, case reports, and review articles published in English and indexed in the PubMed, Google Scholar, and Embase databases were taken into consideration. The key search terms used were ((transgender) OR (transsexual) OR (gender incongruence) OR (gender identity disorder)) AND ((reproductive health) OR (fertility preservation) OR (oocyte cryopreservation) OR (gender-affirming therapy) OR (assisted reproductive technologies)). The references of each selected article were also manually searched. Two authors (L.A.S.L. and E.S.R.) selected the articles to be included, and a third author (M.C.R.A.) judged when there was disagreement between the former two.

#### **Results**

Our search retrieved 1,628 articles. After removing duplicates, 1,426 titles were screened, 112 were considered potential, and 63 were included in this review.

#### **Gender-affirming hormone therapy**

GAHT, consists of the prescription of exogenous T for trans men and estrogen (E) with or without antiandrogens (spironolactone, cyproterone acetate) for trans women.<sup>13</sup> Testosterone is used to induce male secondary sexual characteristics and the possible regression of female secondary sexual characteristics in trans men.<sup>14</sup> Most data available in the literature on the effects of GAHT with T derive from the use of intramuscular testosterone undecylate or undecanoate at a dose of 1000 mg/4.0 mL every 90 days and transdermal T for daily use.<sup>12</sup> In Brazil, the prescription of intramuscular testosterone cypionate at a dose of 200 mg/2.0 mL every 15 or 21 days is more common.<sup>15</sup> However, one study with a small sample size (n=63) evidenced adequate masculinizing effects and good acceptance of subcutaneous T cypionate or enanthate at a dose of 75 mg every 7 days.<sup>16</sup> The serum T levels recommended for trans men are the same as those recommended for cis men.<sup>15</sup> At male levels, T promotes negative feedback leading to the partial blockage of the hypothalamic-pituitary-gonadal (HPG) axis, with subsequent reduction of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels.

The prolonged use of T induces clitoromegaly, increased facial and body hair, voice alterations (deepening), increased sexual desire, and myometrial hypertrophy.<sup>17</sup> Its adverse effects include baldness, acne, increased aggressiveness and sexual desire, and changes in the lipid profile, with increased triglycerides and LDL-cholesterol and reduced HDL-cholesterol, as well as polycythemia with increased hematocrit.<sup>18</sup> The risk of polycythemia seems to be greater in users of transdermal T and other T esters compared to T undecanoate.<sup>19</sup>

GAHT for trans women includes the exogenous administration of estrogen and antiandrogens (cyproterone, spironolactone, 5 $\alpha$ -reductase inhibitors) with the aim of inducing female secondary sexual characteristics. The T and estradiol levels within the normal range for cis women are the same as those recommended for trans women.<sup>12</sup> There are no studies comparing the efficacy and safety of estrogens available for use in transgender women. The ENIGI study, a multicenter, prospective cohort study, provided data from five years of oral estradiol valerate use at a dose of 4.0 mg/day; however, due to the hepatic pathway and thrombogenic effects of the oral route, women aged 45 years or above have started using estradiol patches at a dose of 100 mcg/24 hours, and at lower doses for patients with a history of thrombosis or other clinical conditions.<sup>20</sup> The Endocrine Society guidelines for transgender people recommend using oral estradiol at a dose of 2.0 to 6.0 mg/day and transdermal patches at a dose of 0.025 to 0.2 mg/day, with patch replacement every 3 or 5 days.<sup>12</sup> Gel containing 17 $\beta$ -estradiol can also be used at a dose of 2.0 mg/day for daily use.<sup>21</sup>

# Effects of gender-affirming hormone therapy on the reproductive potential of trans men and women

The American Society for Reproductive Medicine draws attention to the lack of data on the effects of GAHT on fertility in transgender people.<sup>21</sup> There are still no studies in the literature addressing the testosterone-free time period required for trans men to be able to undergo Assisted Reproduction (AR) techniques using their own oocytes. Also, the fecundity and fertility rates after the use of high doses of T remain unknown.<sup>22</sup> Furthermore, there are no data on the reproductive health of offspring resulting from oocytes exposed to T without direct intrauterine exposure.<sup>22</sup> Likewise, there is still a gap in knowledge on the possibility of recovery of the reproductive potential of trans women after discontinuing GAHT.

The chronic use of high doses of T results in suppression of the hypothalamic-pituitary axis (HPA), with reduced levels of LH and FSH,<sup>23</sup> and the consequent suppression of ovarian function, resulting in anovulation and amenorrhea within six months.<sup>24</sup> In animal models, androgens exert pro-atretic and anti-apoptotic effects in growing follicles and granulosa cells, respectively.<sup>25,26</sup> In ovarian specimens obtained from trans men in chronic use of T who underwent GAS, hyperplasia and thickening of the cortex, luteinization of the ovarian stroma,<sup>27</sup> and follicle atresia,<sup>28</sup> similar to the ovarian alterations observed in women with polycystic ovary syndrome (PCOS), have been reported. As for the number of follicles, there are still controversies about whether or not there is an increase during the use of T;<sup>13,27</sup> however, evidence shows that the number of primordial follicles (primary, pre-antral, and early antral) remains unchanged.<sup>26</sup> A microscopic analysis of ovarian specimens from trans men after one year of T use showed a mean count of 90.34 (2 – 614) ± 118.02 follicles, including 68.52% of primordial follicles, 20.26% intermediate follicles, and 10.74% primary follicles. The *cumulus oophorus* presented normal spindle in 94% of the analyzed samples and normal chromosomes in 84%.<sup>28</sup> It is important to highlight that these follicles maintained their *in vitro* maturation capacity. However, it is still unclear whether the results of AR techniques are compromised in this population.

A recent study including 83 trans men in use of T who underwent ovarian stimulation and oocyte collection for intracytoplasmic sperm injection (ICSI) evidenced the occurrence of anomalous cleavage in 45.8% of the zygotes, an *in vitro* maturation rate of 23.8%, a vitrification rate of 21.5%, and 72.6% viability after thawing. ICSI was performed on 139 oocytes, with a fertilization rate of 34.5%; 52.1% of the embryos reached day three of development. In comparison with vitrified donor oocytes, a delay in the disappearance of pronuclei was observed. The authors concluded that oocytes obtained from the ovarian tissue of trans men using T had reduced development capacity in culture medium (*in vitro*).<sup>29</sup> Thus, discontinuation of the drug is recommended for trans men who plan to undergo IVF.

There are still no studies demonstrating the ideal T washout period for performing IVF. LH and FSH levels are not predictive markers of adequate ovarian reserve, and there is controversy regarding the effect of T on anti-Mullerian hormone (AMH) secretion. One study showed AMH suppression that went from  $4.4 \pm 4.4 \mu g/L$  to  $1.4 \pm 2.1 \mu g/L$  after a period of 16 weeks of T use.<sup>30</sup> Another study, on the other hand, did not show a significant difference in the concentration of this hormone in 16 trans men after one year of T use.<sup>31</sup> Therefore, trans men need to be informed that there is no consensus on the necessary time to discontinue T before IVF.

Regarding the transfer of embryos to trans men, it must be clarified that there are few studies on the effects of GAHT on the uterus. One study showed an increase in estrogen receptor expression in the myometrium, which could explain,

in part, the occurrence of myometrial hypertrophy, which has already been demonstrated in 58% of trans men.<sup>32</sup> In the endometrium, T promotes endometrial inactivity and glandular atrophy in the cervical canal and greater expression of androgen receptors in the genitalia during treatment with T.<sup>13</sup> It remains unknown whether these alterations have repercussions on the reproductive capacity of trans men. We emphasize the need for exhaustive discussions regarding the definitive sterility of trans men with the performance of hysterectomy and oophorectomy due to the possibility of future desires to use their uterus for pregnancy.<sup>33</sup>

In spite of all these changes in the reproductive system of trans men, their reproductive potential may return with the recurrence of menstruation after 3 to 6 months of T discontinuation.<sup>34</sup> Another study showed that 80% of trans men began cycling within 6 months after discontinuing testosterone and that 20% became pregnant while still in amenorrhea.<sup>35</sup> Meanwhile, in a study involving 61 trans men seeking natural pregnancy, 88% became pregnant with their own oocytes and 61% became pregnant 4 months after ceasing T administration; 12% required assisted reproductive (AR) techniques.<sup>34</sup> Therefore, even during T therapy and when discontinuing it, it is necessary to offer a contraceptive method to those who do not wish to become pregnant, since unintended pregnancies are also common, occurring in approximately 30% of transgender men.<sup>35</sup> The contraceptive options are the same for cis women (barrier methods like male and female condons, diaphragm, natural methods, fertility awareness methods, rhythm method, avoiding sex, during fertile period, male or female sterilization, conjugated oral contraceptives, monthly injections, patches, vaginal ring, progestogen pills, medroxyprogesterone acetate 150 mg every three months, implant placement, levonorgestrel IUD, cooper IUD).<sup>36,37</sup> Still, it is necessary to individually discuss which method is more suitable for each person since the presence of estrogen in the formulation may increase dysphoria in trans men.

The actual effects of chronic estrogen and antiandrogen use on the testicles are still unclear. The available data are based on case reports and small case series and show from mild alterations to severe impairment of the testicular parenchyma, with hyalinization of the seminiferous tubules, alterations in Sertoli and Leydig cells,<sup>27</sup> and hypogonadism, which interfere with spermatogenesis.<sup>38</sup> The histological examination of the testicles evidences a reduction in the diameter of the seminiferous tubules, germ cell hypoplasia, and changes in spermatogenesis with spermatogonial maturation arrest, even in trans women who were not using estrogen alone or in association with antiandrogens, prior to orchiectomy.<sup>39</sup> In a study evaluating semen samples from 28 patients undergoing GAHT with estrogen, the authors found that parameters such as concentration and motility were abnormal.<sup>40</sup> A retrospective cohort study showed worse pre- and post-freezing semen quality in trans women compared to the general population, although no correlation with GAHT was observed.<sup>41</sup> It is noteworthy that the use of tight underwear and the concealment of the testicles are common practices among trans women; these behaviors increase by 3 and 6 times, respectively, the risk of asthenia and oligospermia, with total sperm counts of less than 5 million.<sup>42</sup> Also, there is a lack of data in the literature on the period of recovery of spermatogenesis after the interruption of estrogen administration.

Cyproterone acetate (CPA) is a synthetic dose-dependent (5-10 mg/day) progestogen with antiandrogenic properties that acts by competitively binding to T receptors in the brain and peripheral tissues, inhibiting spermatogenesis and sperm motility as early as 2 to 4 months.<sup>43</sup> There are no data in the literature on the effects of spironolactone on the reproductive potential of transgender women. Trans women need to be warned about reproductive damage before and during GAHT and be offered the opportunity to have their semen frozen prior to treatment.<sup>38</sup>

There is also a gap in the literature regarding the effects on the reproductive capacity of transgender adolescents treated with GnRH agonists (aGnRH). These substances act on the pituitary gland, initially stimulating GnRH receptors and later promoting their blockage, leading to the suppression of the synthesis of LH and FSH. In cis men, monthly subcutaneous injections of 3.6 mg of aGnRH resulted in a drastic reduction of T production by Leydig cells to levels below 0.5 ng/mL one month after injection.<sup>44</sup> However, after ceasing exposure to aGnRH, sperm concentration returns to baseline levels within 10 to 14 weeks.<sup>45</sup> In the case of blockage with a GnRH agonist in cis women and men, the alterations are totally reversible.<sup>46</sup> Nevertheless, there are no data on the effects of long-term GAHT on fertility in men and women when the treatment is initiated during adolescence,<sup>46</sup> and it remains unknown whether fertility can be restored.

### **Reproductive counseling for transgenders**

An essential form of assistance to transgender people before their transition is reproductive counseling, which aims to clarify the effects of GAHT and GAS on the individual's reproductive capacity. This strategy of care is essential to ensure the reproductive right of this population, with emphasis on fertility preservation for those who desire parenthood.<sup>47</sup> Data from 121 trans women showed that 77% of them consider it important to discuss the preservation of fertility before gender-affirming medical procedures, and 50% stated that they would have preserved spermatozoa if they had been offered the possibility prior to the transition; however, 30% felt discomfort with the seminal freezing procedure.<sup>48</sup>

Several obstacles limit the trans person's access to this form of care. A study conducted in Israel showed that 67.4% of trans women and 61.9% of trans men wanted to have children;<sup>49</sup> nonetheless, the search for fertility preservation was low (40.4%) among trans women and extremely low among trans men (5.8%).<sup>49</sup> A Swedish study including 78 trans women and 164 trans men referred for gamete cryopreservation showed that 69.5% of the women and 82% of the men wanted to have children; however, only 26.2% of the men and 75.6% of the women performed gamete cryopreservation.<sup>50</sup> Young age, the lack of previous hormone treatment, and homosexual orientation were independent factors associated with the decision to cryopreserve oocytes among trans men. Meanwhile, among trans women, the decision to have GAS and being heterosexual were independent factors related to the decision to preserve fertility.<sup>50</sup> Many desist from the procedure in order not to postpone GAHT or due to the discomfort caused by the fertility preservation technique, both of which reinforce the trans condition, and because of the procedure costs, but 44% of trans women and 19% of trans men give up out of fear of the medical team's judgment.<sup>49</sup> These obstacles contribute to a large portion of this population (31.3%) choosing to adopt children.<sup>51</sup> For trans women with dysphoria regarding the genital manipulation required for semen collection, vibratory stimulation or electroejaculation techniques may be proposed.<sup>52</sup>

Discussing already approved techniques, such as sperm cryopreservation for trans women and embryo and oocyte cryopreservation for trans men,<sup>53</sup> not only before initiating GAHT and performing GAS, but throughout the entire follow-up, is recommended so that the individual has the opportunity to make decisions concerning their reproductive life. It is important to be aware that a significant part of this population wants to have biological children through conventional sexual relations<sup>54</sup> and that a considerable amount of trans men want to have children and/or freeze their oocytes.<sup>55</sup> However, assistance regarding the reproductive function of the trans population is a challenge due to the difficulty in finding donors, high procedure costs, financial limitations, and the lengthiness of legal aspects, among others.<sup>56</sup>

## **Reproductive options for transgenders**

The reproductive options for transgender people do not differ from those offered to cis individuals, nor do the techniques for attempting fertility preservation, which include oocyte and embryo cryopreservation, ovarian tissue cryopreservation for trans men, and sperm cryopreservation for trans women. However, there are some particularities in the trans population that need to be addressed. Gamete collection procedures reinforce the trans condition, as is the case with the insertion of the vaginal speculum and transvaginal ultrasound in trans men<sup>57</sup> and masturbation for semen collection in trans women. It is also necessary to mention that ovarian stimulation will raise estradiol levels and can be controlled by the concomitant use of aromatase inhibitors, which do not seem to impair the reproductive outcome.<sup>58</sup>

Considering that the trans woman's seminal quality can be compromised with GAHT, the ideal would be to propose seminal cryopreservation before starting hormone therapy; however, even during GAHT, it is necessary to discuss the method and its limitations regarding sperm quality. In the case of trans men, there are no studies correlating the chronic use of high doses of T with the definitive deterioration of reproductive capacity. Unless trans men have proven infertility, the recurrence of menstruation occurs up to six months after T discontinuation,<sup>34</sup> enabling the possibility of natural pregnancy.

It is recommended that reproductive options for transgender people be categorized according to the stage of the individual's gender affirmation process.<sup>59</sup> Before and during GAHT, as well as concomitantly with GAS<sup>59</sup> (Figure 1), it is important to discuss the individual needs of each person, know their expectations, and demystify and inform them regarding their actual reproductive possibilities based on evidence and considering the ethical aspects of each culture.

For trans men who have male partners and penis-vagina sexual relations, natural pregnancy with the partner's semen can be attempted, as well as the use of AR techniques in cases of proven marital infertility. If there is no penetrative sexual practice, intrauterine insemination or IVF/ICSI can be an alternative. When trans men have female partners, they may use donor semen and their own oocytes, their partner's oocytes, or donated oocytes, their own uterus, their partner's uterus, or a surrogate uterus. Fertility preservation can also be provided through oocyte freezing or ovarian tissue cryopreservation,<sup>46,59</sup> which is still in the experimental phase.

For trans women who performed seminal freezing, this procedure can be used by a female partner in case the trans woman is homosexual or to perform IVF/ICSI using donated oocytes and a surrogate uterus.<sup>48</sup> Gamete donation is an option when sperm alterations have been verified after prolonged estrogen use, as well as the possibility of a surrogate uterus and oocyte donation.<sup>48</sup> Sperm collection procedures may be necessary when testicular dysfunction is present<sup>60</sup> (Figure 1). These discussions should take place even when the person is not interested in reproduction at the time of treatment, which is more common in younger patients. Testicular tissue cryopreservation may be a future option for trans women, but it is still an experimental procedure.<sup>59</sup>



Figure 1. Spreadsheet of the reproductive options for transgenders.

PESA: Percutaneous Epididymal Sperm Aspiration; TESA: Testicular Sperm Aspiration; MESA: Microsurgical Epididymal Sperm Aspiration

### Discussion

The World Professional Association for Transgender Health,<sup>61</sup> the American Society for Reproductive Medicine,<sup>21</sup> and the Society of Endocrinology<sup>12</sup> have established guidelines for reproductive counseling and fertility preservation for transgender people. However, there are few quality studies that support these recommendations, most of which derive from expert opinion. The real risk of infertility associated with GAHT and the real need to use fertility preservation techniques for this population remain unclear. Also, there is a lack of studies on the measures to be taken to reduce dysphoria regarding the suspension of T in trans men.

The reproductive possibilities and fertility preservation techniques for transgenders do not differ from those offered to cis individuals, although they present specific characteristics due to the GAHT and GAS interventions that may lead to infertility in trans men and women. Adequate assistance to this population involves asking about the desire to have biological children, discussing AR techniques, providing information on fertility preservation strategies, clarifying which interventions will be necessary to use their cryopreserved gametes, and, for those who do not opt for fertility preservation, what their future alternatives for having children might be.<sup>50,62</sup> It is also necessary to discuss contraceptive options for trans men who do not wish to become pregnant.

Some factors influence the decision to preserve fertility, such as younger age, opting for the performance of GAS, which involves the excision of the gonads, and the procedures involved in preserving fertility, such as speculum examination and transvaginal ultrasound in trans men and masturbation in trans women; unfortunately, these factors may increase dysphoria in relation to the genitalia. Another difficulty expressed by trans individuals is the need to temporarily suspend GAHT<sup>49</sup> for fear of losing the characteristics of the gender with which they identify. Even so, there is a considerable proportion of trans men and women who wish to have biological children; therefore, this aspect must be discussed before gender affirmation procedures and during the follow-up of these patients.

Despite considerations regarding the need for the healthcare team to discuss reproductive aspects with transgender patients, it seems that this topic has been systematically neglected. In fact, a study with trans adolescents showed that most of them expressed interest in having biological children and wanted to know their options for building their families in the future; however, only 13.5% of them were informed by health professionals about the effects of the gender affirmation process on their fertility.<sup>63</sup> Another study showed that 95% of the participants thought that fertility preservation should be proposed by health professionals, and 33% (114/345) of those who did not have children mentioned a desire to use strategies for fertility preservation, although only 7% were submitted to gamete preservation.<sup>64</sup> It is noteworthy that GAHT can result in transient or permanent changes in semen in trans women. However, there is no study proving that

the chronic use of T can result in infertility in transgender men, and there are no concrete data on the reversibility of morphological changes in the ovaries<sup>27</sup> with the increase in the number of follicles. These modifications, theoretically, could lead to changes in the reproductive capacity of trans men, but the gaps in knowledge make it difficult to develop reproductive counseling protocols for these individuals.<sup>13</sup>

GAS involves oophorectomy and excision of the uterus in trans males, eliminating the possibility of pregnancy. Likewise, orchiectomy in trans women definitively eliminates their chances of having biological children. Therefore, it is recommended that the reproductive aspects be thoroughly discussed with the trans person before starting the gender affirmation procedures and throughout the clinical follow-up period. It is also worth noting that there are several barriers to comprehensive care for this population, especially from the reproductive point of view, such as difficulty in accessing AR services, discrimination, the lack of training of doctors to deal with the trans condition, health system barriers, and socioeconomic hindrances<sup>65</sup> (Table 1).

#### Table 1: Key recommendations in transgender reproductive care

Before initiating cross-hormone therapy for transgenders, it is necessary to discuss reproductive options and fertility preservation possibilities.

It is necessary to discuss assisted reproductive (AR) techniques and offer information on fertility preservation strategies.

For those who do not want to have children or do not want to try to preserve their fertility, it is imperative to discuss future options for having children.

There are few quality studies that support the recommendations regarding the reproductive aspects of transgenders. Most recommendations derive from expert opinion.

High doses of estrogen can permanently compromise the reproductive potential of trans women.

Testosterone (T) suspension may lead to the recurrence of menstruation in trans men over a period varying from 3 to 6 months. As a result, trans men can ovulate again and present uterine receptivity, recovering their potential for natural pregnancy.

It is recommended that T be discontinued before performing oocyte cryopreservation in trans men. However, the duration of the washout time remains unclear.

It is necessary to discuss contraceptive methods for trans men who do not want to become pregnant and who have a penis-vagina relationship.

#### Conclusion

Despite the lack of knowledge regarding the true impact of GAHT on the reproductive function of trans men and women, there are changes in the gonads of trans people caused by estrogen and androgen that can promote infertility in this population, perhaps temporarily or not. Thus, it is necessary to carry out reproductive counseling for this population before starting GAHT and during all medical follow-ups, especially with individuals who will undergo GAS.

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#### **Authors contribution**

Lucia Alves da Silva Lara was responsable for the bibliographic review, data collection, design, written and last review of the paper Paula Andrea Albuquerque Salles Navarro was responsable for the review, design, and last review of the paper Estella Thaisa Sontag dos Reis was responsable for the bibliographic review, data collection, design, written and last review of the paper Thays Marina Roncato Barcelos was responsable for the critical review of the manuscript Rosana Maria dos Reis was responsable for the critical review of the manuscript Maíra Cristina Ribeiro Andrade was responsable for the critical review of the manuscript Ana Carolina Japur de Sá Rosa e Silva was responsable for the critical review of the manuscript Rui Alberto Ferriani was responsable for the critical review of the manuscript