v. 4, n. 90, 2024

International Journal of Health Science

# EVALUATION OF THE BENEFITS AND RISKS RELATED TO HORMONAL THERAPIES FOR GENDER REASSIGNMENT

*Acceptance date: 14/10/2024*

***Aline Martins Teixeira Monteguti***

***Caroline Lianes Martins***

***Fabiana Vidal***

***Guilherme Debaldi***

***Marcos Vinicius dos Santos***

**Abstract:** Hormone therapy for gender transition is a treatment that helps align the body's secondary sexual characteristics with a person's gender identity. Hormone therapy is used by transgender women and men, and non-binary people, to produce physical changes in the body that are caused by hormones that give the gender characteristics. These changes are called secondary sexual characteristics of the desired gender. Individuals entering puberty also need GnRH analogues. Each case is specific. Hormone therapy for gender transition has become very popular due to the media, which sometimes induces individuals to undergo this process without being properly aware of the health risks caused by administering the drugs involved. The aim of the project is to raise awareness among people who are looking to transform their bodies using this method. The research focused on gathering all the information available on the subject in the field of health sciences. It contrasted the risks and benefits of the methodology used in hormone therapy for gender transition. **OBJECTIVE:** The aim of the project is to provide information to people seeking body transformation through hormone therapy, on the main recommendations, pre-preparation, associated risks, and results obtained over the last 20 years.
**Keywords:** "Gender transition hormone therapy", "Gender Specific Need", "Gender Identity Dysphoria", "Gender Identity Disorder", " Social Construction of Gender Identity", "Sexual Disorders and Sexual Identity", "

## INTRODUCTION

Hormone therapy for gender transition is a treatment that helps align the body's secondary sexual characteristics with a person's gender identity. Hormone therapy is used by transgender women and men, and non-binary people, to produce physical changes in the body that are caused by hormones that give the gender characteristics. These changes are called secondary sexual characteristics of the desired gender. Individuals entering puberty also need analogues of the GnRH hormone. Each case is specific.

Eva Moore and her team, in an article published by The Journal of Clinical Endocrinology & Metabolism in 2003, criticize the fact that only six clinical centers reported dosage information in medical journals for endocrinological treatment of M→F transsexual people. The treatment regimens included various forms of estrogen, progestogens and/or antiandrogens. No randomized trials were found. Although the guidelines of organizations such as the International Association of Gender Dysphoria Harry Benjamin, have been useful, management remains complex and experience-driven (MOORE; WISNIEWSKI; DOBS, 2003).

Researchers Michael Mendelsohn and Richard H Karas published data in the journal *Science* in 2005 on their research into "gender differences in the molecular and cellular physiology of the heart and blood vessels in health and disease", highlighting little-studied areas such as hormone replacement therapy to improve cardiovascular health in women. Her research, however, was discontinued. Due to a lack of quantitative and qualitative data on women who have used testosterone and obtained a better prognosis for pre-existing cardiovascular disease (MENDELSOHN & KARAS, 2005).

In 2005, De Cuypere and his team organized a follow-up study of 55 transsexual patients after sex reassignment surgery. Most of the participants reported a change in orgasmic sensation, making it more powerful and shorter in the woman-man relationship and more intense, but softer and longer in the man-woman relationship. More than two thirds of the women reported the secretion of a vaginal fluid during sexual arousal, coming from Cowper's glands, left in place during sur-

gery. In women to men with an erectile prosthesis, sexual expectations were realized, but pain during intercourse was reported more frequently (DE CUYPERE, Griet et al. 2005).

In a study carried out by the *University of Amsterdam UMC*, researchers Henriette A Delemarre-Van De Waal and Peggy Cohen-Kettenis, report that preliminary findings suggest that treatment with a GnRH analog (GnRHa) suppresses endogenous gonadal stimulation of B2-3 and G3-4, and prevents the development of unwanted sex characteristics, in addition to the cross-sex steroid hormones added to the GnRHa medication. There is a decrease in growth rate and bone maturation. Total bone density remains in the same range during the years of puberty suppression, whereas it increases significantly in cross-sex steroid hormone treatment ( DELEMARRE & COHEN-KETTENIS, 2006).

Emily Newfield and her team published a very important paper on health-related quality of life in female-to-male transgender individuals. The analysis of health concepts of quality of life demonstrated statistically significant ($p$ <0.01) decreases in quality of life among FTM transgender participants compared to the US male-to-female population, particularly with regard to mental health. Transgender FTM participants who received testosterone (67%) reported statistically significantly higher quality of life scores ( $p$ <0.01) than those who did not receive hormone therapy (NEWFIELD, Emily et al. 2006).

Wylie Hembree has done a lot of work and research on the subject. With the aim of formulating practical guidelines for the endocrine treatment of people with gender dysphoria/conclusion. In one of his most cited works by the academic community, he concludes that "people seeking to develop the physical characteristics of the desired gender need a safe and effective hormonal regimen. One that suppresses endogenous hormone secretion determined by genetic/biological sex. And maintain sex hormone levels within the normal range for the person's desired gender (HEMBREE, Wylie C. et al.2009) .

In his 8th edition of the book "Sexual Medicine", Annelou LC de Vries reported on his research into the suppression of puberty by means of analogues of gonadotropin-releasing hormone (GnRHa). The aim was to alleviate the suffering caused by the development of secondary sexual characteristics and provide time to make a balanced decision regarding the actual change of gender. The research concluded that puberty suppression can be considered a valuable contribution to the clinical management of gender dysphoria in adolescents (DE VRIES, Annelou LC et al. 2011).

In chapter 6 of the book Principles of Gender-Specific Medicine. The chapter provides an overview of the Standards of Care (SOC) of the World Professional Association for Transgender Health. The doctor's basic competencies are described, as well as the criteria for hormonal and surgical treatment. Healthcare professionals can use the SOC to help patients consider the full range of healthcare services open to them, according to their clinical needs and gender expression goals ( COLEMAN, Eli et al.2012).

In 2012, a qualitative study with participating physicians from Ontario, Canada. Semi-structured interviews were used to capture a progression of ideas related to the barriers faced by physicians when caring for trans patients. The qualitative data was then transcribed verbatim and analyzed with an emergent grounded theory approach. 13 doctors took part in the research. The analysis revealed barriers to care grouped into five themes: access to resources, medical knowledge deficits, ethics of medical care related to transition, diagnosis versus pathologization of trans patients, and health system determinants (SNELGROVE, John W. et al. 2012).

A central theme of "not knowing where to go or who to talk to" was also identified. The findings of this study show that doctors perceive barriers in caring for trans patients, and that these barriers are multifactorial. Access barriers prevent doctors from referring patients to specialists or seeking reliable information about treatment. The clinical management of trans patients is complicated by a lack of knowledge and by ethical considerations regarding treatments that may be unfamiliar or challenging for doctors (SNELGROVE, John W. et al. 2012).

The disciplinary division of responsibilities in medicine further complicates care; few professionals identify trans health as an area of interest and there is a tendency to overemphasize trans status in mental health assessments. The failure to recognize and accommodate trans patients in sex-segregated health systems leads to poor health policies. The findings of this study suggest potential solutions to barriers to trans healthcare at the informational level with greater awareness of clinical guidelines and through the inclusion of trans health issues in medical education - and at the institutional level, with support for both trans-focused and trans-friendly models of primary care (SNELGROVE, John W. et al. 2012).

In the American Journal of Public Health ( AJPH ) a very interesting article was published in October 2013 on "the relationships between social determinants of health and experiences of transgender-related discrimination reported by transgender people in Virginia". The research concluded that transgender people in Virginia experience widespread discrimination in healthcare, employment and housing. Multilevel interventions are needed for transgender populations, including legal protections and training for health care providers (BRADFORD, Judith et al .2013).

In 2013, researcher Lisa Simons and her team presented an interesting article for the journal *Elsevier.* In it, she highlights the importance of parental support and mental health among trans adolescents. According to Lisa, parental support is associated with a higher quality of life and protects against depression in transgender adolescents. Interventions that promote parental support can significantly affect the mental health of transgender young people (SIMONS, Lisa et al. 2013).

In 2014 in the journal *Pediatrics,* Annelou LC de Vries and her team published data from their research on the "psychological outcomes of young adults after puberty suppression and gender reassignment". He concluded that a clinical protocol with a multidisciplinary team, including puberty suppression, followed by cross-sex hormones and gender reassignment surgery, offers gender dysphoric young people who seek gender reassignment from the onset of puberty, the opportunity to develop into well-functioning young adults (DE VRIES, Annelou LC et al. 2014).

Jae Sevelius in her research developed by the *University of Oxford,* on the Barriers and Facilitators to Engagement and Retention in Care among Trans Women Living with Human Immunodeficiency Virus, reports vulnerability of this group to the virus. Jae says that "Our participants faced substantial challenges to adherence to HIV care and treatment, including avoidance of health care due to stigma and past negative experiences, prioritization of hormone therapy, and concerns about adverse interactions between antiretroviral treatment for HIV and hormone therapy" ( SEVELIUS, Jae M. et al.2014).

In 2015, Dr. Johanna Olson and her team conducted a study on the basic physiological and psychosocial characteristics of young trans people seeking care for gender dysphoria. The baseline physiological parameters of the young


International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15949024081010

people assessed were within normal limits for the sex assigned at birth. Transgender young people are aware of the incongruence between their internal gender identity and their assigned sex from an early age. The prevalence of depression and suicide, however, showed that young people could benefit from timely and appropriate intervention. When necessary (OLSON, Johanna et al. 2015).

In 2015, Schneider and his team published part of their research in *The Journal of Sexual Medicine,* on "Testicular functions and clinical characterization of patients with gender dysphoria (GD) undergoing sex reassignment surgery (SRS)". The aim of this study was to compare the effects of three different hormone treatment strategies in relation to endocrinological parameters and testicular histology. Patients who discontinued treatment within 6 weeks. Patients who discontinued within 2 weeks. And the last group were patients who did not discontinue (SCHNEIDER, Florian et al. 2015).

In 2016, researcher Jamie Feldman and his team published some of the results of their research on "Priorities for transgender health and medical research" in *Current Opinion in Endocrinology, Diabetes and Obesity.* Feldman states that transgender individuals experience unique health disparities, but are the subject of little health-focused research. Current research suggests increased mortality and depression in transgender individuals who do not receive optimal care and increased cardiovascular risk related to hormone therapy. Current evidence does not support concerns about the risk of malignancy related to hormones (FELDMAN, Jamie et al. 2016).

One of the best sources on the subject is the work carried out by Oxford University and published in The Journal of Clinical Endocrinology & Metabolism in 2017. It contains a lot of quantitative information obtained through a literature review. In this 2017 article by HEMBREE and his team, they identified 29 eligible studies with a moderate risk of bias. Regarding the effect of sex steroid use in transgender individuals on lipids and cardiovascular outcomes. The second review identified 13 studies regarding the available evidence on the effect of sex steroids on bone health in transgender individuals (WIEPJES, Chantal M. et al. 2018).

A study on gender dysphoria in Amsterdam, which collected information on the subject from the 1970s to 2015. It provided valuable information on trends in prevalence, treatment and regrets. A total of 6,793 people (4,432 men with assigned birth, 2,361 women with assigned birth) visited the gender identity clinic from 1972 to 2015. The number of people assessed per year increased 20-fold, from 34 in 1980 to 686 in 2015. The estimated prevalence in the Netherlands in 2015 was 1:3,800 for men (trans women) and 1:5,200 for women (trans men). The percentage of people who started HT within 5 years of their first consultation decreased over time, from almost 90% in 1980 to 65% in 2010 (WIEPJES, Chantal M. et al. 2018).

There is a role for prenatal/postnatal androgens in gender development, but some studies indicate that it is more likely that prenatal androgens affect gender behavior and sexual orientation more than gender identity itself (FRISEN, Louise et al. 2009). Studies focusing on brain structure suggest that the brain phenotypes of people with gender incongruence differ in various ways from control men and women, but that there is no complete reversal of sex in brain structures (KREUKELS & GUILLAMON, 2018).

The percentage of people who underwent gonadectomy within 5 years of starting HT remained stable over time (74.7% of trans women and 83.8% of trans men). Other relevant data was that only 0.6% of trans women and 0.3% of trans men who underwent gonadec-

tomy were identified as having regrets. This study was carried out at the largest Dutch gender identity clinic, which treats more than 95% of the trans population in the Netherlands (WIEPJES, Chantal M. et al. 2018).

Description of drugs prescribed for hormone therapy in specialized health services for transsexuals and transvestites in Rio Grande do Sul, 2020. Descriptive study, with data collection in these establishments, in the period May-September 2020, using an instrument developed by the researchers. Data was obtained on the profile of users and characteristics of pharmacological care for hormone treatment. The aim of the study was to describe the drugs prescribed for hormonal treatment of the transsexualizing process in specialised healthcare establishments for transsexuals and transvestites in Rio Grande do Sul, Brazil (AUGUSTO; OLIVEIRA; POLIDORO, 2020).

In general, the dosage and type of hormone used in adolescents with dysphoria are often different from those used in adults. The recommendation made by the American Society of Endocrinology Guideline is to carry out treatment with gastrointestinal administration of GnRH (Gonadotrophin Releasing Hormone Agonists) as it promotes blockage of the hypothalamus/pituitary/gonadal hormonal axis, when the individual is at Tanner stage 2. It thus prevents the development of secondary sexual characteristics, allowing time for their desires to mature. However, it must be strictly monitored for the adverse effects of delayed puberty such as growth arrest and bone maturation (DE OLIVEIRA ALVES, Ariane ,2021).

On the other hand, cross-sex hormones, which allow for active masculinization or feminization, can be used when the individual reaches the legal age of medical consent, which varies between countries. For female trans people, oral 17 beta oestradiol is used and for male trans people, intramuscular testosterone is administered. An individualized recommendation by a team of professionals that informs about the benefits and possible risks including cystic acne, diabetes, hypertension, liver problems, adverse changes in lipid profile, anemia, insulin insensitivity and risk of impaired fertility is essential (DE OLIVEIRA ALVES, Ariane, 2021).

In an article published in the *Brazilian Journal of Health Review* in 2021, the authors state that transgender young people have a divergence between their sex at birth and their gender identification, which can cause gender dysphoria. The development of mental disorders is more prevalent in transgender adolescents than in the cisgender population (ALVES; MAGALHÃES; MENDES, 2021). The research indicates a clear greater psychological vulnerability of the group. This reinforces the importance of psychological support before, during and after the process.

Feminizing hormone therapy involves taking drugs to block the action of the hormone testosterone. It also includes taking the hormone oestrogen, which decreases the amount of testosterone the body produces and triggers the development of female secondary sexual characteristics. Masculinizing hormone therapy is used by transgender men and non-binary people to produce physical changes in the body. Masculinizing hormone therapy involves taking the male hormone testosterone, which stops menstrual cycles and decreases the ovaries' ability to produce estrogen (AUGUSTO; OLIVEIRA; POLIDORO, 2022).

In 2023 there was a study on the incidence of contributing factors and implications for the clinical management of polycythemia in trans male patients taking testosterone. This research provided a lot of information and tables of administration and therapeutic dose for trans men. Data collected from each patient inclu-

ded age, body mass index (BMI), nicotine dependence, lung disease status, obstructive sleep apnea (OSA) status, oophorectomy status and route of testosterone administration. For patients who developed polycythemia, data was collected from the polycythemia management strategy (TATARIAN; WALCOTT ; RICHARDSON, 2023)

Data relating to the health profile of people who have used hormone therapy to transform their bodies was used. Also the main recommendations, preparation, associated risks and results obtained over the last 20 years. The aim of this review is to provide scientific data on the subject for people who are interested in undergoing this procedure, and also to inform the general population.

## METHODOLOGY

An integrative review of the main articles related to the topic was carried out, using the DeCs platform as a search tool for keywords, considering PubMed, SciElo, Google Scholar and Science Direct as search criteria. Books and articles were selected on the basis of relevance and the number of citations in other related articles. Preference was given to articles referring to quantitative and qualitative research on the subject, carried out through questionnaires with patients or profiles of tests carried out on patients for follow-up.

The following terminologies were used as a search mechanism in the databases: "Gender transition hormone therapy", "Gender Specific Need", "Gender Identity Dysphoria", "Gender Identity Disorder", "Social Construction of Gender Identity", "Sexual and Sexual Identity Disorders", "Gender Identity Disorder". These keywords were used with direct translation into other languages. Aiming to obtain national and international research on the subject, and prioritizing articles between the years 2003 to 2023.

Based on the definitions, approximately 15,900 results were evaluated, of which per According to the criteria of relevance and number of citations in other articles, 50 papers were selected to carry out a meta-analysis of the results obtained on the subject between 2002 and 2023. The research focused on obtaining the maximum amount of information available in the literature. The search was carried out in books and articles on the subject.

In the initial phase of the project, we defined the main research criteria and selected the key words that would be used. We then carried out a literature search on the topic, reviewing the endocrine system and related subjects.

The second phase of the project involves analyzing the information, results and conclusions of the 50 papers previously selected in stage 1 of the research. The team reviewed all the information, results and conclusions obtained by the authors of the studies selected for the research. Seeking as much information as possible on the general health profile of patients who have undergone treatment and who are now being monitored regularly.

For the third phase, the research group developed a mind map with all the information obtained from the different articles, books and interviews published on the subject. This phase was important for organizing all the information and synthesizing it in a simpler and more illustrative way. Finally, to understand the entire trajectory of a person with gender incongruence, before hormone therapy, during the process and at the end of the process. This process takes place slowly and requires specific care for the patient throughout their life.

In the fourth phase of the project, the main points that need to be worked on in the population, in terms of information on the subject, were classified. The topics in which there were differences between the results obtained were separated out. The main challenges faced by doctors when dealing with this specific group

of people. The main difficulties faced by patients with gender incongruence who seek health services. Finally, what could be done here in Brazil to improve care for this population.

## RESULTS AND DISCUSSION

Hormone therapy for gender transition is not a relatively new procedure. It is possible to observe the relationships between cause and effect in the use of hormones and analogues in the mind map that the group drew up in order to be able to work with the topic more easily. According to the patient's age, primary gender, risk factors and results obtained.

The physiological conditions, drugs used and results achieved change according to the transition and age of the patient. Once the research had been carried out, based on the mind map developed, two tables were drawn up showing the main benefits and risks associated with the use of hormones and GnRH analogues.

In April 2009, the American *Journal of Public Health* presented an article on barriers to care and the use of hormones among male-to-female transgender people living in New York City. The article concluded that the use of healthcare providers by transgender people is associated with a reduction in some high-risk behaviors, but does not result in adherence to standard care recommendations for transgender individuals. (SANCHEZ ; SANCHEZ ; DANOFF, 2009)

It conducted interviews with 101 female--to-male transgender people from 3 community health centers in New York City. It was concluded that hormone therapy regimens pose additional health risks for transgender people, the most serious of which is the hypercoagulability associated with estrogen administration. The incidence of thromboembolism among people on estrogen therapy ranges from 0.4% to 2.6% per year (SANCHEZ ; SANCHEZ ; DANOFF, 2009).

Norman P. Spack in 2012 presented some interesting results related to his research on children and adolescents with gender identity disorder referred to a pediatric medical center. Forty-three patients (44.3%) had a significant psychiatric history, including 20 reporting self-harm (20.6%) and suicide attempts (9.3%). According to Spack "the psychological and physical effects of pubertal suppression and/or cross-sex hormones in patients require further investigation"(SPACK, Norman P. et al.2012).

In 2015, Schneider and his team published part of their research in *The Journal of Sexual Medicine,* on "Testicular functions and clinical characterization of patients with gender dysphoria (GD) undergoing sex reassignment surgery (SRS)". According to the questionnaires, the patients showed desired phenotypic changes, including breast growth (75%) and smooth skin (32%). While the patients who discontinued in the first few weeks had rather virilized hormone levels, the patients who did not discontinue had generally feminized blood serum levels (SCHNEIDER, Florian et al. 2015).

Histological evaluation revealed highly heterogeneous results, with around 24% of patients showing qualitatively normal spermatogenesis. According to the serum endocrine profile, ITT levels were lower in patients who did not discontinue and correlated with testosterone and free testosterone, but not with spermatogenic status. The percentage of cells positive for LHCGR and ITT levels did not correlate.Only patients who did not stop hormone treatment had feminized blood levels on the day of the SRS. Those who stopped revitalized quickly. Interestingly, testicular histology was highly heterogeneous regardless of treatment strategy, a phenomenon that requires further investigation (SCHNEIDER, Florian et al. 2015).

In transgender men, sex steroid therapy was associated with a statistically significant increase in serum triglyceride, cholesterol and low-density lipoprotein cholesterol levels. High-density lipoprotein cholesterol levels decreased significantly in all follow-up periods. In transgender women, serum triglycerides were significantly higher without any changes in other parameters. Cases of myocardial infarction, stroke, venous thromboembolism and death. These events were more frequent in transgender women. However, the quality of the evidence was low (HEMBREE, Wylie C. et al.2017).

In transgender men, there was no statistically significant difference in the BMD of the lumbar spine, femoral neck or total hip at 12 and 24 months, compared to baseline values before starting masculinizing hormone therapy. In transgender women, there was a statistically significant increase in the BMD of the lumbar spine at 12 and 24 months, compared to baseline values before starting feminizing hormone therapy. Information on fracture rates was minimal. The quality of the evidence was also low (HEMBREE, Wylie C. et al.2017).

Other side effects documented in this same study include depression, mood swings, hyperprolactinemia, elevated liver enzymes, migraines and decreased sensitivity to insulin. In 2005, the *Cambridge* University Press Medical Center for Psychiatry carried out a study of 325 adolescents and adults who had consecutively applied for sex reassignment. The results substantiated previous conclusions that sex reassignment is effective (SMITH, Yolanda LS et al. 2005).

As for reproductive preservation. Pregnancy has been reported in transgender men who underwent prolonged treatment with androgens and discontinued testosterone, but did not undergo genital surgery (LIGHT, Alexis D. et al. 2014). A reproductive endocrine gynecologist can counsel patients prior to gender affirming hormone treatment or surgery regarding potential fertility options (DE SUTTER,2003). Cryopreservation techniques for oocytes, embryos and ovarian tissue continue to improve, and the maturation of oocytes from immature tissue is being studied (DE ROO,2018).

On the incidence of contributing factors and implications for the clinical management of polycythemia in trans male patients taking testosterone. A retrospective analysis of medical records of trans male patients taking testosterone for at least 12 months was carried out. Data collected from each patient included age, body mass index (BMI), nicotine dependence, lung disease status, obstructive sleep apnea (OSA) status, oophorectomy status and route of testosterone administration. For patients who developed polycythemia, data was collected from the polycythemia management strategy (TATARIAN; WALCOTT ; RICHARDSON, 2023)

The results showed that of the 511 patients, 113 (22%) had polycythemia. Within the polycythemia group, 77% of the patients were under 40, 56% had a BMI >30.0, 44% had current or previous nicotine dependence, 12% had lung disease, 12% had OSA and 47% had received an oophorectomy. The polycythemia group had a significantly higher mean age, BMI and testosterone dose, and also had a higher proportion of patients with OSA and oophorectomy. These results revealed that polycythemia is a common side effect in trans men taking testosterone (TATARIAN; WALCOTT ; RICHARDSON, 2023).

There is still little research into its use in children and adolescents. Linestrenol monotherapy is considered safe, but metrorrhagia has been reported in approximately half of the subjects, especially in the first 6 months. Acne, headaches, hot flushes and fatigue were other common side effects. Another progestin that has been studied in the United States


International Journal of Health Science ISSN 2764-0159 DOI https://doi.org/10.22533/at.ed.15949024081010

is medroxyprogesterone. This agent is not as effective as GnRH analogs in reducing endogenous sex hormones and may be associated with other side effects (LYNCH; KHANDHERIA; MEYER III, 2015).

Hypertension has been reported as an adverse effect in some women treated with GnRH analogues for precocious puberty (SIOMOU, Ekaterini et al. 2014). Blood pressure monitoring is recommended before and during treatment. There is little data available on the effects of GnRH analogues on brain development. A single cross-sectional study showed no impairment of executive function, but animal data suggest that there may be an effect of GnRH analogues on cognitive function (HOUGH, Denise et al. 2017).

GnRH analogues did not induce a change in the body mass index standard deviation score in adolescents, but caused an increase in fat mass and a decrease in the percentage of lean mass (SCHAGEN, Sebastian EE et al. 2016). Studies in young girls treated for precocious puberty also reported a stable body mass index standard deviation score during treatment and body mass index and body composition comparable to controls after treatment (MAGIAKOU, Maria Alexandra et al. 2010).

In October 2017 in the journal *LGBT Health*, Braun and his team published their work on assessing how concerns about HT-TARV interactions affect treatment adherence. Fifty-four percent live with HIV; 64% have used HT. Only 49% of TTs living with HIV discussed ART-HT IDD with their provider; 40% reported not taking ART (12%), HT (12%) or both (16%) as directed due to concerns about MI. The conclusion was that imperfect use of TH/TARV and limited communication with the provider suggest the need for better integration of HT-TARV (BRAUN, Hannan M. et al. 2017).

In women with gender incongruence, the effect of prolonged treatment with exogenous testosterone on ovarian function is uncertain. There are reports of an increased incidence of polycystic ovaries in transgender men, both before and as a result of androgen treatment (VUJOVIC, Svetlana et al. 2009).

## CONCLUSION

Hormone therapy for transgender men and women carries many of the same risks as sex hormone replacement therapy for non-transgender people. The few data on processes in young individuals report more emblematic visual results of the change, but with various health problems caused by the use of GnRH analogues.

The awareness of oneself as male or female changes gradually during childhood (STEENSMA, Thomas. et al.2013). Studies on individuals with a difference in sex development (DSD) have contributed to understanding the role that hormones play in the outcome of gender identity. In this sense, the research carried out agrees with the article by Wylie Hembree, published in 2017 in "The Journal of Clinical Endocrinology & Metabolism". Hormone therapy for gender transition should not be recommended for children with gender dysphoria. Since there is not enough research on the effects of GnRH analogues in adolescents on bone health, gonadal function and the brain (including the effects on cognitive, emotional, social and cognitive development), it should not be recommended for children with gender dysphoria sexual).

Therefore, it is also suggested that clinicians postpone gender affirming genital surgery involving gonadectomy and/or hysterectomy until the patient is at least of legal age (HEMBREE, Wylie C. et al.2017). In addition to pointing out the importance of ratifying the need to produce information to implement equity policies in the Unified Health System

| Benefits | Risks |
|---|---|
| Relief from gender dysphoria | Significant increase in bone mineral densitometry of the lumbar spine |
| Reduced emotional distress | Anxiety and depression |
| Improved self-acceptance | Increased mortality and depression in individuals who did not receive treatment |
| Increased satisfaction with gender identity | Mood swings |
| Greater comfort with your own body | Hyperprolactinemia |
| Improved health and social well-being | elevated liver enzymes |
| Reduced depression and anxiety | Suppression of puberty |
| Increased self-esteem | Migraine |
| Decreased risk of suicide | Decreased sensitivity to insulin |
| Improved emotional quality of life | Increased incidence of polycystic ovaries |
| Facilitating acceptance by society | Hypertension |
| Greater participation in the LGBTQA+ community | Pain during sexual intercourse |
| Improved relationships with family and friends | Increase in serum triglyceride levels |
| Access to a wider support network | Change in cholesterol levels high density lipoprotein |
| Reducing anxiety and depression associated with gender incongruence | Increased serum levels of low-density lipoprotein |

Table 1 Benefits and risks Source: prepared by the authors

(AUGUSTO; OLIVEIRA; POLIDORO, 2020). This was a great example here in Brazil of a policy to improve care for transgender people.

Despite recent progress in the provision of outpatient and inpatient care for the execution of the procedures of the Transsexualizing Process, through duly authorized health units such as the Midwest (Goiânia/GO), South (Porto Alegre/RS), Southeast (Rio de Janeiro/RJ and São Paulo/SP) and Northeast (Recife/PE) (Revista Brasileira de Bioética 2013;9), Brazil should be inspired and guided in the care of these patients by protocols that already exist in other countries such as the Netherlands and the United States. Where the patient receives all psychological support prior to the diagnosis of gender dysphoria, during the hormonalization process and afterwards.

In 2021, an article published in the *Brazilian Journal of Health Review* concluded that the use of hormone therapy associated with psychological support provides transgender individuals with a reduction in gender dysphoria and an improvement in various symptoms, including depression and anxiety. This emphasizes the need to identify transgender adolescents early in order to refer them to appropriate specialists (DE OLIVEIRA ALVES, Ariane, 2021).

Cross-hormone therapy, however, could result in a subsequent increase in BMD, according to the studies presented. Cognition was studied by Staphorsius and colleagues, showing no effect of GnRHa therapy on the Tower of London test (LD), which assesses executive performance. Fertility, meanwhile, is preserved in 3-5% of patients, according to Cartaya et al. who decide to postpone pubertal blockade.

Hormone therapy is a resource used in gender transition, since it favors an advance in the autonomy and beneficence of the LGBTQIA+ community, in order to enable a gender identity and generate greater physical, mental and emotional well-being. However, there are possible side effects of this resource on sleep-disordered breathing, related to doses and formulations of androgens and estrogens (XAVIER, Eduarda Paula Markus et al. 2022). This thesis was presented in the proceedings of the 2022 Brazilian Online Congress on Medical Care for the LGBTQIA+ Population.

The risk-benefit ratio varies between individuals. In addition, individual response to HRT can be influenced by genetic, metabolic and environmental factors, emphasizing the need for a personalized approach to prescribing and monitoring. Socioeconomic issues related to access and cost of HRT are also crucial, with the need to ensure equity in care (CARNEIRO FILHO, Troy Richard et al. 2023).

In conclusion, although hormone therapy for gender transition is not so recent, there is still a lot of research to be done. The subject generates a lot of controversy in the scientific community. Due to the noted psychological vulnerability of many individuals with gender incongruence, it is important to highlight that a dignified social life free from abuse and discrimination requires combating the pathologization of transsexuality, the attribution of the diagnosis of gender identity disorder and, possibly, additional forms of discrimination. These elements can undermine people's gender self-determination, autonomy and freedom to experience their inner gender identity and belonging to the opposite sex (ANTRA).

## THANKS

We would like to thank all the professionals and teachers who helped us during the research and data analysis. Especially Professor Rafael, who accompanied and instructed us throughout the research and development of the article. The patience and help of everyone who contributed to the research.

Our biggest challenge was to compress such a delicate and complex topic into a six-month research project. To do this, the team worked hard to gather information from reliable, internationally renowned sources. Universities and researchers who had been working on the subject long before the technique arrived here in Brazil and became popular. We carefully translated the articles into foreign languages in order to bring the best content into our language.

## REFERENCES

1. AINSWORTH, Tiffiny A.; SPIEGEL, Jeffrey H. Quality of life of individuals with and without facial feminization surgery or gender reassignment surgery. **Quality of Life Research**, v. 19, p. 1019-1024, 2010.

2. AUGUSTO, R. M.; OLIVEIRA, D. C. DE .; POLIDORO, M.. Descrição de medicamentos prescritos para a terapia hormonal em serviços de saúde especializados para transexuais e travestis no Rio Grande do Sul, 2020. **Epidemiologia e Serviços de Saúde**, v. 31, n. 1, p. e2021502, 2022.

3. American Psychiatric Association . *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Arlington, VA: American Psychiatric Association Publishing.

4. BERENBAUM, S. A.; MEYER-BAHLBURG, H. F. L. Gender development and sexuality in disorders of sex development. **Hormone and Metabolic Research**, p. 361-366, 2015.

5. BRAUN, Hannan M. et al. Transgender women living with HIV frequently take antiretroviral therapy and/or feminizing hormone therapy differently than prescribed due to drug–drug interaction concerns. **LGBT health**, v. 4, n. 5, p. 371-375, 2017.

6. BRADFORD, Judith et al. Experiences of transgender-related discrimination and implications for health: results from the Virginia Transgender Health Initiative Study. **American journal of public health**, v. 103, n. 10, p. 1820-1829, 2013.

7. BERG, Tova. **Development of GABA Inputs to Gonadotropin-Releasing** Hormone (GnRH) Neurons and Effects of Prenatal Androgen Exposure. 2020. Tese de Doutorado.

8. CARNEIRO FILHO, Troy Richard et al. Terapia de Reposição Hormonal: Revisando as indicações, riscos e benefícios da terapia de reposição hormonal em diferentes grupos de pacientes. **Brazilian Journal of Implantology and Health Sciences**, v. 5, n. 4, p. 2595-2606, 2023.

9. COLEMAN, Eli et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, version 7. **International journal of transgenderism**, v. 13, n. 4, p. 165-232, 2012.

10. DE VRIES, Annelou LC et al. Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. **The journal of sexual medicine**, v. 8, n. 8, p. 2276-2283, 2011.

11. DE VRIES, Annelou LC et al. Young adult psychological outcome after puberty suppression and gender reassignment. **Pediatrics**, v. 134, n. 4, p. 696-704, 2014.

12. DELEMARRE-VAN DE WAAL, Henriette A.; COHEN-KETTENIS, Peggy T. Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects. **European Journal of Endocrinology**, v. 155, n. suppl_1, p. S131-S137, 2006.

13. DE OLIVEIRA ALVES, Ariane; MAGALHÃES, Ana Catarina Torres; MENDES, Sabrina Costa. Impacto da terapia hormonal em adolescentes transexuais: uma revisão sistemática. **Brazilian Journal of Health Review**, v. 4, n. 6, p. 24872-24874, 2021.

14. DE ROO, Chloë et al. Fertility options in transgender people. **Gender Dysphoria and Gender Incongruence**, p. 124-131, 2018.

15. DE SUTTER, Paul. Donor inseminations in partners of female-to-male transsexuals: should the question be asked?. **Reproductive BioMedicine Online**, v. 6, n. 3, p. 382-283, 2003.

16. DE CUYPERE, Griet et al. Sexual and physical health after sex reassignment surgery. **Archives of sexual behavior**, v. 34, p. 679-690, 2005.

17. DELEMARRE-VAN DE WAAL, Henriette A.; COHEN-KETTENIS, Peggy T. Clinical management of gender identity disorder in adolescents: a protocol on psychological and paediatric endocrinology aspects. **European Journal of Endocrinology**, v. 155, n. suppl_1, p. S131-S137, 2006.

18. Diagnóstico sobre o acesso à retificação de nome e gênero de travestis e demais pessoas trans no Brasil / **ANTRA (Associação Nacional de Travestis e Transexuais)** – Brasília, DF: Distrito Drag, 2022. 99 f

19. FELDMAN, Jamie et al. Priorities for transgender medical and healthcare research. **Current Opinion in Endocrinology, Diabetes and Obesity**, v. 23, n. 2, p. 180-187, 2016.

20. JOSETH, Filomena De Jesus Souza, *et al.* O Processo Transexualizador no SUS implicações bioéticas. **The Transsexualization Process by the Brazilian Unified Health System - bioethical implications**, v. 9, p. 1-20, 2013.

21. FRISEN, Louise et al. Gender role behavior, sexuality, and psychosocial adaptation in women with congenital adrenal hyperplasia due to CYP21A2 deficiency. **The Journal of Clinical Endocrinology & Metabolism**, v. 94, n. 9, p. 3432-3439, 2009.

22. GOOREN, Louis J.; GILTAY, Erik J.; BUNCK, Mathijs C. Long-term treatment of transsexuals with cross-sex hormones: extensive personal experience. **The Journal of Clinical Endocrinology & Metabolism**, v. 93, n. 1, p. 19-25, 2008.

23. HANAUER, Otto Felipe Dias; HEMMI, Ana Paula Azevedo. Caminhos percorridos por transexuais: em busca pela transição de gênero. **Saúde em Debate**, v. 43, p. 91-106, 2020.

24. HEMBREE, Wylie C. et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. **The Journal of Clinical Endocrinology & Metabolism**, v. 94, n. 9, p. 3132-3154, 2009.

25. HEMBREE, Wylie C. et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: an endocrine society clinical practice guideline. **The Journal of Clinical Endocrinology & Metabolism**, v. 102, n. 11, p. 3869-3903, 2017.

26. HOUGH, Denise et al. Spatial memory is impaired by peripubertal GnRH agonist treatment and testosterone replacement in sheep. **Psychoneuroendocrinology**, v. 75, p. 173-182, 2017.

27. IKEDA, Keiko et al. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. **Human Reproduction**, v. 28, n. 2, p. 453-461, 2013.

28. KREUKELS, Baudewijntje PC; GUILLAMON, Antonio. Neuroimaging studies in people with gender incongruence. **Gender Dysphoria and Gender Incongruence**, p. 132-140, 2018.

29. LYNCH, Mechibelle M.; KHANDHERIA, Mili M.; MEYER III, Walter J. Retrospective study of the management of childhood and adolescent gender identity disorder using medroxyprogesterone acetate. **International Journal of Transgenderism**, v. 16, n. 4, p. 201-208, 2015.

30. LIGHT, Alexis D. et al. Transgender men who experienced pregnancy after female-to-male gender transitioning. **Obstetrics & Gynecology**, v. 124, n. 6, p. 1120-1127, 2014.

31. LEITE, Patrícia Mendonça et al. Impactos do tratamento hormonal em adolescentes transgêneros. **Brazilian Journal of Health Review**, v. 4, n. 2, p. 4777-4784, 2021.

32. MAGIAKOU, Maria Alexandra et al. The efficacy and safety of gonadotropin-releasing hormone analog treatment in childhood and adolescence: a single center, long-term follow-up study. **The Journal of Clinical Endocrinology & Metabolism**, v. 95, n. 1, p. 109-117, 2010.

33. MENDELSOHN, Michael E.; KARAS, Richard H. Molecular and cellular basis of cardiovascular gender differences. **Science**, v. 308, n. 5728, p. 1583-1587, 2005.

34. MOORE, Eva; WISNIEWSKI, Amy; DOBS, Adrian. Endocrine treatment of transsexual people: a review of treatment regimens, outcomes, and adverse effects. **The Journal of Clinical Endocrinology & Metabolism**, v. 88, n. 8, p. 3467-3473, 2003.

35. MURAD, Mohammad Hassan et al. Hormonal therapy and sex reassignment: A systematic review and meta-analysis of quality of life and psychosocial outcomes. **Clinical endocrinology**, v. 72, n. 2, p. 214-231, 2010.

36. NEWFIELD, Emily et al. Female-to-male transgender quality of life. **Quality of life Research**, v. 15, p. 1447-1457, 2006.

37. OLSON, Johanna et al. Baseline physiologic and psychosocial characteristics of transgender youth seeking care for gender dysphoria. **Journal of Adolescent Health**, v. 57, n. 4, p. 374-380, 2015.

38. SARASWAT, Aruna; WEINAND, Jamie D.; SAFER, Joshua D. Evidence Supporting the Biologic Nature of Gender Identity1. **Endocrine Practice**, v. 21, n. 2, p. 199-204, 2015.

39. SEVELIUS, Jae M. et al. Barriers and facilitators to engagement and retention in care among transgender women living with human immunodeficiency virus. **Annals of Behavioral Medicine**, v. 47, n. 1, p. 5-16, 2014.

40. SIMONS, Lisa et al. Parental support and mental health among transgender adolescents. **Journal of adolescent health**, v. 53, n. 6, p. 791-793, 2013.

41. SPACK, Norman P. et al. Children and adolescents with gender identity disorder referred to a pediatric medical center. **Pediatrics**, v. 129, n. 3, p. 418-425, 2012.

42. SIOMOU, Ekaterini et al. Arterial hypertension during treatment with triptorelin in a child with Williams–Beuren syndrome. **Pediatric nephrology**, v. 29, p. 1633-1636, 2014.

43. SMITH, Yolanda LS et al. Sex reassignment: outcomes and predictors of treatment for adolescent and adult transsexuals. **Psychological medicine**, v. 35, n. 1, p. 89-99, 2005.

44. STEENSMA, Thomas D. et al. Gender identity development in adolescence. **Hormones and behavior**, v. 64, n. 2, p. 288-297, 2013.

45. SCHAGEN, Sebastian EE et al. Efficacy and safety of gonadotropin-releasing hormone agonist treatment to suppress puberty in gender dysphoric adolescents. **The journal of sexual medicine**, v. 13, n. 7, p. 1125-1132, 2016.

46. TATARIAN, Joshua; WALCOTT, Quinnlyn; RICHARDSON, Kimberly. Incidence, Contributing Factors, and Implications for Clinical Management of Polycythemia in Transmasculine Patients on Testosterone. **LGBT health**, v. 10, n. 1, p. 72-79, 2023.

47. TOMLINS L. **Prescribing for transgender patients**. Aust Prescr. https://doi.org/10.18873/austprescr.2019.003

48. VAN DEN BOSCH, M. F. et al. Mapping evidence on the effects of gender-affirming hormone therapy on the hard and soft tissues of the craniofacial complex in transgender people: a protocol for a scoping review. **Systematic Reviews**, v. 10, p. 1-8, 2021.

49. VUJOVIC, Svetlana et al. Transsexualism in Serbia: a twenty-year follow-up study. **The journal of sexual medicine**, v. 6, n. 4, p. 1018-1023, 2009.

50. Poteat T, Davis AM, Gonzalez A. **Standards of Care for Transgender and Gender Diverse People**. *JAMA*. 2023;329(21):1872–1874. doi:10.1001/jama.2023.8121

51. SANCHEZ, Nelson F.; SANCHEZ, John P.; DANOFF, Ann. Health care utilization, barriers to care, and hormone usage among male-to-female transgender persons in New York City. **American journal of public health**, v. 99, n. 4, p. 713-719, 2009.

52. SCHNEIDER, Florian et al. Testicular functions and clinical characterization of patients with gender dysphoria (GD) undergoing sex reassignment surgery (SRS). **The Journal of Sexual Medicine**, v. 12, n. 11, p. 2190-2200, 2015.

53. SALIBA William Argolo et al. **EFEITOS COLATERAIS DECORRENTES DA TERAPIA HORMONAL EM TRANSEXUAIS FEMININOS.** Brazilian Journal of Surgery and Clinical Research - BJSCR .Vol.20,n.3,pp.103-110 (Set – Nov 2017)

54. SNELGROVE, John W. et al. "Completely out-at-sea" with "two-gender medicine": A qualitative analysis of physician-side barriers to providing healthcare for transgender patients. **BMC health services research**, v. 12, p. 1-13, 2012.

55. XAVIER, Eduarda Paula Markus et al. DISTÚRBIOS DE SONO EM PACIENTES TRANSEXUAIS EM TERAPIA HORMONAL. In: **Anais do Congresso Brasiliense On-line de Atenção Médica à População LGBTQIA+**. 2022.

56. WIEPJES, Chantal M. et al. The Amsterdam cohort of gender dysphoria study (1972–2015): trends in prevalence, treatment, and regrets. **The journal of sexual medicine**, v. 15, n. 4, p. 582-590, 2018.