

BMJ Best Practice

Care of transgender adults

Straight to the point of care



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Summary

"Transgender" is an umbrella term that is used to describe people whose gender identity is different from their birth-assigned sex (known as gender incongruence/gender dysphoria). Differences and debates about appropriate terminology exist, and there is no single term which effectively and uncontroversially describes all people experiencing gender incongruence/dysphoria.

Many transgender adults will not seek specialist medical intervention, and prevalence is likely underestimated; UK census data from 2021 suggest prevalence to be about 0.5%.

For those seeking gender-affirming medical or surgical treatment, the diagnosis should be confirmed by a medical professional with appropriate experience. Treatment is complex and should only be undertaken as part of a package of care provided by a multidisciplinary team with extensive experience in this area.

Options for gender-affirming care include hormone therapies and surgeries. Adjunctive options include hair removal, speech and language therapy and supportive counseling. Management is highly individualized, and that there is no "one size fits all" approach to treatment. Transgender people may choose to undergo all, some, or none of the above interventions to support their gender affirmation.

Although gender incongruence is not in itself a mental disorder, transgender people are at increased risk of certain mental health conditions, for example, depression and anxiety, compared with the general population; rates of autism spectrum disorder are also elevated.

Definition

Transgender people (often called trans people) experience gender incongruence to at least some degree.

Gender incongruence, as defined in ICD-11, is characterized by a marked and persistent discordance between an individual's experienced gender and their birth-assigned sex, which often leads to a desire to "transition," in order to live and be accepted as a person of the experienced gender, for example, through hormonal treatment, surgery or other healthcare services.^[1] The ICD diagnosis does not require distress or dysfunction to be present.^[1]

In contrast, gender dysphoria (as defined in DSM-5-TR) is characterized by a marked gender incongruence that is accompanied by distress or dysfunction.^[2]

The precise nature of gender transition may vary widely between individuals. Although gender transition can involve a change in physical characteristics, it may additionally (or alternatively) involve social aspects such as changing styles of clothing and hair, changing name, arranging new identity documents, or simply the use of a more suitable gendered pronoun.^[3]

It is important to note that only some gender nonconforming people experience gender dysphoria at some point in their lives.^[4]

Differences and debates about appropriate terminology are common, and, given the diversity of presentation, there is no single term which effectively and uncontroversially describes all people experiencing gender dysphoria and incongruence.^[4]

Inclusive language and environments are important in enabling optimal access to care for transgender adults.^[5]

This topic uses the terminology "transgender person" to refer to people experiencing gender incongruence/dysphoria, whether or not there is distress or dysfunction present.

The term "transgender man" is used to mean a person who was assigned female at birth, but who identifies as a man or trans man.

The term "transgender woman" is used to mean a person who was assigned male at birth, but who identifies as a woman or trans woman.

Note that gender identity and sexual orientation are separate; transgender people may identify as heterosexual, homosexual, bisexual, or none of the above.^[6]

The historical terms "transvestite" and "transsexual" are considered outdated and stigmatizing, and their use should generally be avoided, unless a person specifically claims or identifies with these terms. "Gender identity disorder" (as defined in DSM-IV) is also now considered an obsolete term.

Note: This topic covers the care of transgender adults only. In children and adolescents, presentation is particularly complicated, may be associated with higher levels of comorbidity, and may change form as patients mature, making specialist multidisciplinary assessment especially important.

Epidemiology

It is difficult to estimate the size of the transgender population, given the diversity within this group, including the fact that many individuals do not seek care from specialized centers.[2] [10] For both those assigned male and those assigned female at birth, prevalence is estimated to be <0.1%.[2] This figure is based on gender-affirming treatment-seeking populations, and is therefore likely to be an underestimation.[2] According to (anonymous) UK census data from 2021, around 0.5% of the population disclosed that their gender identity and sex registered at birth were different.[11]

In the US, there seems to be no significant association with social class, intelligence, or ancestry. Presentations to gender identity clinics are becoming more common, but this may reflect better awareness of, and access to, treatment, rather than increasing incidence.[4]

Some observations suggest children and adults with gender incongruence and gender dysphoria show more features of autism spectrum disorder than the general population.[12] [13] Gender incongruence and dysphoria may be associated with intersex, genetic, or sex chromosome abnormalities. These should not be assumed to be causative, and their presence rarely alters clinical management.

As a group, transgender people experience an increased risk of general mental health issues, including depression, anxiety, post-traumatic stress disorder, suicidality, and substance use disorders.[1] [2][14] A number of external social factors including stigma, discrimination, and minority stress have been suggested as contributors.[15]

Etiology

The causes of gender incongruence/gender dysphoria are unknown. At first, hypotheses about causation addressed psychological factors and came mostly from a psychoanalytic perspective. Over the decades, though, available evidence has suggested a multifactorial etiology, with biological and social factors rising in importance.[16] [17]

There is known to be a slightly elevated rate of gender incongruence and dysphoria among people with Klinefelter syndrome and congenital adrenal hyperplasia.[18] [19] [20] [21] [22] It is also known that birth-assigned males with gender incongruence and dysphoria are more likely than the general population to be left-handed.[23] A genetic association has been postulated as one possible cause of gender incongruence and gender dysphoria; a review of case report studies suggests higher rates in monozygotic twins versus dizygotic twins.[24] There is some evidence to suggest that CYP17 is a gene associated with the development of gender incongruence and gender dysphoria in birth-assigned females.[25]

Some observations suggest children and adults with gender incongruence and gender dysphoria show more features of autism spectrum disorder (ASD) than the general population.[12] [13] [26] At one gender clinic prevalence of autistic traits consistent with a clinical diagnosis of ASD among individuals undertaking treatment was 5.5%, compared with reports of 0.5% to 2.0% ASD diagnoses in the general population.[26] Transgender people with ASD sometimes have an atypical presentation of gender dysphoria/incongruence, which makes a correct diagnosis and determination of treatment options for gender dysphoria/incongruence more difficult.[12] [27]

Pathophysiology

As a general rule, neurologic and physiologic function in transgender people appear to be the same as in the general population.

However some small differences in brain structure have been suggested. One small study showed that the size of the bed nucleus of the brain's stria terminalis was in keeping with the person's sense of gender rather than their birth-assigned sex.^[28] Another study showed white matter changes in birth-assigned female transgender people prior to hormone treatment that were akin to those seen in nontransgender males.^[29]

Magnetic resonance imaging of transgender women suggests the presence of a larger, female-like putamen compared to that found in controls (nontransgender males).^[30]

Case history

Case history #1

A 45-year-old transgender person, who is birth-assigned as male, requests a prescription for estrogens and a rapid referral for gender reassignment surgery. She identifies as a transgender woman, and uses the pronouns "she/her." She is dressed as a woman, and gives a lifelong history of lifelong cross-dressing, which became sexually exciting at puberty. The sexual excitement diminished in her 20s, to be replaced by a sense of relaxation and comfort when in a female role, described as being able to express her feminine side. She is married to a woman, but separated, and together they have 2 children. The sexual content of their marriage (never very great) diminished after their birth. She hid her cross-dressing from her wife until she discovered her female clothes and assumed that she was having an affair. Although initially accepting of her dressing in female clothes, her wife became increasingly dissatisfied as she spent more time in a female role and suggested that they might live together as sisters. Moving away from her wife and children, she began to purchase estrogens from the internet. She lived as a woman for all purposes aside from at work, where nothing was known of her female life outside work. She began to feel increasingly unhappy in her male work life, feeling that she was only truly herself when living as a woman.

Case history #2

A 35-year-old transgender person, who is birth-assigned as female, requests treatment with androgens and a bilateral mastectomy. He identifies as a transgender man, and uses the pronouns "he/him." He looks masculine and is often taken to be a male somewhat younger than his chronological age. He gives a history of being a "tomboy" as a child, and at high school he was widely assumed to be lesbian. Declaring himself to be a lesbian in his late teens, he moved in lesbian social circles for some years and made relationships with women with some ease. These tended to founder after a few months because partners complained that, rather than being a masculine woman, he was more like a man. Although his libido was good and he was an attentive sexual partner, he could not bear attention being paid to his own (female) sexual characteristics, and the one-sided nature of the sexual relationship became, after a time, disturbing to his partners. Eventually he felt that his sense of masculinity could no longer be denied, and he decided to live as a man. He is desperate to halt his menstrual periods, seeking treatment with androgens to increase facial and body hair, and to lose his breasts.

Other presentations

The majority of birth-assigned male people with gender incongruence/dysphoria (i.e., transgender women) present with a background of cross-dressing. A smaller number give a history of earlier, very feminine homosexuality associated with a low libido and an ever-increasing sense of femaleness that drove them to live as a woman and to be viewed by others (including gay men) as a woman. Birth-assigned female transgender people (i.e., transgender men) very often have a history of childhood masculine behavior, and many have (for a while at least) been identified by themselves or others as masculine lesbian women.

A small proportion of people of either birth-assigned sex present with pronounced gender incongruence or gender dysphoria in childhood, even from their earliest years. They were often taken to be members of the other sex in childhood and very often experienced sexual attraction to others with the same birth-assigned sex. However it is important to note that childhood gender incongruence or gender dysphoria does not necessarily continue into adulthood.^[4] A number of studies in prepubescent children with gender dysphoria/incongruence suggest that persistence into adulthood occurs in 12% to 27% of children.^{[7] [8] [9]}

Approach

Only a proportion of transgender people will present to a medical professional with the aim of accessing gender-affirming care. For transgender people seeking gender-affirming treatment, the initial presentation is usually to a primary care clinician, endocrinologist or mental health specialist. Consensus recommendations from international guidelines recommend that when a transgender person seeks gender-affirming treatment with hormones or surgery, the diagnosis of gender incongruence or gender dysphoria should be made by qualified healthcare providers who are familiar with the diagnostic criteria, and who are experienced in assessing for the presence of any confounding/coexisting mental or physical health problems which may complicate the diagnosis.[4] [31]

The role of the primary care clinician is typically to carry out the initial assessment before referring to specialist services; alternatively patients may be referred to specialist gender services by a psychologist, nonspecialist psychiatrist or sexual health clinician. Service models vary substantially according to location, but as an overarching principle, diagnostic assessment within a specialist multidisciplinary team is strongly recommended.[31] In practice, if a specialized gender service is unable to assess a patient within a reasonable timeframe, referral to endocrinology or mental health services may be required as an interim measure, depending on the unique clinical scenario and circumstances of the individual.[32] It is important to note that in parts of the world, specialist services for transgender people are limited or entirely unavailable, and so primary care providers may need to take on a much greater role in the assessment and management of transgender people seeking gender affirming care, indicating an often unmet need for specialized professional education and training.[4]

Transgender people may be more likely to engage in risky sexual practices, particularly those experiencing social marginalization.[33] [34] Sexual history taking may therefore be important to assess risk and guide screening for sexually transmitted infections (STIs), but requires sensitivity and awareness of the person's comfort level and nonverbal cues. This may take place in either primary or secondary care, but note that in some circumstances it may be appropriate to defer sexual history taking to a follow-up consultation, in order to first establish a good therapeutic alliance. Sexual practices vary greatly, and should not be assumed. Transgender people may have male, female or other transgender partners.

Initial primary care assessment

A full history, including mental state assessment, is recommended as part of the initial primary care assessment.[32] Clinicians should ask about past and present use of hormones and gonadal surgeries, and about any future plans for hormones or surgeries. It is not uncommon for people to self-administer medically unsupervised hormones and/or hormone blockers obtained from the internet, particularly if there is limited access to care, carrying an increased risk of adverse effects compared to medically supervised treatment.[35] [36] Clinicians should ask about the use of any herbal remedies or dietary supplements, and ask about any use of silicone injections, which may be administered using unsterile techniques, increasing the risk of bloodborne infection.

Transgender people may experience an increased risk of general mental health issues, including depression, anxiety, post-traumatic stress disorder, suicidality and substance use disorders.[1] [2][14]

A number of external social factors including stigma, discrimination and minority stress have been suggested as contributing factors.[15] Primary care may represent a safe space for the disclosure of mental health symptoms and concerns, and primary care screening and assessment for mental health conditions is therefore likely to be valuable on an ongoing basis. It is important not to assume that all

mental health concerns are necessarily related to the person's gender identity.[37] Social history taking may identify important sources of support or stress, including family and economic factors.

Secondary care assessment, including diagnosis

As the diagnosis is the gateway to potentially irreversible treatment, it is necessary to identify any comorbidities, exclude differential diagnoses, and make a proper diagnosis using the relevant diagnostic criteria (see Diagnostic criteria).[4] [31] Diagnosis is typically made by a mental health professional, but, depending on local service models, another healthcare professional (e.g., endocrinologist or primary care provider) may make the diagnosis, providing that they have appropriate experience, training, and knowledge of diagnostic criteria. Ideally, diagnosis should be made by a clinician who is working within the context of a specialist, multidisciplinary gender identity team.

Clinicians should follow local guidance relevant to their country of practice; for example, US guidance from the Endocrine Society offers detail on the criteria necessary to make a diagnosis of gender dysphoria/incongruence in adults.[31] Clinicians should establish whether relevant diagnostic criteria for gender dysphoria/gender incongruence are met, according to the diagnostic criteria relevant to their location of practice.[1] [2]

It is important that all mental health concerns or differential diagnoses (e.g., body dysmorphic disorder) which may complicate/otherwise explain the diagnosis are assessed and potentially treated, prior to considering gender-affirming treatment.[4] [31] Assess whether there is a serious intention to change social gender role, or whether the stated desire for hormone treatment or surgery is aimed at removing the characteristics of one sex without seeking the characteristics of the other, or acquiring the characteristics of both, and vitally, with no change of social gender role at all. This last aspect is more in keeping with body dysmorphic disorder or autogynephilia.[27]

Clinicians should identify and assess any underlying medical conditions or risk factors (e.g., cardiovascular risk factors, history of breast cancer) which may complicate or preclude hormonal treatment.[4] Those receiving endocrine treatment who have relative contraindications to hormones such as smoking, diabetes, liver disease, should have an in-depth discussion with their physician concerning the risks and benefits of therapy.[31]

Clinicians should assess capacity to consent for gender-affirming treatment, explore the patient's goals for treatment including expectations of treatment, establish that the desire for transition is appropriate and persistent, confirm their understanding of the risks versus benefits, and discuss the potential impact on future fertility including fertility preservation options.[4] [31]

Clinical presentation

Determine whether there is a preceding history of gender dysphoria or incongruence of childhood, using informants if possible. As children, transgender people may have demonstrated marked gender nonconformity in peer preferences, mannerisms, role-playing, dreams, fantasies, and gender-typed play and toy preferences. They may have stated that they did not wish to develop secondary sexual characteristics of their assigned gender, asked to have primary sexual characteristics removed, or hoped that they would grow into an adult of their experienced gender.[2]

The history should elicit whether the person has adopted the behaviors of their experienced gender and whether they have taken measures to alter their primary and secondary sexual characteristics. Individuals assigned male at birth may shave their facial, body, and leg hair, and/or bind their genitals. Individuals

assigned female at birth may bind their breasts. Transgender people are often reluctant to let sexual partners see or touch their genitals.^[2]

The most common manifestation of gender dysphoria/incongruence in birth-assigned males is cross-dressing. Cross-dressing can be described as the wearing of clothes of the other sex in order to enjoy the temporary experience of membership of the other sex.

Transgender people may adopt a first name consistent with their experienced gender.^[2]

Physical examination is usually unremarkable. Clothing, hairstyle, vocal style, and mannerisms may resemble those of the patient's experienced gender.^[2]

Laboratory investigations

Serum androgens should be checked in both birth-assigned women and birth-assigned men, both as a baseline and during any hormonal treatment.^[32] At diagnosis, the presence of elevated serum testosterone and dihydrotestosterone and unsuppressed follicle-stimulating hormone and luteinizing hormone suggests a partial androgen insensitivity syndrome, which requires genetic counseling for the family. Low testosterone and elevated gonadotropins in males suggests Klinefelter syndrome. Elevated androgens in birth-assigned females may suggest polycystic ovary syndrome.

Recommended baseline blood tests include liver function tests, lipids, hematocrit and hemoglobin (to evaluate for polycythemia), and prolactin.^[32]

In some locations it is common practice to measure prostate-specific antigen (PSA) in birth-assigned males at the age of 45 years and over prior to initiation of hormone therapy, to obtain a baseline level, and to rule-out undiagnosed prostate cancer. It is important to note that following the initiation of hormone treatment, PSA may be a less-useful measuring tool for prostate cancer, given that PSA levels ordinarily plummet in those taking gender-affirming hormone therapy; extra care is needed in interpreting results.^[38]

Vitamin D levels are routinely measured in some centers, given the high rate of vitamin D deficiency within the transgender population.^[39]

A routine sexual health screen to assess for STIs may be carried out in either primary or secondary care, as guided by any specific risk factors noted in the sexual history.

History and exam

Key diagnostic factors

incongruence between birth-assigned sex and experienced gender (common)

- Gender incongruence, as defined in ICD-11, is characterized by a marked and persistent discordance between an individual's experienced gender and their birth-assigned sex, which often leads to a desire to "transition," in order to live and be accepted as a person of the experienced gender, for example, through hormonal treatment, surgery or other healthcare services.^[1]

altered appearance or affect (common)

- Patients may adopt the clothing, hairstyles, vocal styles, and mannerisms of their experienced gender.[\[2\]](#)

Risk factors

Weak**autism spectrum disorder (ASD)**

- Some observations suggest people with gender incongruence and gender dysphoria show more features of ASD than the general population.[\[12\]](#) [\[13\]](#) [\[26\]](#) At one gender clinic prevalence of autistic traits consistent with a clinical diagnosis of ASD among individuals undertaking treatment was 5.5%, compared with reports of 0.5% to 2.0% ASD diagnoses in the general population.[\[26\]](#)

congenital adrenal hyperplasia

- Associated with a slightly elevated rate of gender incongruence/dysphoria.[\[20\]](#) [\[21\]](#) [\[22\]](#)

Klinefelter syndrome

- Associated with a slightly elevated rate of gender incongruence/dysphoria.[\[18\]](#)

Tests

1st test to order

Test	Result
serum testosterone <ul style="list-style-type: none"> Used to exclude associated conditions. High testosterone with high or normal follicle-stimulating hormone and luteinizing hormone suggests partial androgen insensitivity syndrome. Low testosterone and elevated gonadotropins in males suggests Klinefelter syndrome. High androgens in females may suggest polycystic ovary syndrome. Morning draw of the specimen is recommended. 	normal
serum dihydrotestosterone <ul style="list-style-type: none"> Routinely measured in some (but not all) centers. May be used to exclude associated conditions. High testosterone and dihydrotestosterone with high or normal follicle-stimulating hormone and luteinizing hormone suggests partial androgen insensitivity syndrome. Morning draw of the specimen is recommended. 	normal
serum follicle-stimulating hormone (FSH) and luteinizing hormone (LH) <ul style="list-style-type: none"> Used to exclude associated conditions. High testosterone with high or normal FSH and LH suggests partial androgen insensitivity syndrome. Low testosterone and elevated gonadotropins in males suggest Klinefelter syndrome. 	normal
serum prolactin <ul style="list-style-type: none"> Used to exclude associated conditions. Elevation may suggest prolactinoma or drug use. Post-treatment, prolactin should not rise above 1000 IU. Should be repeated every 6 months while the patient is on hormonal therapy. 	normal
serum liver function tests <ul style="list-style-type: none"> Serum aspartate aminotransferase, alkaline phosphatase, and gamma glutamyl transpeptidase should be followed up every 6 months while the patient is on hormonal therapy. 	normal baseline
serum lipid screen <ul style="list-style-type: none"> LDL-cholesterol may rarely rise with hormone treatment. Dyslipidemia should be treated as it would be for any other cause. Should be repeated every 6 months. 	should be normal initially
CBC <ul style="list-style-type: none"> Elevated mean corpuscular volume (MCV) denotes possible alcohol use disorder. Hemoglobin (Hb) may rise following androgen treatment, particularly in smokers. Should be followed up every 6 months. 	MCV and Hb should be normal initially

Other tests to consider

Test	Result
<p>serum prostate-specific antigen (PSA) in birth-assigned males</p> <ul style="list-style-type: none">• In some locations, it is common practice to measure PSA in birth-assigned males at the age of 45 years and over prior to initiation of hormone therapy, in order to obtain a baseline level, and to rule-out undiagnosed prostate cancer.• Note that following the initiation of hormone treatment, PSA may be a less-useful measuring tool for prostate cancer, given that PSA levels ordinarily plummet in those taking gender-affirming hormone therapy; extra care is needed in interpreting results.[38]• Total PSA is the initial test of choice (i.e., the sum of both the free and bound forms).	<p>elevated PSA (value should be correlated with patient age and exposure to gender-affirming hormone treatment) indicates suspicion of prostate cancer</p>
<p>Serum 25-hydroxyvitamin D</p> <ul style="list-style-type: none">• Vitamin D levels are routinely measured in some centers, given the high rate of vitamin D deficiency within the transgender population.[39]• 25-hydroxyvitamin D is the major circulating form of vitamin D used to determine vitamin D status.[40]	<p>vitamin D deficiency: ≤20 ng/mL; vitamin D insufficiency: 21-29 ng/mL</p>

Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
Autogynephilia	<ul style="list-style-type: none"> Defined as sexual arousal in a birth-assigned male associated with the thought or image of themselves as a woman.[2] This is a controversial diagnosis and is not listed specifically as a paraphilic disorder in DSM-5-TR, and is instead given as a specifier to transvestic disorder (see below).[2] The person may seek hormone treatment and/or surgery to obtain female bodily characteristics (usually breasts) but either does not want to change social gender role or makes no more than token gestures in this regard. Often a greater degree of earlier sexual activity than in gender incongruence/dysphoria. The sexualized element to the desire for female characteristics may not be disclosed to medical professionals. May be present in addition to gender dysphoria, according to DSM-5-TR.[2] 	<ul style="list-style-type: none"> No distinguishing tests: diagnosis is clinical.
Body dysmorphic disorder	<ul style="list-style-type: none"> Patient may abhor and seek the removal of either primary or secondary sexual characteristics but has no sense of wanting any other gender role or plan to change social gender role. Aside from this preoccupation, function in birth gender role has often been quite good. 	<ul style="list-style-type: none"> Diagnosed according to DSM-5-TR or ICD-11 criteria.[1] [2]
Psychosis	<ul style="list-style-type: none"> Patient's presentation has the psychological texture of a delusion. Patient is not very worried about how others perceive him/her as a member of the other sex. Often a history of psychosis or delusions. Sometimes 	<ul style="list-style-type: none"> Diagnosed according to DSM-5-TR or ICD-11 criteria.[1] [2]

Condition	Differentiating signs / symptoms	Differentiating tests
	negative symptoms or affective symptoms present at the time of interview. <ul style="list-style-type: none"> Gender-related delusions may also occur in up to 20% of people with schizophrenia.[2] 	
Transvestic disorder	<ul style="list-style-type: none"> Wearing of the clothes of the other sex is associated with sexual arousal. The clothes are often sexualized. The behavior may be accompanied by masturbation. After orgasm there is often a sense of shame and the rapid removal of the clothes, accompanied by a (transitory) resolution never to cross-dress again. Found almost exclusively in males. May occasionally be accompanied by gender dysphoria/incongruence, or be a precursor to gender dysphoria/incongruence in prepubertal birth-assigned males.[2] 	<ul style="list-style-type: none"> Diagnosed according to DSM-5-TR criteria.[2] (Diagnosis does not appear in its own right in ICD-11)

Criteria

International classification of diseases 11th revision (ICD-11)[1]

Published by the World Health Organization, ICD-11 represents a significant shift in the classification of gender identity-related health compared to ICD-10. Outdated diagnostic categories including "gender identity disorder of children" and "transsexualism" have been replaced to reflect modern understanding of sexual health and gender identity. The new diagnostic categories have also been moved out of the "Mental and behavioral disorders" chapter and into the new "Conditions related to sexual health" chapter, as it is stigmatizing to associate gender diversity with mental ill health.

Gender incongruence

- Characterized by a marked and persistent incongruence between an individual's experienced gender and the assigned sex.
- Gender variant behavior and preferences alone are not a basis for assigning the diagnoses in this group.

Gender incongruence of adolescence or adulthood

- Characterized by a marked and persistent incongruence between an individual's experienced gender and the 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 hormonal treatment, surgery or other health care services to make the individual's body align, as much as desired and to the extent possible, with the experienced gender.

- The diagnosis cannot be assigned prior the onset of puberty.
- Gender variant behavior and preferences alone are not a basis for assigning the diagnosis.

Separate ICD-11 criteria exist for the diagnosis of children; however, children with gender dysphoria/incongruence are not covered by this topic.

[WHO: International Classification of Diseases 11th Revision] (<https://icd.who.int/en>)

[WHO: FAQs Gender incongruence and transgender health in the ICD] (<https://www.who.int/standards/classifications/frequently-asked-questions/gender-incongruence-and-transgender-health-in-the-icd>)

Diagnostic and statistical manual of mental disorders, 5th edition, text revision (DSM-5-TR)[2]

Gender dysphoria in adolescents and adults

- A marked incongruence between one's experienced/expressed gender and assigned gender, of at least 6 months' duration, as manifested by at least two of the following:
 - A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).
 - A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).
 - A strong desire for the primary and/or secondary sex characteristics of the other gender.
 - A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).
 - A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).
 - A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).
- The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- Two specifiers exist:
 - With a disorder of sex development (e.g., congenital adrenal hyperplasia or androgen insensitivity syndrome).
 - Post-transition: the individual has transitioned to full-time living in the experienced gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one gender-affirming medical procedure or treatment regimen (e.g., regular gender-affirming hormone treatment or gender reassignment surgery confirming the experienced gender).
- Separate DSM-5-TR criteria exist for the diagnosis of children; however, children with gender dysphoria/incongruence are not covered by this topic.

"Gender identity disorder" and related terms should be avoided due to their connotations with mental ill health and the associated stigma. [APA: gender dysphoria] (https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/DSM/APA_DSM-5-Gender-Dysphoria.pdf)

Approach

The aim of treatment is to improve the quality of life to the maximum attainable degree by means of the safe and sustainable relief of gender incongruence/dysphoria. Options for gender-affirming care include hormone therapies and surgeries. Adjunctive options include hair removal, speech and language therapy and supportive counseling. Management is highly individualized, and that there is no "one size fits all" approach. Transgender people may choose to undergo all, some, or none of the above interventions to support their gender affirmation.

Meta-analysis evidence demonstrates that, for the majority of transgender people, gender-affirming treatment (including hormonal therapy) results in significant improvements in quality of life and psychosocial functioning.[43] [44] [45]

Several large professional medical bodies have published guidance on care of transgender people, including gender-affirming care; this includes US guidance from the Endocrine Society and American College of Obstetricians and Gynecologists (ACOG), and international guidance from the World Professional Association for Transgender Health (WPATH).[4] [31] [41]

An overarching general principle is that reversible steps are successfully negotiated before irreversible steps are contemplated.[4] A multidisciplinary approach to management is strongly recommended; relevant disciplines include (but are not limited to) endocrinology, surgery, voice and communication, primary care, reproductive health, sexual health, and mental health.[4] All transgender people seeking gender-affirming medical treatment should be given information on options for fertility preservation prior to treatment with hormones or surgery.[31]

It is important to note that transgender people as a group experience relatively poorer access to health services compared to other patient groups. Barriers include bias and stigma by healthcare professionals as well as lack of knowledge around best practices, including safety and efficacy of treatments.[46] [47]

An open, nonjudgemental and inclusive approach is important and may help to encourage people to be forthcoming with their concerns, and less likely to obtain hormones from unlicensed sources.[41] As with any patient group, effective patient-clinician collaboration and shared decision making can facilitate development of therapeutic alliance.

When caring for transgender people use their patient-identified name and gender-neutral terminology until pronoun preferences are made clear. The most straightforward way to determine pronouns is simply to ask, "What are your preferred pronouns?" Using the wrong pronoun can cause transgender people to feel invalidated or disrespected, particularly if it occurs repeatedly. If you make a mistake, apologize and carry on, aiming to get it right thereafter.[48]

Healthcare workers should also be aware of the lack of standardization in recording gender identity and that there may be insufficient options in electronic health record platforms.

Outside of specific transgender-related care, transgender people have similar health care needs to the general population. However, depending on their history of gender-affirming care (e.g., hormone therapy), some specific primary and preventive care considerations may be required. When treating people who take gender-affirming hormones, it is important to remember these may affect laboratory test results (e.g., liver function tests, prostate specific antigen [PSA]) and modify disease-specific risk factors or increase the risk of in-hospital complications (e.g., venous thromboembolism).[49]

Social transition

Social transition is the process of adopting a new or evolving gender role or gender presentation in everyday life. Whether social transition should necessarily precede hormone treatment is a matter of some debate. Usually, clinicians maintain that hormone treatment should generally not be started unless the patient has already changed gender role.[31] This may include legally changing registration to that of the preferred sex and changing the person's name on all documents, as well as making friends, family, and other contacts aware of this change and asking them to treat the person as the chosen sex. Based on clinical experience, advantages of this approach are that it can allow both patient and clinician to appreciate the degree to which the change in gender expression and role can be practically applied. Regrets following gender-affirming treatment are rare, but do occur; regret is more likely to occur in those who experience difficulties with social transition.[43] [50] Furthermore, changes of social gender role to a nonbinary role may be harder to accomplish than people anticipate, and after experiencing an initial period of social transition to a nonbinary role, some people may prefer to modify their social transition in favor of developing a more distinct, social gender role.

Less commonly, hormone treatment is used for patients who do not wish to make a social gender role transition, or who are unable to do so.[4] Some patient groups maintain that hormone treatment should precede a change of gender role. Clinical experience suggests that potential disadvantages of this approach are that it involves a prolonged period of treatment with hormones, with associated potential for adverse effects, that may result in the person being unhappy with the degree of bodily change (which may be permanent), and indefinitely postponing any change of role.

Patients with autogynephilia may seek hormone treatment without any change of gender role and may put forward this argument (explicitly or covertly) to achieve that aim. Their autogynephilia may subsequently dissipate, leaving them with unwanted feminization.

There is universal agreement that a period of social transition of at least 6 months to 1 year (including at least 1 year of consistent hormone treatment, unless unsuitable or contraindicated) should precede any genital surgery.[4] [31] Longer periods may be needed if there are any problems living in the new gender role, to allow time for these problems to be addressed. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

Note that legal transition should not be dependent on use of medication or surgery, and varies according to local (i.e., national or state) laws; clinicians and patients should consult their relevant local legal guidance.[41]

Fertility and contraception

Pretreatment discussion of the consequence of medical and surgical treatment on fertility is essential, including a discussion of fertility preservation options, including sperm banking, oocyte preservation, embryo preservation and (less commonly) ovarian or testicular tissue cryopreservation.[31] [41] All patients should be counseled on barrier methods of contraception for prevention of sexually transmitted infections. Gender-affirming hormone therapy is not effective contraception; transgender people with retained gonads should be counseled about the possibility of pregnancy if they are having sexual activity that involves sperm and oocytes. Testosterone therapy is contraindicated during pregnancy, but transgender men may safely achieve pregnancy after cessation of testosterone.[41]

Gender-affirming hormone treatment

Hormone therapy for transgender people is given with the aim of achieving one or more of the following goals:[4][31]

- Reduce endogenous hormone levels (with a resultant reduction in secondary sex characteristics of the person's birth-assigned sex).
- Replace these endogenous hormones with those of the reassigned sex following principles of hormone replacement for hypogonadal patients.
- Provide hormone replacement therapy (HRT) to prevent the effects of hypogonadism following surgical treatment.

Individualized treatment is required based on the patient's goals, any medical contraindications, and the side effect profile of the medications used. According to the WPATH, criteria for starting hormone therapy include:[4]

- Gender incongruence is marked and sustained.
- The individual meets diagnostic criteria for gender incongruence prior to gender-affirming hormone treatment in regions where a diagnosis is necessary to access health care.
- The individual demonstrates capacity to consent for the specific gender-affirming hormone treatment.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of treatment have been assessed, with risks and benefits discussed.
- The individual understands the effect of gender-affirming hormone treatment on reproduction and they have explored reproductive option.

Transgender care is an interdisciplinary field, and so coordination of care and referral for hormone treatment within a patient's overall care team is recommended.

Hormone treatment varies with the birth sex of the patient.

Clinicians should stress the importance of smoking cessation, as smoking increases the thromboembolic risk from estrogen treatment and polycythemia with testosterone treatment (see Smoking cessation).

Feminizing treatment for transgender women

The term "transgender woman" is used to mean a person who was assigned male at birth, but who identifies as a woman or trans woman.

A thorough discussion of the risks versus benefits of treatment is essential prior to treatment initiation, and guides shared decision-making.

Gender-affirming hormone treatment aims to elicit in a birth-assigned male patient the secondary sexual changes seen in birth-assigned females at puberty. These changes will be superimposed on whatever male pubertal changes have already occurred and will not reverse them. Effects of treatment may include breast growth, increased body fat percentage, decreased libido, decreased testicular size and decreased erectile function.[41] There is no effect on vocal quality.[41] Facial and bodily hair growth is slowed only slightly and never stopped. For information on expected timing of feminizing effects of estrogen (see Patient discussions).

According to the Endocrine Society in the US, risks associated with estrogen therapy in transgender women include:[31]

- Very high risk of adverse outcomes
 - Thromboembolic disease
- Moderate risk of adverse outcomes
 - Macroprolactinoma
 - Breast cancer
 - Coronary artery disease
 - Cerebrovascular disease
 - Cholelithiasis
 - Hypertriglyceridemia

ACOG advises that there are no absolute contraindications to feminizing therapy in transgender women.^[41] However, clinicians should evaluate for (and potentially treat) a number of conditions at baseline, given that relative risks may be increased with hormone treatment; these include hormone sensitive cancer, coronary artery disease, cerebrovascular disease, hyperprolactinemia, hypertriglyceridemia, and cholelithiasis.^[4]

WPATH advises that people seeking feminizing treatment who have a history of thromboembolic events (e.g., deep vein thrombosis or pulmonary embolism) should undergo evaluation and treatment prior to the initiation of hormone therapy.^[4] For those with nonmodifiable risk factors which may increase the risk of thromboembolic disease, for example, a known history of thrombophilia, a past history of thrombosis, or a strong family history of thromboembolism, WPATH advise that offering an anticoagulant in addition to treatment with transdermal estrogen may decrease the risk of thromboembolism, although data to guide treatment decisions are extremely limited.^[4]

- Estrogen, with or without an agent to suppress androgen, is used as feminizing treatment in transgender women. However, there are no randomized controlled trials to assess the safety and efficacy of this treatment.^[51] A wide variety of different formulations and preparations are available, and local formularies vary considerably. In practice, both oral and transdermal estrogens are commonly used. In theory, transdermal estrogen may be associated with a lower risk of venous thromboembolism (VTE) and stroke (based on knowledge of the "first pass effect" and from extrapolation of data derived from postmenopausal women receiving HRT).^[52] Any absolute risk will be dependent on the individual's baseline risk for VTE. In clinical practice, oral estrogen is commonly used in transgender women who have a low baseline risk for VTE. For those ages 45 years or over, or with other risk factors for VTE, transdermal preparations are usually preferred.^[41]
- Currently available data do not provide clear guidance on dose titration; instead this should generally be based on patient goals.^[41] As with any medication, use of the lowest dose possible to achieve the desired results is recommended.^[41] Based on clinical experience, one approach is to start treatment with a low/moderate dose and build over time. Ultimately the goal is to reach a dose that produces a serum estradiol in the normal female premenopausal range.^[41] Clinical experience suggests that high-dose treatment from the outset may be associated with early duct fusion and the eventual formation of small, hard, conical breasts that cannot be made larger or more naturally textured with any subsequent hormonal manipulation.
- Usually, adjunctive therapy is required to achieve testosterone levels in the normal female range (androgen suppression), particularly in younger people (<40 years).^[31] Androgen suppression using a gonadotropin-releasing hormone (GnRH) agonist is preferred where available, given favorable safety and efficacy data.^{[31] [53]} This treatment carries fewer adverse effects than when used for prostate cancer and is usually well tolerated, with bone density being protected

by the parallel sex steroid therapy. Disadvantages of GnRH agonists are the requirement for parenteral administration and a relatively greater cost, which sometimes prevents placement on available formularies. GnRH agonists are used routinely in some countries, including the UK, but in other parts of the world, including the US, their use is limited due to cost and insurance coverage difficulties.

- Alternative options for androgen suppression where GnRH agonists are not available include spironolactone, cyproterone, and 5-alpha reductase inhibitors.[4] [31] Spironolactone is commonly used in the US.[41] Cyproterone is available in most countries, but not the US; overall, its use is decreasing due to its association with a number of adverse effects, including hyperlipidemia and raised prolactin levels.[54]
- Progesterone is not indicated, as there is insufficient evidence that the benefits outweigh the risk; although there are anecdotal reports of its use for breast development, there is currently insufficient evidence as to the efficacy of this, and it is known to raise the risk of breast cancer and has been associated with depression.[4]
- It typically takes 2 or more years for patients to achieve maximal feminizing results from hormones. If there was gonadal suppression with a GnRH agonist, the same dose will be needed after any genital surgery, although in later life doses might need to be lowered to achieve the same hormone levels as hepatic sex steroid metabolism can decrease with age. For patients who go on to have orchidectomy, hormone therapy with estrogen is usually continued lifelong, unless contraindications develop.[4]
- For recommended blood test monitoring regimens for patients newly started and established on hormone therapy (see Monitoring).

Masculinizing treatment for transgender men

The term "transgender man" is used to mean a person who was assigned female at birth, but who identifies as a man or trans man.

A thorough discussion of the risks versus benefits of treatment is essential prior to treatment initiation, and guides shared decision-making.

Gender-affirming hormone treatment aims to elicit in a birth-assigned female patient the secondary sexual changes seen in birth-assigned males at puberty. These changes will be superimposed on whatever female pubertal changes have already occurred and will not reverse them. Goals of treatment may include development of facial hair, deepening of the voice, and increasing body hair and muscle mass. Other effects of treatment may include fat redistribution, hairline recession, changes in body odor, reduced libido, cessation of menses, vaginal atrophy and increased clitoral size.[41] Vaginal atrophy may increase susceptibility to small amounts of vaginal tearing during penetrative sexual intercourse (similar to in postmenopausal women), and so prescription of a topical lubricant/estrogen may be required.[41] For information on expected timing of masculinizing effects of testosterone (see Patient discussions).

According to the US Endocrine Society, risks associated with testosterone therapy in transgender men include:[31]

- Very high risk of adverse outcomes
 - Polycythaemia (hematocrit > 50%)
- Moderate risk of adverse outcomes
 - Severe liver dysfunction (transaminases > threefold upper limit of normal)

- Coronary artery disease
- Cerebrovascular disease
- Hypertension
- Breast or uterine cancer

According to the ACOG, the only absolute contraindications to masculinizing treatment with testosterone are current pregnancy, unstable coronary artery disease and polycythemia (hematocrit greater than 55%).^[41] WPATH note that relative contraindications to masculinizing treatment with testosterone include severe hypertension and sleep apnea, since both may be exacerbated by testosterone administration.^[4]

- Preparations, doses, and licensing restrictions for testosterone vary according to country of practice. A variety of preparations and routes of administration are available, including injectables, gels, patches, and buccal tablets.
- The aim of therapy is to achieve serum testosterone levels in the normal physiologic range for young males at all times.^[41]
- Data from studies reported in the literature between 1980 and 2010 suggest that treatment of female-to-male transgender people with supra-physiologic doses of testosterone is associated with minimal adverse effects and no increase in mortality, breast cancer, vascular disease, or other major health problems.^[55] However clinicians can achieve a good clinical response and minimize the risk of adverse effects by avoiding supraphysiologic levels of testosterone.
- Androgens are administered in doses sufficient to induce menopause, usually once monthly but, more rarely, as often as once every 2 weeks. Once menopause is achieved, it is often possible to decrease the frequency without menstrual periods returning.
- Gonadotropin suppression is not usually needed in transgender men, as androgens alone suppress ovarian function very well. All patients should be offered the opportunity for gamete storage before hormone treatment, as is the case for any medically mandated treatment that removes natural fertility.^[4]
- It typically takes 2 or more years for patients to achieve maximal masculinizing/feminizing results from hormones. If there was gonadal suppression with a GnRH agonist, the same dose will be needed after any genital surgery; although, in later life doses might need to be lowered to achieve the same hormone levels, as hepatic sex steroid metabolism can decrease with age.
- For patients who go on to have gonadectomy, hormone therapy with estrogen or testosterone is usually continued lifelong, unless contraindications develop.^[4]
- For recommended blood test monitoring regimens for patients newly started and established on hormone therapy (see Monitoring).

Gender-affirming surgery

Some transgender people live successfully in their preferred gender role without surgery, but for others, genital surgery is the final (and most considered) step in the treatment process.^[4]

According to the WPATH, criteria for genital surgery include:^[4]

- Gender incongruence is marked and sustained.
- Meets diagnostic criteria for gender incongruence prior to gender-affirming surgical intervention in regions where a diagnosis is necessary to access health care.
- Demonstrates capacity to consent for the specific gender-affirming surgical intervention.
- Understands the effect of gender-affirming surgical intervention on reproduction and they have explored reproductive options.
- Other possible causes of apparent gender incongruence have been identified and excluded.

- Mental health and physical conditions that could negatively impact the outcome of gender-affirming surgical intervention have been assessed, with risks and benefits have been discussed.
- Stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).*

*This was graded as a suggested criterion. Note that there is an absence of consensus as to whether or not hormone treatment should always precede certain surgical procedures, and if so, for what duration. WPATH notes that gender-affirming hormone treatment leads to anatomic, physiologic and psychologic changes. The onset of anatomic changes (clitoral growth, vaginal atrophy) may begin early after initiation of treatment, with peak effects expected at 1-2 years. Depending on the surgical result required, a period of hormone treatment may be necessary prior to surgery for anatomic reasons, for example, to cause clitoral virilization prior to phalloplasty, or may be desired, for example, to cause breast growth and skin expansion prior to breast augmentation. Hormone treatment prior to surgery may also be preferred for psychologic reasons.[4] For patients not taking hormone treatment, an individualized approach is required, ideally with multidisciplinary input, and it is important that surgeons carefully review the impact that a lack of prior hormone therapy may have on any proposed surgery. Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role prior to surgery.[32]

Counseling to discuss expectations and limitations of surgery is essential, including likely effects on sexual function. Requirements on clinical authorization of gender-affirmation procedures differ according to location of practice, and clinicians should consult local guidance; for example, in some locations (e.g., the US), agreement between a mental health professional and a physician overseeing hormone therapy is required for authorization and medical clearance prior to surgery.[31] Genital surgeries should be performed within centers with specialist expertise wherever possible.

Ongoing mental health and psychosocial support may be required before and after surgery, as appropriate. Lifelong urologic follow-up is encouraged for transgender men who have undergone metoidioplasty/phalloplasty.[4] Long-term follow-up by the primary surgeon/gynecologist/primary care physician is encouraged for transgender women who have undergone vaginoplasty.[4]

The percentage of people who regret their gender-affirming surgical intervention is low (estimated to be between 0.3% and 3.8%).[4] Regret may be temporary or permanent; in this scenario multidisciplinary input is recommended in order to explore this further, with possible outcomes being medical and/or surgical treatment to continue the transition, or revision surgery to return anatomy to the sex assigned at birth.[4]

Transgender women: feminizing treatments and surgeries

Hair removal

- This can be done with electrolysis or laser treatment. All other methods are non-permanent.

Speech and language therapy

- Transgender women wishing to achieve increased congruence between their voice and experienced gender may benefit from referral to a speech and language therapist/pathologist with specific training and experience in this field.[41]

Aesthetic procedures

- Options are varied, and include liposuction, lipofilling, gluteal augmentation, and hair reconstruction.[41]

Head and neck surgery

- Thyroid cartilage reduction surgery is sometimes needed in tall, thin, patients whose thyroid cartilage is unacceptably prominent. It is usually an unproblematic procedure. It can be combined with a cricothyroid approximation.
- Cricothyroid approximation can be done alone or combined with a thyroid cartilage reduction. It alters vocal quality to a more feminine pitch. It should only be attempted when speech therapy has failed, and usually requires follow-up speech therapy.^[41]
- Craniofacial surgery is a complex and sometimes very radical surgery that is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.

Augmentation mammoplasty

- Although not a formal prerequisite, it is desirable that patients receive feminizing hormone treatment (for a minimum of 12 months) prior to surgery.^[32] Based on clinical experience, a minimum of 2 years is preferable. This is because it can be aesthetically problematic if natural breast development under estrogen stimulation follows an augmentation mammoplasty.

Genital surgery

- Patients should be stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).
- Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role. The patient must, over that period of time, have shown improved psychologic, social, and, probably, occupational function.^[32]
- Genital surgery typically involves penectomy and orchidectomy. The surgery uses the existing genitals to fashion a vulva, neoclitoris and hood, labia, and (often) neovagina.^[41]
- Preoperative genital hair removal is sometimes needed, particularly in patients who have been circumcised. Clinical experience suggests that the cosmetic results can be very good.

Transgender men: masculinizing treatments and surgeries

Aesthetic procedures

- Options are varied, and include liposuction, lipofilling, and pectoral implants.^[41]

Bilateral mastectomy ("top surgery")

- There is no consensus about when patients should undergo bilateral mastectomy.^[31] Although hormone therapy is not a formal prerequisite to bilateral mastectomy, nearly all practitioners take the view that bilateral mastectomy should come after a change of gender role and treatment with androgens. Some patient groups argue that it should precede both. Body weight and shape can change considerably when patients are treated with androgens, and it may be that an initially good postsurgical appearance alters negatively with subsequent androgen treatment. Difficulties may arise when a patient initially asserts that a non-binary role is desired and requests bilateral mastectomy and chest reconstruction without preceding treatment with testosterone. There may then be a subsequent evolution to a more clearly male role and corresponding need for testosterone treatment, which may have a negative impact on the patient's postsurgical appearance.

Hysterectomy and bilateral oophorectomy

- Previously, total hysterectomy and oophorectomy were recommended for transgender men taking testosterone therapy, but WPATH now recommends against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender people undergoing testosterone treatment and who have an otherwise average risk of malignancy.[4] [31] Gender-affirming hormones have not been shown to affect cancer risk, but the quality of evidence is low and longer-term studies are needed.[56]
- The route of hysterectomy is dependent on clinical findings, surgical, and patient preference.[41]
- Approaches include laparoscopic, transvaginal, and transabdominal. An advantage of the laparoscopic approach is that it avoids leaving a large abdominal scar. Vaginal access may be difficult if patients are nulliparous and have often not experienced penetrative intercourse. A transabdominal approach may utilize any incision other than a Pfannenstiel incision, as this incision is pathognomonic of gynecologic surgery and the resulting scar may look unusual in a male.

Phalloplasty

- This complex, often multistage procedure is typically considered only when the patient has received continuous hormone treatment, unless contraindicated, for 1 year at the very minimum.[32] Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role. The patient must over that period of time have shown improved psychological, social, and, probably, occupational function.
- Donor sites for phalloplasty can include the forearm, abdominal skin, or tissue from elsewhere on the body. The complexity, duration, and expense of the procedure are such that only a minority of patients choose to undergo this surgery. Clinical experience suggests that the cosmetic and functional results are fairly good, but the result in even the best centers is clearly distinguishable from a native penis.

Primary care: special considerations

The primary health care needs of transgender people are similar to those of any other patient.[4] However for people receiving gender-affirming care, some additional considerations may be required. Depending on service arrangements, primary care practitioners may be involved in the prescription of gender-affirming hormone therapy, preferably in conjunction with a specialist secondary-care based team, and with access to an endocrinologist if necessary.[32] Physical assessment and ongoing monitoring of hematologic, endocrinologic and biochemical parameters are essential, and ideally should be carried out under shared/collaborative care arrangements with secondary care (see Monitoring).

Note that in some (less common) clinical circumstances, a nonspecialist, for example, primary care clinician may consider prescribing a "bridging prescription" of hormonal treatment to cover the patient's care until they are able to access specialist services, as part of a harm reduction approach. This provides the opportunity to undertake blood tests and health checks to screen for contraindications to treatment. The suitability of this approach depends on the training and experience of the individual clinician, as well as on local guidelines and policy, and should only typically be considered when:[57]

- The patient is already self-prescribing, or seems highly likely to self-prescribe, with hormones obtained from an unregulated source (online or otherwise on the black market).
- The bridging prescription is intended to mitigate a risk of self-harm or suicide.
- The clinician has sought the advice of a gender specialist and prescribes the lowest acceptable dose in the circumstances.

It is important to note that in some parts of the world, speciality services for transgender people are limited or wholly unavailable, highlighting a need for all health providers to undergo training in the safe provision of gender-affirming care.^[4]

With respect to preventive health care, evidence on the long-term impact of gender-affirming hormone treatment is currently lacking. Cancer screening should commence, in general, according to local guidance, although there are a few specific issues to consider for people on hormonal therapy and/or those who have received surgery (e.g., with respect to breast, cervical, and prostate cancer screening, and osteoporosis screening) (see Monitoring).^[4]

Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Ongoing		(summary)
transgender women (male-to-female transgender persons whose sex assigned at birth was male)		
	1st	individualized multidisciplinary management
	adjunct	estrogens
	adjunct	androgen suppression therapy
	adjunct	speech and language therapy
	adjunct	hair removal
	adjunct	head and neck surgery
	adjunct	augmentation mammoplasty
	adjunct	genital surgery
	adjunct	other aesthetic procedures
transgender men (female-to-male transgender persons whose sex assigned at birth was female)		
	1st	individualized multidisciplinary management
	adjunct	androgens
	adjunct	bilateral mastectomy
	adjunct	hysterectomy and bilateral oophorectomy
	adjunct	phalloplasty
	adjunct	other aesthetic procedures

Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Ongoing

**transgender women (male-to-female
transgender persons whose sex
assigned at birth was male)**

1st individualized multidisciplinary management

» A multidisciplinary approach to management is strongly recommended; relevant disciplines include (but are not limited to) endocrinology, surgery, voice and communication, primary care, reproductive health, sexual health, and mental health.[4] However it is important to note that in some parts of the world, speciality services for transgender people are limited or wholly unavailable; in this setting, nonspecialist clinicians, for example, primary care providers may need to take on a greater role in the provision gender-affirming care, highlighting the need for continuing training and professional development in line with current best practices.[4]

» Options for gender-affirming care include hormone therapies and surgeries. Adjunctive options include hair removal, speech and language therapy and supportive counseling. Management is highly individualized, and that there is no "one size fits all" approach. Transgender people may choose to undergo all, some, or none of the above interventions to support their gender affirmation.

» Transgender people as a group experience relatively poorer access to health services compared to other patient groups. Noted barriers include bias and stigma by healthcare professionals and a lack of knowledge around best practices, including safety and efficacy of treatments.[46] [47] An open, nonjudgemental and inclusive approach is important and may help to encourage people to be forthcoming with their concerns, and less likely to obtain hormones from unlicensed sources.[41]

» Transgender people also experience an increased risk of general mental health issues, including depression, anxiety, post-traumatic stress disorder, suicidality, and substance use disorders.[1] [2][14] Ongoing screening, assessment, and management of any mental health conditions is therefore important.

Ongoing

» Usually, clinicians maintain that hormone treatment should generally not be started unless the patient has already changed gender role.[31]

This may include legally changing registration to that of the preferred sex and changing the person's name on all documents, as well as making friends, family, and other contacts aware of this change and asking them to treat the person as their experienced sex.

» Based on clinical experience, advantages of this approach are that it can allow both patient and clinician to appreciate the degree to which the change in gender expression and role can be practically applied. Regrets following gender-affirming treatment are rare, but do occur; regret is more likely to occur in those who experience difficulties with social transition.[43] [50]

» Less commonly, hormone treatment is used for patients who do not wish to make a social gender role transition, or who are unable to do so.[4]

» There is universal agreement within international standards of care that social transition of at least 1 year (plus 1 year of continuous hormone treatment) should precede any genital surgery.[4][31] Longer periods may be needed if there are any problems living in the new gender role. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

» Note that legal transition should not be dependent on use of medication or surgery, and varies according to local (i.e., national or state) laws; clinicians and patients should consult their relevant local legal guidance.[41]

adjunct estrogens

Treatment recommended for SOME patients in selected patient group

» Hormonal treatment is preferably done working as part of a multidisciplinary team containing (or having easy access to) an endocrinologist.

» Criteria for hormone therapy include the following:[4]

- Gender incongruence is marked and sustained.
- The individual meets diagnostic criteria for gender incongruence prior to gender-affirming hormone treatment in regions

Ongoing

where a diagnosis is necessary to access health care.

- The individual demonstrates capacity to consent for the specific gender-affirming hormone treatment.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of treatment have been assessed, with risks and benefits discussed.
- The individual understands the effect of gender-affirming hormone treatment on reproduction and they have explored reproductive options.

» A thorough discussion of the risks versus benefits of treatment is essential prior to treatment initiation, and guides shared decision-making.

» Gender-affirming hormone treatment aims to elicit in a birth-assigned male patient the secondary sexual changes seen in birth-assigned females at puberty. These changes will be superimposed on whatever male pubertal changes have already occurred and will not reverse them. Effects of treatment may include breast growth, increased body fat percentage, decreased libido, decreased testicular size, and decreased erectile function.^[41] There is no effect on vocal quality.^[41] Facial and bodily hair growth is slowed only slightly and never stopped. For information on expected timing of feminizing effects of estrogen see Patient discussions .

» Estrogen is either used alone, or with adjunctive androgen suppression therapy. A wide variety of different formulations and preparations are available, and local formularies vary considerably. In practice, both oral and transdermal estrogens are commonly used. In theory, transdermal estrogen may be associated with a lower risk of venous thromboembolism (VTE) and stroke (based on knowledge of the "first pass effect" and from extrapolation of data derived from postmenopausal women receiving hormone replacement therapy).^[52] Any absolute risk will be dependent on the individual's baseline risk for VTE. In clinical practice, oral estrogen is commonly used in transgender women who have a low baseline risk for VTE. For those ages over 45 years or

Ongoing

with other risk factors for VTE, transdermal preparations are usually preferred.[41]

» Currently available data do not provide clear guidance on dose titration; instead this should generally be based on patient goals.[41] As with any medication, use of the lowest dose possible to achieve the desired results is recommended.[41] Based on clinical experience, one approach is to start treatment with a low/moderate dose and build over time. Ultimately the goal is to reach a dose that produces a serum estradiol in the normal female premenopausal range.[41] Clinical experience suggests that high-dose treatment from the outset is associated with early duct fusion and the eventual formation of small, hard, conical breasts that cannot be made larger or more naturally textured with any subsequent hormonal manipulation.

» It typically takes 2 or more years for patients to achieve maximal feminizing results from hormones. If there was gonadal suppression with a gonadotropin-releasing hormone agonist, the same dose will be needed after any genital surgery, although in later life doses might need to be lowered to achieve the same hormone levels as hepatic sex steroid metabolism can decrease with age.

» For patients who go on to have orchidectomy, hormone therapy with estrogen is usually continued lifelong, unless contraindications develop.[4]

» For recommended blood test monitoring regimens for patients newly started and established on hormone therapy see Monitoring .

» Consult your guidelines and drug formularies for estrogen options and formulations.

adjunct androgen suppression therapy

Treatment recommended for SOME patients in selected patient group

» Used in transgender women in whom native androgen production is not suppressed by full-dose estrogen therapy.[58] These tend to be younger patients (<40 years). Androgen suppression using a gonadotropin-releasing hormone (GnRH) agonist is preferred where available, given favorable safety and efficacy data.[31] [53] This treatment carries fewer side effects than when used for prostate cancer and is usually well tolerated, with bone density being protected by the parallel sex steroid therapy.

Ongoing

» Disadvantages of GnRH agonists are the requirement for parenteral administration and a relatively greater cost, which sometimes prevents placement on available formularies. GnRH agonists are now used routinely in some countries, including the UK, but in other parts of the world, including the US, their use is limited due to cost and insurance coverage difficulties.

» Alternative options for androgen suppression where GnRH agonists are not available include spironolactone, cyproterone, and 5-alpha reductase inhibitors.[4] [31] Spironolactone is commonly used in the US.[41] Cyproterone is available in most countries, but not the US; overall, its use is decreasing due to its association with a number of adverse effects, including hyperlipidemia and raised prolactin levels.[54]

» It typically takes 2 or more years for patients to achieve maximal feminizing results from hormones. If there was gonadal suppression with a GnRH agonist, the same dose will be needed after any genital surgery, although in later life doses might need to be lowered to achieve the same hormone levels as hepatic sex steroid metabolism can decrease with age.

» For patients who go on to have orchidectomy, hormone therapy with estrogen is usually continued lifelong, unless contraindications develop.[4]

» For recommended blood test monitoring regimens for patients newly started and established on hormone therapy see Monitoring .

» Consult your guidelines and drug formularies for GnRH agonist options and formulations.

adjunct **speech and language therapy**

Treatment recommended for SOME patients in selected patient group

» Transgender women wishing to achieve increased congruence between their voice and experienced gender may benefit from referral to a speech and language therapist/pathologist with specific training and experience in this field.[41]

adjunct **hair removal**

Treatment recommended for SOME patients in selected patient group

» This can be done with electrolysis or laser treatment. All other methods are nonpermanent.

adjunct **head and neck surgery**

Ongoing

Treatment recommended for SOME patients in selected patient group

» Thyroid cartilage reduction is a usually unproblematic procedure that is sometimes needed in tall, thin, patients whose thyroid cartilage is unacceptably prominent. It can be combined with a cricothyroid approximation.

» A cricothyroid approximation procedure can be done alone or combined with a thyroid cartilage reduction. It alters vocal quality to a more feminine pitch. It should only be attempted when speech therapy has failed, and usually requires follow-up speech therapy.[41]

» Craniofacial surgery is a complex and sometimes very radical surgery that is sometimes helpful but should only be contemplated when treatment with hormones has been fully utilized and when simpler cosmesis has failed.

adjunct augmentation mammoplasty

Treatment recommended for SOME patients in selected patient group

» Although not a formal prerequisite, it is desirable that patients receive feminizing hormone treatment for a minimum of 12 months prior to augmentation mammoplasty.[32]

Based on clinical experience, a minimum of 2 years is preferable. This is because it can be aesthetically problematic if natural breast development under estrogen stimulation follows an augmentation mammoplasty.

adjunct genital surgery

Treatment recommended for SOME patients in selected patient group

» Some transgender people live successfully in their preferred gender role without surgery, but for others, genital surgery is the final (and most considered) step in the treatment process.

» Criteria for genital surgery include the following:[4]

- Gender incongruence is marked and sustained.
- Meets diagnostic criteria for gender incongruence prior to gender-affirming surgical intervention in regions where a diagnosis is necessary to access health care.

Ongoing

- Demonstrates capacity to consent for the specific gender-affirming surgical intervention.
- Understands the effect of gender-affirming surgical intervention on reproduction and they have explored reproductive options.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of gender-affirming surgical intervention have been assessed, with risks and benefits have been discussed.
- Stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).*

» *This was graded as a suggested criterion.

» Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role. The patient must over that period of time have shown improved psychological, social, and, probably, occupational function.[32]

» Genital surgery typically involves penectomy and orchiectomy. The surgery uses the existing genitals to fashion a vulva, neoclitoris and hood, labia, and (often) a neovagina. Preoperative genital hair removal is sometimes needed, particularly in patients who have been circumcised. Clinical experience suggests that the cosmetic results can be very good.

» Ongoing mental health and psychosocial support may be required before and after surgery, as appropriate. Long-term follow-up by the primary surgeon/gynecologist/primary care physician is encouraged for transgender women who have undergone vaginoplasty.[4]

adjunct other aesthetic procedures

Treatment recommended for SOME patients in selected patient group

» Options are varied, and include liposuction, lipofilling, gluteal augmentation, and hair reconstruction.[41]

Ongoing

transgender men (female-to-male transgender persons whose sex assigned at birth was female)

1st

individualized multidisciplinary management

» A multidisciplinary approach to management is strongly recommended; relevant disciplines include (but are not limited to) endocrinology, surgery, voice and communication, primary care, reproductive health, sexual health, and mental health.[4] However it is important to note that in some parts of the world, speciality services for transgender people are limited or wholly unavailable; in this setting, nonspecialist clinicians, for example, primary care providers may need to take on a greater role in the provision of gender-affirming care, highlighting the need for continuing training and professional development in line with current best practices.[4]

» Options for gender-affirming care include hormone therapies and surgeries. Adjunctive options include hair removal, speech and language therapy and supportive counseling. Management is highly individualized, and that there is no "one size fits all" approach to treatment. Transgender people may choose to undergo all, some, or none of the above interventions to support their gender affirmation.

» Transgender people as a group experience relatively poorer access to health services compared to other patient groups. Noted barriers include bias and stigma by health care professionals and a lack of knowledge around best practices, including safety and efficacy of treatments.[46] [47] An open, nonjudgemental and inclusive approach is important and may help to encourage people to be forthcoming with their concerns, and less likely to obtain hormones from unlicensed sources.[41]

» Transgender people also experience an increased risk of general mental health issues, including depression, anxiety, post-traumatic stress disorder, suicidality and substance use disorders.[1] [2][14] Ongoing screening, assessment, and management of any mental health conditions is therefore important.

» Usually, clinicians maintain that hormone treatment should generally not be started unless the patient has already changed gender role.[31] This may include legally changing registration

Ongoing

to that of the preferred sex and changing the person's name on all documents, as well as making friends, family, and other contacts aware of this change and asking to treat the person as their experienced sex.

» Based on clinical experience, advantages of this approach are that it can allow both patient and clinician to appreciate the degree to which the change in gender expression and role can be practically applied. Regrets following gender-affirming treatment are rare, but do occur; regret is more likely to occur in those who experience difficulties with social transition.[43] [50]

» Less commonly, hormone treatment is used for patients who do not wish to make a social gender role transition, or who are unable to do so.[4]

» There is universal agreement within international standards of care that social transition of at least 6 months to 1 year (plus a year of continuous hormone treatment) should precede any genital surgery.[4] [31]

Longer periods may be needed if there are any problems living in the new gender role. Patients should not undergo surgical treatment until they are thriving (not merely surviving) in their new gender role.

» Note that legal transition should not be dependent on use of medication or surgery, and varies according to local (i.e., national or state) laws; clinicians and patients should consult their relevant local legal guidance.[41]

adjunct androgens

Treatment recommended for SOME patients in selected patient group

» Treatment is preferably done working as part of a multidisciplinary team containing (or having easy access to) an endocrinologist.

» Criteria for hormone therapy include the following:[4]

- Gender incongruence is marked and sustained.
- The individual meets diagnostic criteria for gender incongruence prior to gender-affirming hormone treatment in regions where a diagnosis is necessary to access health care.

Ongoing

- The individual demonstrates capacity to consent for the specific gender-affirming hormone treatment.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of treatment have been assessed, with risks and benefits discussed.
- The individual understands the effect of gender-affirming hormone treatment on reproduction and they have explored reproductive options.

» A thorough discussion of the risks versus benefits of treatment is essential prior to treatment initiation, and guides shared decision-making.

» Gender-affirming hormone treatment aims to elicit in a birth-assigned female patient the secondary sexual changes seen in birth-assigned males at puberty. These changes will be superimposed on whatever female pubertal changes have already occurred and will not reverse them. Goals of treatment may include development of facial hair, deepening of the voice, and increasing body hair and muscle mass. Other effects of treatment may include fat redistribution, hairline recession, changes in body odour, reduced libido, cessation of menses, vaginal atrophy and increased clitoral size.[41] Vaginal atrophy may increase susceptibility to small amounts of vaginal tearing (similar to in postmenopausal women), and so prescription of a topical lubricant/estrogen may be required.[41] For information on expected timing of masculinizing effects of testosterone see Patient discussions .

» Androgens are administered in dosages sufficient to induce menopause, usually once monthly but, more rarely, as often as once every 2 weeks. Once menopause is achieved, it is often possible to decrease the frequency without menstrual periods returning.

» Gonadotropin suppression is generally not needed, as androgens alone usually suppress ovarian function very well.

» The aim of therapy is to achieve serum testosterone levels in the normal physiologic range for young males at all times.

Ongoing

- » It typically takes 2 or more years for patients to achieve maximal masculinizing results from hormones.[4]
- » For patients who go on to have oophorectomy, hormone therapy with testosterone is usually continued lifelong, unless contraindications develop.[4]
- » For recommended blood test monitoring regimens for patients newly started and established on hormone therapy see Monitoring .
- » Consult your guidelines and drug formularies for testosterone options and formulations. Preparations, doses, and licensing restrictions for testosterone vary according to country of practice. A variety of preparations and routes of administration are available, including injectables, gels, patches, and buccal tablets.

adjunct bilateral mastectomy

Treatment recommended for SOME patients in selected patient group

- » There is no consensus about when patients should undergo bilateral mastectomy. Although hormone therapy is not a formal prerequisite to bilateral mastectomy, most practitioners take the view that it should come after a change of gender role and treatment with androgens. Some patient groups would argue that it should precede both.

adjunct hysterectomy and bilateral oophorectomy

Treatment recommended for SOME patients in selected patient group

- » Some transgender people live successfully in their preferred gender role without surgery, but for others, genital surgery is the final (and most considered) step in the treatment process.

- » Criteria for genital surgery include the following:[4]

- Gender incongruence is marked and sustained.
- Meets diagnostic criteria for gender incongruence prior to gender-affirming surgical intervention in regions where a diagnosis is necessary to access health care.
- Demonstrates capacity to consent for the specific gender-affirming surgical intervention.

Ongoing

- Understands the effect of gender-affirming surgical intervention on reproduction and they have explored reproductive options.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of gender-affirming surgical intervention have been assessed, with risks and benefits have been discussed.
- Stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).*

» *This was graded as a suggested criterion.

» The aim of hormone therapy prior to oophorectomy and hysterectomy is principally to introduce reversible estrogen suppression, before the patient undergoes irreversible surgical intervention.

» Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role. The patient must, over that period of time, have shown improved psychologic, social, and, probably, occupational function.[\[32\]](#)

» Some transgender men desire hysterectomy and/or oophorectomy as part of masculinizing surgery. Previously, consideration of hysterectomy and bilateral oophorectomy was recommended within 2 years to obviate the risk of gynecologic malignancy.[\[31\]](#) However, the World Professional Association for Transgender Health now recommends against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender people undergoing testosterone treatment and who have an otherwise average risk of malignancy.[\[4\]](#)

» The route of hysterectomy is dependent on clinical findings, surgical, and patient preference.[\[41\]](#) Approaches include laparoscopic, transvaginal, and transabdominal. An advantage of the laparoscopic approach is that it avoids leaving a large abdominal scar.

Ongoing

» Vaginal access may be difficult if patients are nulliparous and have often not experienced penetrative intercourse. A transabdominal approach should utilize any incision other than a Pfannenstiel incision because this incision is pathognomonic of gynecologic surgery and the resulting scar may look unusual in a male.

adjunct phalloplasty

Treatment recommended for SOME patients in selected patient group

» Some transgender people live successfully in their preferred gender role without surgery, but for others, genital surgery is the final (and most considered) step in the treatment process.

» Criteria for genital surgery include the following:[4]

- Gender incongruence is marked and sustained.
- Meets diagnostic criteria for gender incongruence prior to gender-affirming surgical intervention in regions where a diagnosis is necessary to access health care.
- Demonstrates capacity to consent for the specific gender-affirming surgical intervention.
- Understands the effect of gender-affirming surgical intervention on reproduction and they have explored reproductive options.
- Other possible causes of apparent gender incongruence have been identified and excluded.
- Mental health and physical conditions that could negatively impact the outcome of gender-affirming surgical intervention have been assessed, with risks and benefits have been discussed.
- Stable on their gender affirming hormonal treatment regime (which may include at least 6 months of hormone treatment or a longer period if required to achieve the desired surgical result, unless hormone therapy is either not desired or is medically contraindicated).*

» *This was graded as a suggested criterion.

Ongoing

» Furthermore, many clinics prefer that the patient has experienced 1-2 years in the desired gender role. The patient must, over that period of time, have shown improved psychologic, social, and, probably, occupational function.^[32]

» This is a complex, often multi-stage procedure.

» Donor sites for phalloplasty can include the forearm, abdominal skin, or tissue from elsewhere on the patient's body. The complexity, duration, and expense of the procedure are such that only a large minority of patients chose to undergo this surgery.

» Clinical experience suggests that the cosmetic and functional results are fairly good, but the result in, even the best centers, is clearly distinguishable from a native penis.

adjunct other aesthetic procedures

Treatment recommended for SOME patients in selected patient group

» Options are varied, and include liposuction, lipofilling, and pectoral implants.^[41]

Secondary prevention

Patients taking hormonal therapies should avoid prothrombotic states such as obesity, smoking, or inactivity.

Hormone therapy may increase cardiovascular risk, particularly for transgender women taking feminizing hormone therapy. For those with nonmodifiable risk factors which may increase the risk of thromboembolic disease, for example, a known history of thrombophilia, a past history of thrombosis, or a strong family history of thromboembolism, offering an anticoagulant in addition to treatment with transdermal estrogen may decrease the risk of thromboembolism, although data to guide treatment decisions are extremely limited.^[4]

Note that traditional cardiovascular risk calculators do not take into account the use of current or past hormones. Factors to consider when estimating cardiovascular risk include the dose, length and age of onset of hormone therapy.^[4] As a general guide, when estimating cardiovascular risk, it may be appropriate to use birth-assigned sex for those who have transitioned in later life, and to use a patient's affirmed gender for those who have been taking hormone therapy since adolescence/young adulthood.^[62]

Patient discussions

Terminology

The terminology used to describe transgender people is complex, changing, and has the potential to cause distress if used inappropriately. Healthcare professionals are advised to address transgender people as they would prefer to be addressed, whether or not they have officially changed their name. A simple way to do this is to ask the person what pronouns they use. It may also be helpful to share your own pronouns too, if you wish. Some transgender people prefer gendered pronouns such as "she", "her," and "hers" or "he", "him", and "his". Others prefer gender-neutral pronouns such as "they", "them," and "theirs." A change in pronouns may be an important aspect of transition.^[61] Clinicians may be concerned

about the possibility of using the wrong pronoun when talking to a transgender person (often described as "misgendering"). If this happens, often the best way to approach this is simply to apologize and carry on with the conversation, and aim to use the correct pronouns in future.

Fertility, pregnancy, and contraception

Pretreatment discussion of the consequence of medical and surgical treatment on fertility is essential, including a discussion of fertility preservation options, including sperm banking, oocyte preservation, embryo preservation and (less commonly) ovarian, or testicular tissue cryopreservation.^[31] ^[41] All patients should be counseled on barrier methods of contraception for prevention of sexually transmitted infections. Gender-affirming hormone therapy is not effective contraception; transgender people with retained gonads should be counseled about the possibility of pregnancy if they are having sexual activity that involves sperm and oocytes. Testosterone treatment is contraindicated during pregnancy, but transgender men may safely achieve pregnancy after cessation of testosterone.^[41]

Thromboembolic disease

Transgender people receiving hormone therapy should be educated on the symptoms and signs of thromboembolic disease and advised to present promptly for investigation, should these symptoms occur.

Timing of hormone-induced changes

People receiving hormone treatment require information on the likely extent and timing of hormone-induced changes. Although the data on this is limited, and a large degree of natural variation can be expected, the following information from the Endocrine Society is helpful as a general guide.^[31]

Expected timing of masculinizing effects of testosterone^[31]

- Onset in the first 1-6 months:
 - Increased skin oiliness/acne (maximum effect 1-2 years)
 - Fat redistribution (maximum effect 2-5 years)
 - Cessation of menses
 - Clitoral enlargement (maximum effect 1-2 years)
 - Vaginal atrophy (maximum effect 1-2 years).
- Onset in the first 6-12 months:
 - Facial/body hair growth (maximum effect 4-5 years)
 - Scalp hair loss
 - Increased muscle mass/strength (maximum effect 2-5 years)
 - Deepening of voice (maximum effect 1-2 years).

Expected timing of feminizing effects of estrogen and antiandrogen therapy^[31]

- Onset in the first 1-3 months:
 - Decreased sexual desire (maximum effect 3-6 months)
 - Decreased spontaneous erections (maximum effect 3-6 months).
- Onset in the first 3-6 months:
 - Redistribution of body fat (maximum effect 2-3 years)
 - Decreased muscle mass and strength (maximum effect 1-2 years)
 - Softening of skin and decreased oiliness (maximum effect unknown)
 - Breast growth (maximum effect 2-3 years)
 - Decreased testicular volume (maximum effect 2-3 years).
- Onset in the first 6-12 months:

- Decreased terminal hair growth (maximum effect greater than 3 years).
- Variable timing of onset:
 - Male sexual dysfunction
 - Decreased sperm production (maximum effect greater than 3 years)
 - Scalp hair.

Monitoring

Monitoring

Clinical review

- For patients receiving hormone treatment, medical evaluation by the hormone-prescribing physician every 2-3 months in the first year, and every 6-12 months thereafter, is recommended.[4][31] [41] This is to monitor for appropriate signs of masculinization/feminization, and for the development of any adverse reactions (e.g., venous thromboembolism, cardiovascular impairment). It typically takes at least 2 years for patients to achieve maximal masculinizing/feminizing results from hormones.[31]
- Patients who undergo gonadectomy require hormone replacement treatment, surveillance, or both, to prevent adverse effects associated with chronic hormone deficiency.[31]

Blood tests

- For patients receiving hormone treatment, laboratory (blood test) monitoring is recommended every 2-3 months in the first year, and every 6-12 months thereafter.[4][31] [41] A clinical priority is maintaining testosterone/estrogen levels within the physiologic range for birth-assigned female/birth-assigned male patients respectively, given that supraphysiologic doses may lead to an increased risk of adverse effects.[31] Long-term monitoring of lipids, prolactin, liver functional tests (plus hematocrit in transgender men only) from baseline is advisable, although derangements are rare. The Endocrine Society guidelines contain detailed standard monitoring plans for patients on both testosterone and estrogen cross-hormone therapy, including recommended serum hormone levels.[31]
- Note that there are particular considerations with regard to testosterone monitoring according to whether a topical or injected preparation is used. With topical testosterone preparations levels should be measured at least 6 hours after the preparation was applied, making sure the blood is drawn from a different site to the one the preparation was earlier applied. Injected preparations need a peak and trough level. The trough is the level that pertains to the day the injection is due and should be at the bottom end of the normal male range. The peak level is that which applies a week after the injection is given, and should be at the top end of the normal male range. This ensures that at no point in the dosing cycle is the level supraphysiologically high or low. Longer acting preparations need a single, trough, measurement that should be at the bottom end of the normal range.

Mammography in transgender women

- It is not clear whether there is any need for mammographic breast cancer screening in transgender women. Data are sparse, but only five breast cancers have ever been reported in this patient group, and these were in patients on unsupervised treatment regimes that included progesterone (which raises the risk of cancer in birth-assigned females on hormone replacement therapy). Avoiding the use of progesterone in treatment seems greatly to decrease the risk of breast cancer.[58] Based on a potential increased risk of breast cancer with feminizing hormones, the Endocrine Society guidelines suggest that transgender taking feminizing hormones follow breast screening guidelines recommended for birth-assigned women.[31] It may be necessary to take into consideration the length of time of hormone use, dosing, current age, and the age at which hormones were initiated.[4]

Mammography in transgender men

- If mastectomy has not been performed, standard breast screening guidance applies.[4]

Prostate screening in transgender women

- Transgender women treated with estrogens should follow screening guidelines for prostatic disease and prostate cancer recommended for birth-assigned men.[31] Manual prostate checks may be performed via the vaginal canal in transgender women who have received genital surgery, as

the prostate is located on the anterior wall of the vagina.[4] Although there are case reports of prostate cancer in transgender women, most were in people who started hormone therapy after the age of 50 years, and it is considered likely that these people had pre-existing lesions before initiating hormone treatment.[60] It is important to note that following the initiation of gender-affirming hormone treatment, prostate-specific antigen (PSA) may be a less-useful measuring tool for prostate cancer, given that PSA levels ordinarily plummet in transgender women taking gender-affirming hormone therapy, meaning that extra care is needed in interpreting results.[38] Guidance on screening and recommended PSA ranges in transgender women is currently lacking; establishment of a baseline PSA level prior to hormone therapy is often recommended.

Gynecologic monitoring

- Anyone with an intact uterus, cervix, or ovaries should be offered the usual screens for malignancies of these organs.[4] Gender-affirming hormones have not been shown to affect cancer risk, but the quality of evidence is low and longer-term studies are needed.[56]
- Previously, total hysterectomy and oophorectomy were recommended for transgender men taking testosterone therapy, but the World Professional Association for Transgender Health now recommends against against routine oophorectomy or hysterectomy solely for the purpose of preventing ovarian or uterine cancer for transgender men undergoing testosterone treatment and who have an otherwise average risk of malignancy.[4] [31]
- Patients re-registered as male may be automatically dropped out of cervical cancer screening programs and should be advised to proactively seek such screening.

Bone mineral density measurement

- This is recommended for patients with risk factors for osteoporosis, and in particular for those who stop hormone treatment following gonadectomy.[31]

Aortic aneurysm screening

- Transgender women should be offered abdominal aortic aneurysm screening in keeping with routine screening programs for birth-assigned men.

Complications

Complications	Timeframe	Likelihood
estrogen- or androgen-related obesity	long term	high
Both estrogens and androgens increase appetite, so unless actual consumption is kept constant, weight gain will result.		
estrogen-related thromboembolic disease	long term	low
Estrogen treatment raises the risk of thromboembolic disease, particularly in smokers.[31] Nonsmoking status should be strongly recommended prior to treatment. For those with nonmodifiable risk factors which may increase the risk of thromboembolic disease, for example, a known history of thrombophilia, a past history of thrombosis, or a strong family history of thromboembolism, offering an anticoagulant in addition to treatment with transdermal estrogen may decrease the risk of thromboembolism, although data to guide treatment decisions are extremely limited.[4]		
androgen-related polycythemia	long term	low
<p>Particularly before hysterectomy and oophorectomy, when higher doses of androgens may sometimes be employed to achieve menopause.</p> <p>The American College of Obstetricians and Gynaecologists list polycythemia (hematocrit greater than 55%) as an absolute contraindication to testosterone treatment.[41]</p> <p>Androgen treatment raises hematocrit, particularly in smokers. Hysterectomy and oophorectomy may allow dose reduction, or phlebotomy may be needed.[58]</p>		
estrogen- or androgen-related hyperprolactinemia	long term	low
<p>Particularly at outset of treatment.</p> <p>Estrogens and androgens can cause prolactin to rise. Only levels of over 1000 IU require endocrine advice.[58]</p>		
estrogen- or androgen-related dyslipidemia	long term	low
Dyslipidemia is not common, but is worthwhile monitoring. If apparent it is treated in the usual manner with diet and statins.		
bone loss	long term	low
Bone mass is generally preserved with use of either sex steroid. The risk of osteoporosis is increased for patients who stop sex hormone treatment following gonadectomy.[31] Screening for osteoporosis is recommended for patients with risk factors, and in particular for those who stop hormone treatment following gonadectomy.[31]		
mental health disorders	variable	medium
Transgender people are at increased risk for mental health problems, including suicidal ideation, prior to gender-affirming treatment and legal gender change. This risk may persist after gender reassignment if the individual struggles to adjust.[2] Furthermore, a number of external social factors including stigma,		

Complications	Timeframe	Likelihood
discrimination, and minority stress have been suggested as contributing factors.[15] Primary care screening and assessment for mental health conditions is likely to be valuable on an ongoing basis.		

Prognosis

In general, transgender people are at increased risk of stigmatization and discrimination which can lead to depression, suicidality, relationship difficulties, and economic consequences such as unemployment.[15] Mental health problems may persist after gender reassignment in some individuals, particularly if they struggle to adjust to their new identity.[2]

Meta-analysis evidence demonstrates that, for the majority of transgender people, gender-affirming treatment (including hormonal therapy) results in significant improvements in quality of life and psychosocial functioning.[43] [44] [45] The percentage of people who regret their gender-affirming surgical intervention is low (estimated to be between 0.3% and 3.8%).[4] Regret may be temporary or permanent; in this scenario multidisciplinary input is recommended in order to explore this further, with possible outcomes being medical and/or surgical treatment to continue the transition, or revision surgery to return anatomy to the sex assigned at birth.[4]

A retrospective cohort study found that adult transgender people who received hormone treatment were at a 2-fold increased mortality risk compared to the general population. The increased risk was not attributable to hormone treatment, but rather emphasized the importance of holistic transgender healthcare, including appropriate treatment of cardiovascular disease.[59]

Diagnostic guidelines

International

Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, Text Revision (DSM-5-TR) (<https://ebooks.appi.org/product/psychiatric-statistical-manual-mental-disorders-fifth-edition-text-revision-dsm5tr>) [2]

Published by: American Psychiatric Association

Last published: 2022

Health care for transgender and gender diverse individuals (<https://www.acog.org/clinical/clinical-guidance/committee-opinion>) [41]

Published by: The American College of Obstetricians and Gynecologists

Last published: 2021
(Reaffirmed 2024)

Assessment and treatment of gender dysphoria and gender variant patients: a primer for psychiatrists (<https://www.psychiatry.org/Psychiatrists/Search-Directories-Databases/Resource-Documents/2018/Assessment-and-Treatment-of-Gender-Dysphoria-and-G>) [17]

Published by: American Psychiatric Association

Last published: 2018

Standards of care version 8 (<https://www.wpath.org/publications/soc>) [4]

Published by: World Professional Association for Transgender Health

Last published: 2022

International Classification of Diseases 11th revision (ICD-11) (<https://icd.who.int/en>) [1]

Published by: World Health Organization

Last published: 2022

European Society for Sexual Medicine Position statement "assessment and hormonal management in adolescent and adult trans people, with attention for sexual function and satisfaction" (<https://academic.oup.com/jsm/article-abstract/17/4/570/6973560?redirectedFrom=fulltext&login=false>) [42]

Published by: European Society for Sexual Medicine

Last published: 2020

Treatment guidelines

International

Health care for transgender and gender diverse individuals (<https://www.acog.org/clinical/clinical-guidance/committee-opinion>) [41]

Published by: The American College of Obstetricians and Gynecologists

Last published: 2021
(Reaffirmed 2024)

Assessment and treatment of gender dysphoria and gender variant patients: a primer for psychiatrists (<https://www.psychiatry.org/Psychiatrists/Search-Directories-Databases/Resource-Documents/2018/Assessment-and-Treatment-of-Gender-Dysphoria-and-G>) [17]

Published by: American Psychiatric Association

Last published: 2018

Endocrine treatment of gender-dysphoric/gender-incongruent persons (<https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines>) [31]

Published by: Endocrine Society

Last published: 2017

Guidelines for psychological practice with transgender and gender nonconforming people (<https://www.apa.org/practice/guidelines>) [37]

Published by: American Psychological Association

Last published: 2015

Standards of care version 8 (<https://www.wpath.org/publications/soc>) [4]

Published by: World Professional Association for Transgender Health

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European Society for Sexual Medicine Position statement "assessment and hormonal management in adolescent and adult trans people, with attention for sexual function and satisfaction" (<https://academic.oup.com/jsm/article-abstract/17/4/570/6973560?redirectedFrom=fulltext&login=false>) [42]

Published by: European Society for Sexual Medicine

Last published: 2020

Online resources

1. WHO: International Classification of Diseases 11th Revision (<https://icd.who.int/en>) (*external link*)
2. WHO: FAQs Gender incongruence and transgender health in the ICD (<https://www.who.int/standards/classifications/frequently-asked-questions/gender-incongruence-and-transgender-health-in-the-icd>) (*external link*)
3. APA: gender dysphoria (https://www.psychiatry.org/File%20Library/Psychiatrists/Practice/DSM/APA_DSM-5-Gender-Dysphoria.pdf) (*external link*)

Key articles

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- American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 5th edition (DSM-5). Washington, DC: American Psychiatric Publishing; 2022.
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Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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DISCLOSURES: LS has received an honorarium for giving a lecture in a nonpromotional meeting on the subject of gender dysphoria by Besins healthcare.

Jack Drescher, MD

Clinical Professor of Psychiatry

Columbia University, NY

DISCLOSURES: JD declares that he has no competing interests.

Rebecca Luff, BSc(Hons)

Individual with lived experience of gender dysphoria.

DISCLOSURES: RL declares that she has no competing interests.