OUTpatients
The UK's LGBTIQ+ Cancer Charity

British Oncology Pharmacy Association
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TRANScribing

Clinical considerations for safe and inclusive prescribing for transgender and non-binary patients

British Oncology Pharmacy Association

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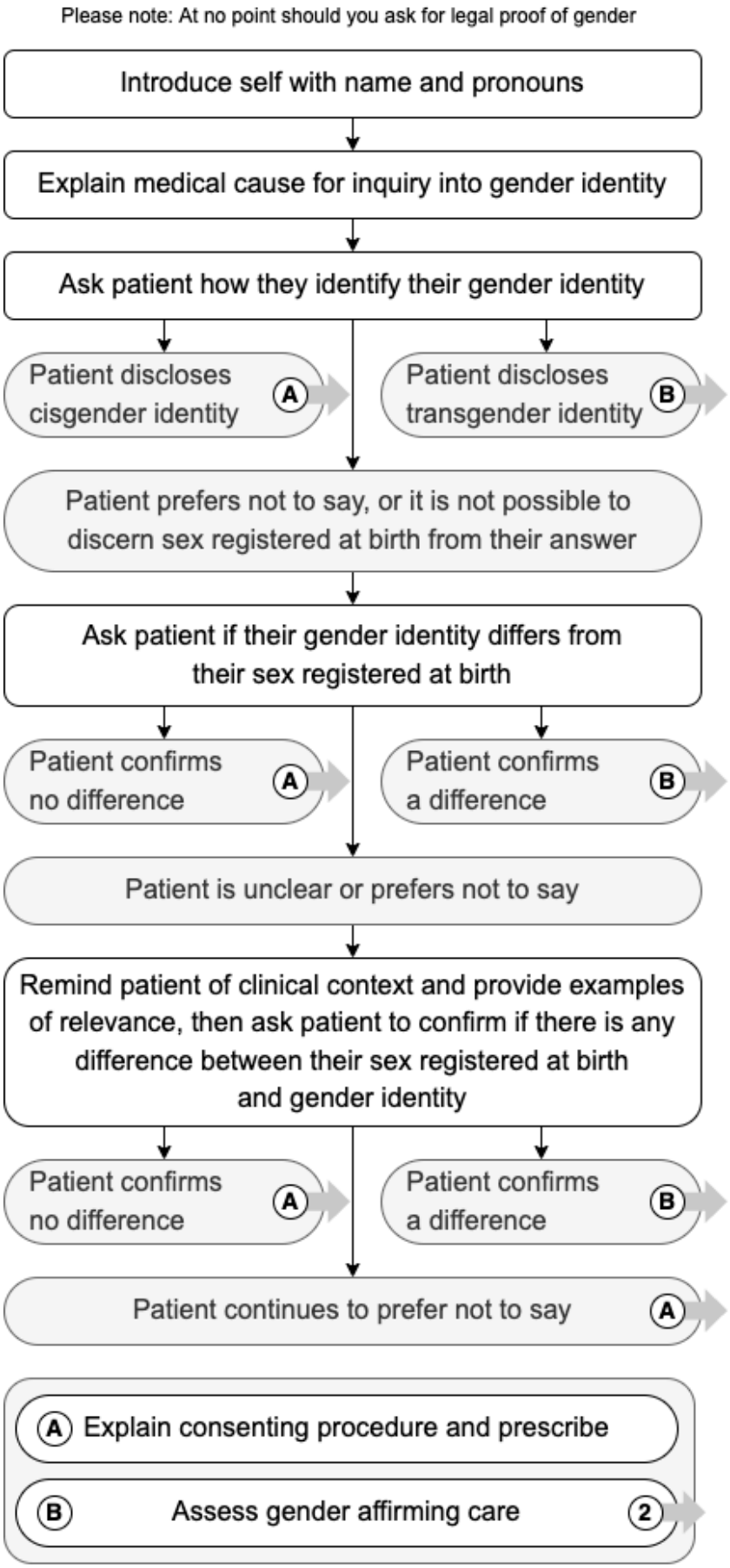
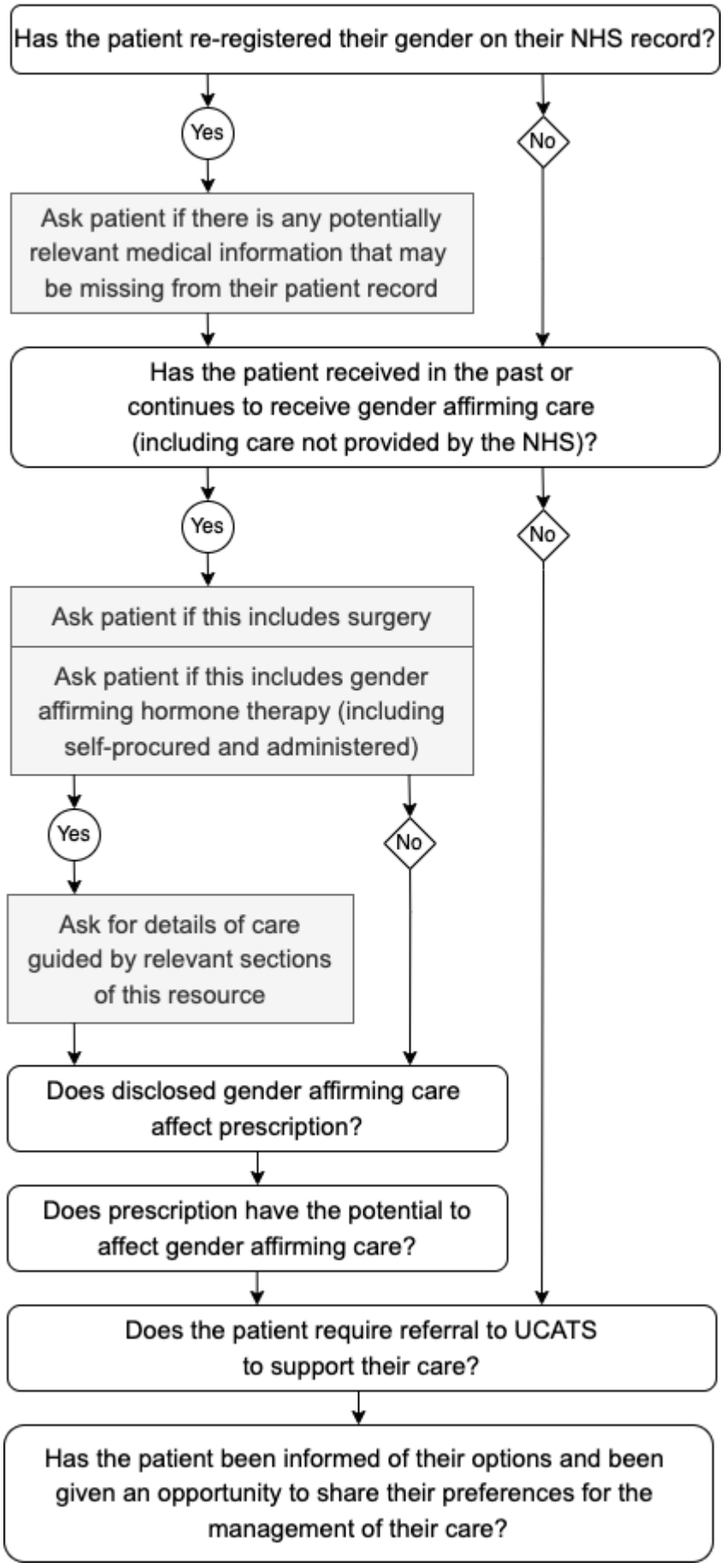


2. Quick guide: Gender affirming care assessment



3. Glossary of Terms

Agender
A lived experience that does not relate to gender.

Ally
A person who supports and advocates for LGBTIQ+ people.

Assigned Female at Birth (AFAB) / Registered Female at Birth
Any person whose sex registration at birth resulted in a declaration of female.

Assigned Male at Birth (AMAB) / Registered Male at Birth
Any person whose sex registration at birth resulted in a declaration of male.

Cisgender
A person whose gender identity aligns with the sex they were registered at birth.

Deadname
A trans person's previous or birth name. It is considered offensive to use this name. 'Deadname' can be used as a noun and a verb.

Enby
Colloquialism for non-binary.

Gender
A social construct informed by the norms, roles and behaviours that we attribute to being masculine, feminine, or third gender.

Gender affirming care
Refers to medical, psychological, and social interventions that are provided to transgender and gender-diverse individuals, to help align their physical and social characteristics with their gender identity. Replacing the terms 'Sex Reassignment' and 'Gender Reassignment'.

Gender dysphoria
The discomfort felt between one's gender and their sex registered at birth. This may be experienced mentally, physically or socially.

Gender-fluid
A form of gender identity and expression that is not fixed.

Gender identity
An individual's personal sense of having a particular gender.

Intersectionality
Theory introduced by Prof. Kimberlé Crenshaw to describe how multiple facets of a person's identity can overlap to make unique forms of oppression and discrimination.

LGBTIQ+
Lesbian, Gay, Bisexual, Transgender, Intersex, Queer, and other sexual orientations and

gender identities and expressions signified by the '+'.

Non-binary
A term to describe a gender identity that does not fit within the traditional categories of being exclusively male or female. Non-binary individuals may identify as a combination of both genders, neither gender, a different gender entirely, or as having a gender identity that is fluid and may change over time.

Outing someone
Identifying someone as LGBTIQ+ without their consent.

Pronoun
A word that takes the place of a noun in a sentence. The most common third-person pronouns we encounter are "he, she and they". Correct pronoun use corresponding to a person's gender identity is important.

Sex
Refers to the underlying biological characteristics including genitalia, chromosomes, and secondary sexual characteristics (such as breast development and facial hair growth).

Third Gender
A distinct form of gender from that of male or female found around the world, including the Hijra, Māhū, Fa'afafine, Two-Spirit, and Muxe.

Top surgery
Community term for bilateral mastectomy with masculine chest reconstruction undergone as gender affirming care.

Transgender man / Trans man
A person who was registered female at birth but has the gender identity of male.

Transgender woman / Trans woman
A person who was registered male at birth but has the gender identity of female.

Transfeminine
A person who was registered male at birth but identifies and expresses their gender identity in ways that align more closely with a female gender, femininity, or feminine characteristics.

Transgender
An umbrella term for a person whose gender identity differs from the sex they were registered at birth.

Transmasculine
A person who was registered female at birth but identifies and expresses their gender identity in ways that align more closely with a male gender, masculinity, or masculine characteristics.

Transphobia
Prejudice, discrimination, fear, or dislike towards someone that is transgender based on their identity.

4. Introduction

In 2022, The Office for National Statistics UK Census reported that 0.5% of the UK population identified as transgender. NHS surveys like the GP Patient Survey report the percentage of trans people accessing GP services as 0.8%, averaged across all age groups. If younger people are viewed as a separate cohort, this rate increases to 2.2%.

The variations in these figures may be attributed to varying methodologies, greater trust in the NHS than the census, or an over-representation of trans people in healthcare. Either way, according to these figures around one in a hundred patients may be transgender so it is important to understand their needs and how to support their health and patient safety.

5. Defining transgender

To be transgender (trans) is to have a difference in your **sex assigned at birth** and your **gender identity**. The term 'assigned at birth' is a community developed term that tries to describe the feeling of having your identity assumed based on your sex characteristics observed at birth. For clarity in a clinical space, we tend to use the phrase **sex registered at birth**, as this better describes the process that occurs when a child is born.

> A person's sex is understood as the classification we make based upon physical factors, such as their genitalia, chromosomes and hormones. This is only ever recorded as male or female in the UK.
>
> Gender identity refers to the way we understand ourselves within our society's view of norms, behaviours, and relationships that are associated with masculine and feminine traits. These experiences may inform how they identify and the label(s) they may choose to use, such as male, female, non-binary, or in another way.

When there is a difference between a person's sex registered at birth and their gender identity, this is clinically known as **gender incongruence**. Gender incongruence was introduced as a term in 2019 by the World Health Organisation to replace previously stigmatising clinical labels of transgender identity.

Non-binary and gender diverse

Assuming that all people are somewhere on a fixed line between 'male' and 'female' has the potential to incorrectly assume a level of androgynous gender expression from non-binary individuals. Instead it is better to understand gender as a spectrum and acknowledge there are numerous ways a person can identify that sit outside of normative gender expression.

6. Language

Correct use of community language demonstrates respect for the individuals and is associated with greater levels of disclosure and patient reported experience measures (PREMs).

Pronouns

Pronouns are a common feature of the English language and are used to replace a noun in a sentence. This may be a proper noun, such a name (Example 1), or it can be for other types of nouns (Example 2).

1. **Stacy** parked her car | **She** parked her car
2. **The driver** delivered the package | **They** delivered the package

In Example 2, we see the use of a gender neutral singular 'they' as the gender of the driver is not known.

> The use of singular 'they' dates as far back as 1375 in recorded texts, and potentially further in common speech. As a point of comparison, 'you' functioned as a polite singular for centuries, but it was not until the seventeenth century that it was used more widely in common speech, replacing thou and thee.

Some people prefer to use the singular 'they' as a gender neutral pronoun for themselves. Writing in the singular 'they' also allows us to make our patient information applicable to more people who might otherwise be excluded by some gendered language.

Supporting an individual's personal pronouns is important. The Trevor Project's 2022 National Survey on LGBTQ Mental Health showed that affirming a young person's gender identity (eg. through affirming pronoun use) reduces the individual's risk of attempting suicide by half.

Common ways to ask a person's pronouns include:

- "Hi, my name is _____ and my pronouns are ___/___, can I ask yours?"
- "May I ask your name and pronouns?"
- "Can I ask which pronouns you use?"

When people share their pronouns, this is done in the grammatical subject/object method i.e. he/him, she/her, they/them. A rising feature of pronoun use in younger cohorts is the sharing of multiple pronoun forms that they are comfortable with using (e.g. she/they). When people share multiple pronouns, this does not follow the subject/object method. Instead, people typically share their pronouns in order of preference. So, someone using she/they may prefer 'she' but is also comfortable with 'they'. If you're not sure which one to use, just ask politely to check by asking:

- "Which pronouns would you prefer that I use today?"
- "Hey, I noticed you use she/they pronouns, do you have a preference?"
- "Are there any specific situations where you would prefer me to use one pronoun instead of the other?"

Appropriate language

Learning an individual's cultural or personally significant language can be a delicate task for any patient. For those in the transgender community, there can be specific sensitivity due to many similar sounding words or apparently non-offensive words being weaponised against

the community. Below are some examples of correctly used community terms for trans and non-binary individuals.

- Transgender man
- Transgender woman
- Non-binary person
- Trans man
- Enby
- Transmasculine
- Transfeminine
- Transition
- Trans woman
- Trans person

Inappropriate language

Inappropriate language targeted at transgender people tends to revolve around a focus on their sex registered at birth as a means to deny their gender identity, such as referring to a trans woman as a 'biological male'.

There can also be incorrect grammatical use of transgender terms and language. Transgender is an adjective and should follow this grammatical use. If you are not sure if you are using the word correctly, consider substituting in the word 'tall' to check your grammar. For this reason, the following examples are not appropriate: transman, transgendered man.

Some phrases that were previously common have since fallen out of popularity. These terms may be used by individuals of particular generations or subsections of the transgender community, but for appropriateness it is best not to lead with them. Examples are below with appropriate alternatives.

Inappropriate language		**Appropriate language**
Transsexual		Transgender (trans)
Sex change	→ use →	Transition
Male to female		Transgender woman
Female to male		Transgender man
Sex change operation		Gender affirming surgery / Top surgery / Lower surgery

Some of the systems used within the clinical environment may still use outdated terminology and diagnostic codes. These systems are usually slow to be updated, so it is important to remember to use affirming and appropriate language with patients, even if the systems are not up to date. If the patient may potentially see these outdated terms and codes, it may be worth discussing this with them why our systems continue to use these terms and reaffirm our commitment to using the right language with them.

7. Disclosure

Opportunities for disclosure

In order to be clear of potential prescribing risks, we must ascertain if the patient is transgender, non-binary or gender diverse and has undergone or is presently undergoing gender affirming care. This will involve asking questions related to their gender identity and healthcare in appropriate ways that gain trust and disclosure from the patient.

The process of getting to know transgender and non-binary patients may take additional consideration to build a positive rapport. Transgender patients often look for cues about the safety of their environment before revealing information and being transgender or non-binary.

Using inclusive language, as described in the preceding section, can be a useful way to demonstrate safety for these patients. Additionally, some patients may prefer to reveal their transgender identity through self-report measures such as consent forms.

You may also wish to display or share your pronouns, wear LGBT+ related paraphernalia such as rainbow badges, or assess your workplace on its ability to provide for transgender and non-binary patients (e.g. gender neutral bathrooms).

Legal protections

If a patient has applied for or is in possession of a Gender Recognition Certificate they receive certain protections under UK law. This certificate is achievable through the Gender Recognition Act (2004) and allows a patient to update their legal gender on their birth certificate and will affect aspects of marital law, state benefits, and pensions.

- **A person with a GRC is protected against people working in a professional capacity revealing their transgender identity without their consent**
- **A patient does not need to present their Gender Recognition Certificate and it may be considered discrimination if they are asked to see it**

These two protections together create a circumstance whereby we must act with respect of all trans people and gain consent from each individual before sharing their identity. This is an appropriate model of best practice.

The Equality Act 2010 also affords transgender and non-binary people protection from discrimination, harassment or victimisation in employment, and as users of private and public services. This community is covered by the protected characteristic of “gender reassignment” which protects those proposing to undergo, undergoing or having undergone transition. The protection of non-binary people was confirmed under the Equality Act by case law.

Patients records

In England and Wales, when transgender patients re-register their gender on their patient record they are provided with a new NHS number and clinical record. The newly allocated NHS number will not be linked in any way to the patient’s previous NHS number. This method conceals the individual’s sex registered at birth, affects their screening invitations, and

creates a potential situation by which their clinical history may be incomplete if not manually transferred to the new record. For this reason, it is especially important that taking clinical history is thorough to avoid any potential omissions affecting patient safety when prescribing.

In Northern Ireland, the Health and Care Number (H&C Number) is the equivalent of the NHS number in England and Wales. When a patient chooses to change their H&C number a new patient record and Health and Care Number for the patient. Similar issues around screening and clinical information apply.

In Scotland, the Community Health Index (CHI) number is the equivalent of the NHS number in England and Wales. In CHI numbers, the ninth digit is always an even number for people registered as female and an odd number is for people registered male. When the CHI number is requested to be changed by a trans person, a new medical record is created with a CHI number which reflects the trans patient's gender. The old record and the new record are initially linked and GPs are encouraged to transfer notes. If a patient chooses they may refuse this link between the new and old records. Doing so affords greater privacy, however also gives rise to the potential issues in screening and incomplete records or medical history.

There may also be instances where an individual is acquiring and self-administering medical transition related care, such as gender affirming hormone therapies (GAHT). This is often motivated by the incredibly long waiting times for assessment at the NHS Gender Identity Clinics (GICs). As a result, it is important that we are able to respectfully and safely ask about any self-administration of gender affirming care that may affect how we prescribe to the individual.

Gender affirming care and oncology

There may be circumstances where the individual's gender affirming care and transition changes how we prescribe. There may also be times that GAHT is at risk of driving cancer growth. These factors will be described in more detail in the following sections.

In some circumstances, oncological intervention may preclude transition. Where this is the case, it is important that patients are consulted and given the opportunity to make an informed decision about their care. Many patients feel that their transition is life-saving so may require additional support when discussing potential cessation of transition to pursue oncological therapies. Some patients have been known to refuse care to prioritise their transition.

8. Transition

The rate of people disclosing gender incongruence is rising. Likewise, the rate of referrals to the Gender Identity Clinics provided by the NHS is also increasing. People are referred to these clinics to access gender affirming care to support their transition.

Transition is the process by which a person may bring their gender expression or physical characteristics in line with their gender identity. Each individual will take their own personal path through transition. In the UK, there are minimum ages and

thresholds that must be met before treatment can begin on the NHS.

Transition can be grouped into three main categories:

Social transition

Changing a person's gender expression is the first form of transition taken by the individual. This may involve modification of their clothing, hair, and other gendered markers of presentation. It may also involve adoption of gendered roles and behaviours. Some individuals may also compress or conceal parts of their anatomy for aesthetic and gender affirming reasons such as 'binding' (compression of breast tissue) and 'tucking' (concealment of the penis).

Medical transition

Some trans people may choose to undergo gender affirming hormone therapy (GAHT). The World Professional Association for Transgender Health (WPATH) recommends health care professionals prescribing GAHT to monitor patients' endogenous and administered sex steroids so that they are safely maintained at levels appropriate for the treatment goals of transgender and gender diverse people according to their tanner stage.

Trans Men

In trans men and transmasculine people, this will involve taking exogenous testosterone, but may also include a gonadotropin releasing hormone (GnRH) analogues to reduce oestrogen and progesterone levels. Testosterone can be accessed in an injectable form which is either shorter acting and given every 3-4 weeks, or longer acting and given every 12 weeks. Testosterone can also be used as a gel which is applied daily, causing less fluctuation in hormone levels. GnRH analogues are usually delivered as an injection every 12 weeks.

Some trans men and non-binary individuals will take progesterone-containing medications either to stop menstruation prior to starting testosterone, to prevent cramping on testosterone, and/or as contraception. These include medroxyprogesterone acetate and norethisterone, progesterone-only contraceptive pills, the contraceptive implant, the levonorgestrel intrauterine system (IUS) commonly known as the Mirena coil and the Jaydess coil, and Depo-Provera. Some may choose to be on the combined oral contraceptive, but this is less common due to its oestrogen content which may disrupt the effect of GAHT. However the extent of this interaction requires more research.

Rapidity and degree of change from masculinising endocrine therapy depends on the agents used, dosage, and the patient's responsiveness to endocrine therapy. Typically, within the first 1-3 months, patients experience oilier skin/acne, increased muscle mass and upper body strength, redistribution of fat to a more masculine pattern (shifting from the hips and buttocks to the abdomen) and clitoral growth.

Trans women

Trans women and transfeminine people usually take exogenous oestrogen in the form of tablets, gel, patches, or a 12 weekly injection. Many trans women will also take GnRH analogues to suppress the release of testosterone. Other drugs alpha-reductase inhibitors like finasteride) are used instead of GnRH analogues to limit the conversion of testosterone to its active form dihydrotestosterone. Finasteride also has the effect of preventing hair loss and thinning body hair, which may be desirable to the patient. Spironolactone, used to suppress testosterone production.

Cyproterone acetate is a drug that shares some activities with progesterone but is used as an antiandrogen. It is usually given for two weeks to stop the initial surge of testosterone that can occur with GnRH analogues. However, it has also been used as longer term antiandrogen. It is currently subject to an European Medicines Agency warning due to an increased frequency of meningiomas (benign brain tumours) in long term administration.

Rapidity and degree of change from feminising endocrine therapy depends on the agents used, dosage, and the patient's responsiveness to endocrine therapy. Typically, within the first 1-6 months there is a gradual redistribution of body fat to more closely approximate a female body habitus, decreased muscle mass and decreased upper body strength, and softening of the skin.

Surgical transition

Trans Men

Trans men and some non-binary people registered female at birth may choose to have masculinising chest reconstruction, commonly referred to as 'top surgery'. In most cases this removes the majority of breast tissue, but a small amount remains. Top surgery can be achieved by multiple methods, often relating to the amount of tissue to be removed and also the surgeon's preferred method. As a result, there may be instances where it is not immediately apparent that a person has undergone top surgery if their scars are minimal.

A number of trans men and some non-binary people registered female at birth may undergo a hysterectomy. However, this number has been declining in recent years as coincidentally the rates of trans pregnancy increase. In the past, hysterectomy was motivated by a perceived risk of endometrial cancer, but now it is more common to see an observation schedule with ultrasound recommended. After hysterectomy with or without oophorectomy, trans men may no longer need a GnRH analogue or progesterone.

Around ⅓ of trans men and non-binary people registered female at birth in the UK also undergo genital reconstruction surgery ('lower surgery'). Phalloplasty is the surgical creation of a penis whereby a surgeon harvests one or more "flaps" of skin

and other tissues from a donor site on the body (usually the forearm but sometimes from the lower abdomen or buttocks) and uses it to form a penis.

Metoidioplasty is the surgical creation of a penis using existing genital tissue. It is considered a less-extensive procedure than phalloplasty and is performed after the clitoris has been enlarged through the use of testosterone therapy. Not all trans men and non-binary people registered female at birth will undergo hysterectomy and/or vaginectomy, even if they have opted for a phalloplasty or metoidioplasty.

Trans women

In the UK around ⅔ of trans women will access genital reconstruction surgery. This often takes the form of a vaginoplasty, which creates the potential space of a vagina and moves the prostate anteriorly in doing so. The vaginal canal is most often achieved through the penile inversion method or the less common sigmoid colon graft. Externally, the vulva is often indistinguishable from cisgender female anatomy.

Some people may not opt for vaginoplasty and instead choose to access vulvoplasty (sometimes referred to as shallow-depth or zero-depth vaginoplasty) which creates the appearance of a vulva, but there is no potential space created for a vagina.

After genital surgery, trans women no longer require a GnRH analogue and often need lower doses of oestrogen to reach therapeutic levels. This is because genital surgery for trans women includes the removal of the testes, which lowers the levels of testosterone in the body.

Transition in young people

As per the interim service specification for the NHS Gender Identity Development Service (GIDS), published June 2023, access to GAHT for new referrals will require patients to consent to a research protocol if they are under 18. Those patients already receiving this care from the NHS before the introduction of the research protocol should not need to change protocols.

A person would have to be 18+ to access gender affirming surgery on the NHS, however the reality is that these surgeries typically do not happen until the patient is 20+ due to waiting times and the very few surgical hubs for trans patients in the UK.

Although this stepped care model is the standard for NHS gender services, some people will access medical and surgical transition via private routes due to the significant delays on the NHS gender care pathway.

9. Clinical considerations when caring for transgender patients

WPATH recommends health care professionals evaluate and address medical

conditions that can be exacerbated by lowered endogenous sex hormone concentrations and treatment with exogenous sex hormones for transgender and gender diverse people.

However, transgender patients often face health disparities due to a lack of research and evidence-based guidelines regarding their specific health needs. To address this, important clinical considerations from recent research related to caring for the transgender population are summarised below.

1. Conducting inclusive consultations

Taking medication history

Transgender and non-binary patients may be receiving (prescribed or self-medicating) gender-affirming hormone therapy (GAHT; previously referred to as Cross-Sex Hormone Therapy, CSHT) to produce secondary sex characteristics aligning with their gender identity.

Using a patient-centred approach, clinicians are encouraged to take a proper medication history to note the type, dose, route, and duration of any GAHT as these factors will impact the clinical approach and treatment decisions of trans gender patients.

Inappropriate curiosity

During consultations with transgender and non-binary patients, it is important to make sure that the cause of our enquiry is always known and justifiable. Without this, the individual may feel that they are being subjected to inappropriate curiosity about transgender identity, particularly their sex registered at birth.

Whilst some patients may take this as an opportunity to support and educate the healthcare professional, this should not be assumed of all patients. Many trans patients report this as being an issue that can negatively impact the patient-professional relationship.

To support oneself when conducting a consultation with a trans patient that may have relevance to their sex registered at birth, effort should be made to the patient to describe the logic in doing so, supported by robust research or published guidelines where available.

2. GAHT and pharmacokinetic considerations

Due to the lack of clinical data in the transgender population, clinicians may supplement this with data extrapolated from the general adult population to predict the effect of hormone therapy on other prescribed medications.

Absorption

Emerging research suggests that it may be medically relevant to know the patient's

sex registered at birth due to the potential for sex-related differences in absorption and bioavailability of certain drugs. However, consensus on the impact of this factor for trans patients is still in development.

Distribution

Among transgender women, most studies support associations between oestrogen therapy and decreased lean mass with an increased fat mass and body mass index (BMI). Within transgender men, studies support associations between testosterone therapy and increased lean mass, and although not as consistent, increased BMI and fat mass. No consistent changes in bone mineral density has been noted for either group.

Some reports summarise changes in plasma protein concentrations during hormone therapy however no studies to date have characterised these on tissue or plasma drug binding for any specific medication taken by transgender adults.

Metabolism

Drug-drug interactions can either enhance or inhibit the metabolism of oestrogen and progesterone, leading to an increase or decrease in their levels in the body. Clinicians need to remain vigilant of potential drug-drug interactions. These are often related to drug metabolism by the CYP family of enzymes.

Below is a table highlighting the most common drug-drug interactions and their impact on the levels of hormonal therapy when co-administered. There were no relevant interactions found with GnRH analogues, finasteride, and testosterone.

Interactions between spironolactone with other drugs does not cause significant changes in the drug levels within the body. Instead, it primarily affects electrolyte imbalance, specifically hyperkalemia and reduced blood pressure. Therefore, if feasible, it is advisable to avoid co-administration of spironolactone with other medications that have similar side effects.

Table 1. Brief summary table of alterations in hormonal therapy levels due to drug-drug interactions.

Hormone therapy affected	Confirmed interaction (Moderate - **Severe**)		Theoretical or Anecdotal interaction	
Combined oestrogen and progesterone* **Cyproterone acetate**	↓ **Aprepitant** ↑ **Atazanavir** ↓ **Bosentan** ↓ **Carbamazepine** ↑ **Cobicistat** ↓ **Efavirenz** ↓ **Eslicarbazepine** ↑ Etoricoxib ↓ Etravirine ↓ **Fosaprepitant** ↓ **Fosphenytoin** ↓ **Modafinil** ↓ **Nevirapine**	↓ **Oxcarbazepine** ↓ **Perampanel** ↓ **Phenobarbital** ↓ **Phenytoin** ↓ **Primidone** ↑ Rasagiline ↓ **Rifabutin** ↓ **Rifampicin** ↓ **Ritonavir** ↓ **Rufinamide** ↓ **Topiramate**	↓ Belzutifan ↓ Brigatinib ? Cabozantinib ↓ Carfilzomib ? Cenobamate ↓ Dabrafenib ? Encorafenib ↓ Etravirine ↓ Ivosidenib** ↓ Larotrectinib	↓ Lorlatinib ↓ Lumacaftor ? Neratinib ? Olaparib ↓ Pitolisant ? Ponatinib ↓ Pralsetinib ↓ Sarilumab ↓ St John's Wort ↓ Vemurafenib
Conjugated oestrogens (equine)			↓ Aprepitant ↓ Carbamazepine ↑ Cobicistat ↓ Efavirenz ↓ Etravirine ↓ Fosphenytoin ↓ Lumacaftor ↓ Modafinil ↓ Nevirapine ↓ Perampanel ↓ Phenobarbital	↓ Phenytoin ↓ Primidone ↓ Rifabutin ↓ Rifampicin ↓ Ritonavir ↓ Rufinamide ↓ St John's Wort ↓ Topiramate
Progestogens (Desogestrel***, Levonorgestrel, Norethisterone)	↓ Lamotrigine***		↓ Aprepitant ↓ Carbamazepine ↑ Cobicistat ↓ Efavirenz ↓ Etravirine ↓ Fosphenytoin ↓ Lamotrigine ↓ Lumacaftor ↓ Modafinil ↓ Nevirapine ↓ Perampanel ↓ Phenobarbital	↓ Phenytoin ↓ Primidone ↓ Rifabutin ↓ Rifampicin ↑ Ritonavir ↓ Rufinamide ↓ St John's Wort ↓ Topiramate ↓ Ulipristal

Progestogen (Drospirenone, Medroxyprogesterone, Etonogestrel, Levonorgestrel)	↑ **Atazanavir** ↑ **Berotralstat** ↑ **Clarithromycin** ↑ **Cobicistat** ↑ **Crizotinib** ↑ **Darunavir** ↑ **Diltiazem** ↑ **Dronedarone** ↑ **Erythromycin** ↑ **Fedratinib** ↑ **Fluconazole** ↑ **Fosamprenavir** ↑ **Idelalisib**	↑ **Imatinib** ↑ **Itraconazole** ↑ **Ketoconazole** ↓ Lamotrigine ↑ **Letermovir** ↑ **Lopinavir** ↑ **Netupitant** ↑ **Nilotinib** ↑ **Posaconazole** ↑ **Verapamil** ↑ **Voriconazole**	↓ Aprepitant ↓ Carbamazepine ↑ Cobicistat ↓ Efavirenz ↓ Etravirine ↓ Fosaprepitant ↓ Fosphenytoin ↓ Lumacaftor ↓ Modafinil ↓ Nevirapine ↓ Perampanel ↓ Phenobarbital	↓ Phenytoin ↓ Primidone ↓ Rifabutin ↓ Rifampicin ↑ Ritonavir ↓ Rufinamide ↓ St John's Wort ↓ Topiramate ↓ Ulipristal
Testosterone	↑ Dutasteride**** ↑ Finasteride****		↑ Cobicistat ↓ Efavirenz ↓ Etravirine ↓ Nevirapine ↑ Ritonavir ↓ Somapacitan ↓ Somatrogon ↓ Somatropin ? Tesamorelin	

Legend

↓: Decreases effect of hormone therapy
↑: Increases effect of hormone therapy
?: May alter levels of hormone therapy but directionality is unpredictable, variable or unclear from current research

Severe: Interaction that may result in a life-threatening event or have a permanent detrimental effect.
Moderate: Interaction could cause considerable distress or partially incapacitate a patient; they are unlikely to be life-threatening or result in long-term effects.
Theoretical: Interactions predicted based on sound theoretical considerations. The information may have been derived from in vitro studies or based on the way other members in the same class act.
Anecdotal: Interactions based on either a single case report or a limited number of case reports.

Notes

This table primarily reports data from the British National Formulary. It is recommended that multiple databases are consulted to compare for contrast or consensus on matters related to GAHT-related DDIs. In particular, Stockley's Drug Interactions is recommended.

*

Combined oestrogen and progesterone preparations **decrease** the exposure to Chenodeoxycholic acid, Lamotrigine, Metyrapone, Ulipristal.

Combined oestrogen and progesterone preparations **increase** the effect of Agomelatine, Aminophylline, Anagrelide, Chlorpromazine, Clozapine, Erlotinib, Lomitapide (take 12 hours apart), Loxapine, Melatonin, Olanzapine, Pirfenidone, Riluzole, Roflumilast, Ropinirole, Ropivacaine, Selegiline, Theophylline, Tizanidine, Zolmitriptan.

Combined oestrogen and progesterone preparations oppose the action of Ospemifene and Raloxifene.

**

Manufacturer advises to use alternative hormonal therapies during treatment with, and for at least 28 days after stopping Ivosidenib.

***
Lamotrigine might decrease the effects of Desogestrel and Desogestrel is predicted to increase the exposure to Lamotrigine. Moderate studies have been conducted on Desogestrel while interactions of Lamotrigine and Norethisterone/ Levonorgestrel are theoretical.

**** Testosterone levels are increased by 5-alpha reductase, however, as the drug has poor bioavailability this interaction can positively affect its levels.

Elimination

An accurate assessment of kidney function is important to appropriately dose medications and to monitor the progression and development of medical conditions. Transgender patients with Chronic Kidney Disease (CKD) require special attention to their renal function to appropriately guide hormone therapy and to assess the necessity for renal replacement therapies, dose adjustments, or medications to be stopped.

Research has indicated that transgender individuals undergoing GAHT, experience physiological changes within 6-12 months of commencing hormonal therapy. In transgender men there is a rise in serum creatinine, which is a byproduct of muscle metabolism, deriving from increase in muscle mass, while, transgender women will exhibit the opposite pattern.

Renal function assessment commonly relies on equations like the Cockcroft-Gault (CG) formula provided below:

Cockroft-Gault equation

$$eGRF = \frac{(140 - \text{age}) \times weight \times constant}{serum\ creatinine}$$

Constant = 1.23 for men and 1.04 for women

As shown above, serum creatinine is factored into the equation. However, when it comes to the constant for men and women, there may be confusion on how to account for the degree of physiological changes after starting GAHT.

When considering which constant to use, it is important to consider the length of the GAHT as mentioned above as changes are expected to be visible after a minimum of 6 months.

As an example, if a transgender man has undergone testosterone treatment for more than six months without interruption, the male constant should be employed in the formula.

When assessing renal function in individuals using lower levels of GAHT, as seen in some non-binary people, the CG formula needs careful consideration. Lower levels of GAHT may result in less pronounced changes in muscle mass and fat redistribution. The formula's constants will therefore depend on the type of hormonal regimen the individual is following.

Therefore, the formula should be assessed based on clinical judgement determined by the extent of physiological changes, in order to accommodate diverse scenarios and ensure a comprehensive evaluation.

If an accurate estimation of the renal function is required, there is potential to use a nuclear medicine GFR, however, it is crucial not to delay initiating appropriate care as this could adversely impact the patient's health.

3. Special safety concerns in transgender patients

Cardiovascular diseases (CVD) among transgender adults on GAHT
Existing research in transgender populations, like in cisgender individuals, suggests that CVD risk factors are affected by hormone therapy. Transgender men receiving GAHT might experience worsening of their CVD risk factors, such as increased blood pressure, insulin resistance, and other metabolic dysregulation. For transgender women, extensive literature comparing various routes and formulations of hormonal therapy is scarce which limits knowledge of any associations between GAHT and CVD. Therefore, proper consideration of baseline risk factors (e.g. high blood pressure, smoking, unfavourable lipid levels, high BMI, and diabetes) and the age of first administration of exogenous hormones is strongly recommended due to concern regarding an increased risk for myocardial infarction and stroke. Special considerations should also be applied when prescribing potential cardio-toxic anticancer medicines, for example anthracyclines and tyrosine kinase inhibitors (TKIs).

Thromboembolic risks in transgender women
GAHT has known thromboembolic risk. The incidence of venous thromboembolism (VTE), in trans women can be increased up to 20-fold when the patient is on GAHT.

Transdermal oestrogen formulations are preferred over oral formulations where risk is indicated, as they have demonstrated lower VTE rates. Doses may also be minimised in high risk individuals. Although not usually prescribed in the UK, conjugated oestrogens, e.g. Premarin, have been previously used in GAHT and may continue to be accessed by those self-medicating, however conjugated oestrogens should be avoided as they confer the highest risk.

In cases where there is particularly high VTE risk from the cancer type or location, and/or from the anti-cancer therapy, clinical teams may wish to consider prescribing prophylactic low molecular weight heparin to enable patients to safely continue GAHT. Particularly contraindicated, is the concurrent use of Linalidomide and combined oestrogen and progesterone preparations, which should be avoided and alternative treatments explored.
Risks and benefits can be discussed further with the local haematology team.

Thromboembolic risk in transgender men
Studies suggest that the rate of venous thromboembolism in transgender men on GAHT is comparable to cisgender men using testosterone HRT. Studies in cisgender men have shown a slightly increased VTE risk in the first 6 months of testosterone. Clinical vigilance is therefore advised, with the option to use prophylactic anticoagulation in high-risk individuals.

The Faculty of Sexual and Reproductive Healthcare (FSRH) has published evidence-based recommendations and practice points on the use of hormonal therapies currently available in the UK by transgender patients. Please see the Useful Links section for this resource.

GAHT dosage modulation related to HIV
Where the patient is diagnosed with HIV and is receiving antiretroviral treatment, there may be modifications to their GAHT. For more information on this, see the Useful Links section from www.hiv-druginteractions.org

This reinforces the importance of appropriate terminology and supporting behaviours that can instil trust in the individual to the healthcare professional and lead towards better disclosure of concurrent medically relevant information.

Potential for GAHT to drive hormone receptor positive cancer
There may be instances where a patient is diagnosed with a hormone receptor positive cancer and thus any additional levels of circulating hormones have the potential to drive tumour growth. This is most commonly indicated in breast cancers, but can also include others such as ovarian cancer. In these instances, GAHT is typically paused whilst the tumour is tested, but this can result in opposition from the transgender patient if the reasoning and risk is not explained clearly to them. UCATS can help support healthcare providers and their patients in these instances.

Case Study - Mike, trans man in his 50s
Mike's breast cancer was identified during his top surgery (bilateral mastectomy with masculine chest reconstruction). While he had been on testosterone for four years by the time he was diagnosed with breast cancer, he was taken off his gender affirming hormone therapy until he had his treatment pathway organised. Delays due to the lack of established pathways for patients like Mike, compounded

by the pandemic, resulted in him being off of GAHT for seven months.

Fertility

Some consultations will involve discussions regarding the patient's fertility. Each person, inclusive of their gender identity, is entitled to have this conversation. Yet oftentimes, the information and consenting procedures supporting these consultations can underserve trans people.

For example, many forms will discuss "male sperm" and a "female uterus" which may equate with sex registered at birth, but does not consider transgender people and the way they may identify their bodies. Often, we see that trans patients find the gendering of body parts associated with their sex registered at birth as off-putting, and can become a barrier in communication in a clinical setting.

Alternatively, these terms could be simplified to "sperm" and "uterus" without any sex or gender ascribed to them, facilitating consultations with both cisgender and transgender patients. Work to explore this approach is being undertaken by BOPA.

Some transgender patients receiving gender affirming care may have already had conversations regarding their fertility and its potential preservation. WPATH recommends health care professionals inform and counsel all individuals seeking gender-affirming medical treatment about the options available for fertility preservation prior to initiating puberty suppression and prior to treating with hormone therapy.

However, it should not be assumed these conversations have occurred with all transgender patients receiving GAHT in order to account for the various routes that it is sometimes acquired due to significant delays in gender affirming care on the NHS.

10. Contacting GICs or UCATS

WPATH recommends that health care providers involve professionals from multiple disciplines who are experts in transgender health and in the management of the care required for transgender and gender diverse people.

You may find it necessary to seek further advice from the UK Cancer and Transition Service (UCATS) or the patient's Gender Identity Clinic (GIC) regarding the patient's hormonal therapy, if they are receiving this treatment.

At the time of writing there are 7 adult GICs in England, 1 in Wales, 3 in Scotland and 1 in Northern Ireland. There are also 4 GIC Pilots in England. In the case of patients under 18, care is managed by the Gender Identity Development Service, which is presently undergoing restructure but continues to support eligible patients with GAHT.

The role of the GIC/GIDS is to provide psychological assessment on suitability for hormones and provide endocrinological advice on potential side effects, risks, interactions with other health conditions and suitable preparations.

In most cases, prescribing is done by a GP on recommendation from the GIC under a Shared Care Agreement. This means that there will be several clinicians involved, in addition to the team treating the patient's cancer, who have a responsibility to satisfy themselves that continuing to prescribe hormones is safe.

We recommend that any prescribing of medicines that could affect gender affirming care are discussed with the GIC, with the patient's consent.

A list of services and contact details can be found here:
https://www.nhs.uk/nhs-services/how-to-find-an-nhs-gender-identity-clinic/

Usually it is best to address any correspondence to the core clinician who last assessed the patient, as well as the GIC endocrinology team where applicable.

Some patients may not be under the care of a GIC. The patient may also be accessing gender-affirming care from a private clinic or from outside of the UK. In some cases the patient may be self-medicating. Furthermore, gender identity clinicians may not have a working knowledge of oncology.

For this reason, the UK Cancer and Transition Service (UCATS) was set up to bring together patients and all the clinicians involved in the individual's gender-affirming cancer care. It is currently a monthly virtual clinic and involves multidisciplinary team (MDT) meetings with experts from around the country. Any healthcare professional, or patient, can make a referral.

11. Useful links

UK Cancer and Transition Service (UCATS)
https://www.wearetransplus.co.uk/uk-cancer-and-transition-service/
Or the service can be contacted directly at: chelwest.ucats@nhs.net

General Pharmaceutical Council
Equality Guidance for Pharmacies (2022)
https://www.pharmacyregulation.org/sites/default/files/document/gphc-equality-guidance-for-pharmacies-december-2022_0.pdf

General Pharmaceutical Council: Regulate
Gender identity: pharmaceutical care for children and young people (2023)
https://www.pharmacyregulation.org/regulate/article/gender-identity-pharmaceutical-care-children-and-young-people

The Pharmacists' Defence Association
LGBT+ Pharmacists' Network Position Statement: Support for patients with gender incongruence (including those accessing gender identity services) (2023)
https://www.the-pda.org/wp-content/uploads/LGBT-Network-Gender-Affirming-Care-statement.pdf

The World Professional Association for Transgender Health
Standards of Care 8 (2022)
https://www.wpath.org/publications/soc

www.hiv-druginteractions.org
Hormone therapy for gender affirmation
https://liverpool-hiv-hep.s3.amazonaws.com/prescribing_resources/pdfs/000/000/219/original/Hormone_Chart_2022_Oct.pdf

The Faculty of Sexual and Reproductive Healthcare
Contraceptive Choices and Sexual Health for Transgender and Non-Binary People
https://www.fsrh.org/documents/fsrh-ceu-statement-contraceptive-choices-and-sexual-health-for/

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13. Document control

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