## CONTENTS

01. Approach to Care ........................................................................................................ 4

02. Transgender Health Program Structure and Functions ........................................... 5

03. General Considerations for Hormone Therapy ...................................................... 6

3.1 Initiation of GAHT ..................................................................................................... 7

3.2 Providers of GAHT ................................................................................................... 8

  Medical Provider .......................................................................................................... 8

  Behavioral Health Clinicians ......................................................................................... 9

04. Medical Recommendations Prior to Initiation of GAHT ........................................ 9

  Screening/baseline laboratory testing ........................................................................... 11

05. Hormone Treatment Regimens ............................................................................... 13

  Testosterone Treatment ............................................................................................... 13

  Estrogen and Anti-Androgen Treatment ...................................................................... 17

  Dosing options ............................................................................................................. 22

  Patients on Preexisting GAHT When Entering Care ................................................... 26

    Provider-Prescribed GAHT: .................................................................................... 26

    Self-Prescribed GAHT: ............................................................................................ 26

    GAHT for Nonbinary/Genderqueer Individuals ......................................................... 26

06. Follow-up Care and Monitoring .............................................................................. 27

  Follow Up Visits .......................................................................................................... 27

  Laboratory monitoring by Visit Timelines .................................................................... 29

07. Health Maintenance Care ....................................................................................... 33

  7.1 Mental Health ......................................................................................................... 33

  7.2 Sexual Health and Safety ....................................................................................... 34

  7.3 Cancer Screening .................................................................................................... 35

    7.3.1 Breast/Chest Health ....................................................................................... 35

    7.3.4 Prostate Cancer ............................................................................................. 37

    7.3.5 Cervical Cancer ............................................................................................. 38

    7.3.6 Endometrial Cancer ....................................................................................... 40

    7.3.7 Ovarian Cancer ............................................................................................... 41

  7.4 Unexplained Pelvic Pain ....................................................................................... 41

  7.5 Cardiovascular Health ........................................................................................... 42

  7.6 Diabetes .................................................................................................................. 43

  7.7 Bone Health ............................................................................................................ 44
01. Approach to Care

Fenway Health is a federally qualified community health center providing primary medical care, along with integrated mental health, specialty medical care (obstetrics, podiatry, endocrinology, dermatology), addictions treatment, and complementary services (acupuncture, massage, optometry, dental care, and nutrition counseling). The mission of Fenway Health is to enhance the well-being of the LGBTQIA+ communities and all people in our neighborhoods and beyond through access to the highest quality health care, education, research, and advocacy. As part of this larger mission, the Trans Health Program (THP) seeks to promote and support comprehensive and patient-centered care to transgender, nonbinary, and gender diverse (TGD) people in an environment that is comfortable, safe, and affirming.

The THP operates within a multidisciplinary and integrated health care system to support all departments, programs, and clinical providers at Fenway. The aim is to ensure collaborative, and holistic care of TGD individuals across the health center, and to ensure that access to informed, low barrier gender affirming care and services is available at all touch-points within the health center.

Fenway Health provides preventative, acute, solution-focused, and continuing medical and behavioral health care to all TGD persons, whether or not they pursue hormonal or surgical treatment as part of gender affirmation. Fenway practices an integrated approach to gender affirming care within primary care, maintaining a clinical environment where all primary care providers are trained in gender affirming medicine, with the goals of increasing access to health care, thereby decreasing health disparities for TGD populations. Though not all people seek medical gender affirmation, for many hormonal treatment and surgery play a vital role in the care of individuals with gender dysphoria and/or gender diverse identities. Fenway views hormonal treatment and pre-, peri-, and post-surgical care in the context of, and as a part of, overall primary care. By acknowledging the importance of providing gender affirming care and access to hormone therapy across primary care, and intentionally building skills and knowledge in this field, primary care providers have the unique ability to decrease barriers to care, increase access, and engage TGD community in comprehensive, holistic health care.

Fenway Health seeks to promote the wellbeing of all its patients, regardless of gender identity. Gender diversity should not be pathologized, and we acknowledge that gender diversity is not synonymous with a clinical diagnosis of gender dysphoria. Not all patients with a diverse gender identity will necessarily experience a sense of gender dysphoria that might impair their functioning or compel them to seek treatment that specifically addresses their gender. There is a spectrum of gender identities beyond the Western cultural customs of binary gender norms, and we support the varied and evolving expression of each person’s individual identity. Fenway Health and the THP seek to support individuals with their own personal exploration of gender and with the decisions they make regarding their individual treatment needs. Gender identity evolves and develops across the lifespan of all individuals, and this developmental process may not follow a linear progression along any set gender affirmation or expression pathway. We collaborate with each patient to create treatment plans that are responsive to
particular and presenting concerns of the person while ensuring a professional level of competence, sensitivity, and responsibility to accepted standards of ethical and scientifically grounded care for medical and behavioral health professionals.

The Fenway Health protocols for the Provision of Gender Affirming Medical Care and the Medical Care of Gender Diverse Children and Adolescents (hereafter Protocols) were developed after careful and extensive review of current research and in consultation with other medical and mental health professionals who have demonstrated experience and expertise working with TGD persons. These Protocols are informed by the WPATH Standards of Care and by the protocols of other facilities that specialize in the medical and behavioral health care of TGD persons. Fenway Health’s Protocols strive to reflect current knowledge and research on transgender health, while acknowledging that the data and research are limited, often scientifically imperfect, and continuously evolving. In addition, no medications or other treatments are currently approved by the Food and Drug Administration (FDA) for the purposes of gender affirmation. Given this reality, these protocols should not be viewed as a rigid or exclusive approach to gender affirming care, but as a dynamic document that continues to be updated and revised as knowledge, research, and experience in this field progresses.

02. Transgender Health Program Structure and Functions

The Transgender Health Program (THP) Medical Director, the THP Manager, and the THP Patient Advocate lead the Transgender Health Program. The THP staff conducts Trans Clinical Team (TCT) meetings for the medical and behavioral health departments with the goal of providing on-going education, training, and case consultations for new and established providers. These meetings consist of clinical case conference meetings and monthly didactic presentations on various topics within the field. THP staff additionally provide consultations on demand and regularly scheduled educational seminars to all Fenway staff. The THP also creates internal and external facing educational documents and pamphlets for the support of Fenway staff and our patients. The THP Patient Advocate provides on-going practical support to Fenway providers, nurses, case managers, BHS staff, and Patient Services staff, as well as ongoing training in working with trans and gender diverse individuals. The THP Patient Advocate also provides direct health navigation and advocacy supports for all TGD community members in the geographic area as needed and when appropriate.

Additional services provided for the community by the THP include:

- All-access drop-in clinics for support with self-advocacy issues, resource provision, referrals and recommendations for outside supports or services
- Recurring series of public information sessions on a variety of legal, health, and wellness topics with a specific focus on TGD experiences and needs
- Free, drop-in support groups designed to support members of the TGD community and their loved ones
03. General Considerations for Hormone Therapy

Gender affirmation for many TGD individuals is a multidimensional process involving aspects of social, emotional, and physical affirmation to decrease internal distress. Often the goal of gender-affirming hormone therapy (GAHT) for physical affirmation is to create the internal hormone environment that best aligns with one’s gender identity, with the aim of achieving physical characteristics that are culturally accepted and expected as a presentation of that gender. The TGD population is a diverse group of individuals, and therefore creating a low-barrier, welcoming environment to discuss nuances of each patients’ needs and goals for gender-affirming care can allow for an individualized approach to treatment, health education, and support. Several studies have shown significant reductions in mental health co-morbidities (depression, suicidality, substance use) and an overall improvement in the quality of life with the ability to access GAHT. As such, for many individuals, access to GAHT is an important and necessary part of their process.

Hormonal and other treatments for gender affirmation may have both desired and undesired physical and psychological effects, some with potential negative health implications, while many others may be lifesaving. Discussing realistic expectations, risks, and benefits is in an important part of medical gender affirmation and should focus on empowering patients to make informed decisions. This is best achieved when providers understand a patient’s goals and priorities.

Fenway provides gender affirming hormone therapy (GAHT) through an informed consent model. Informed consent is the conversation between the patient and medical or behavioral health clinician during which there is a thorough explanation of the benefits, risks, and realistic expectations for the full range of treatment options available to the patient. There is no one way to provide informed consent; rather, it should be individualized to a patients’ cognitive and emotional needs, age, and cultural context. By establishing clear expectations, evidenced based knowledge and recommendations, as well as limitations of medications and research, Fenway allows for patients to assess beneficence of these options and consent for treatment. We respect the individual’s sense of self and agency. Patients will be given the opportunity to discuss how these expectations, known outcomes, and unknowns may align with their current and future goals and expectations. Fenway also recognizes that identities, goals, health risks, and general safety may change throughout the time in care, and therefore a flexible approach to treatment is imperative. We acknowledge the importance of behavioral health care for TGD patients who may experience gender dysphoria and the effects of stigmatization and discrimination. For some patients, mental health care may be an integral and recommended part of their gender affirmation process. Therapeutic and/or supportive mental health care and the provision of GAHT will be achieved with a patient-centered approach that balances individual needs within a harm reduction philosophy.

Fenway also recognizes that caring for TGD patients is more than just the provision of GAHT and gender-affirming surgical procedures. Fenway Health is committed to providing comprehensive primary preventive medical care and general mental health services with the knowledge and understanding of the unique needs and challenges of TGD people.
### 3.1 Initiation of GAHT

Those interested in gender affirming hormone therapy (GAHT) under these adult protocols must be 18 years old, and demonstrate understanding of the short- and long-term expectations of the medications. (NOTE: Fenway Health provides care for all individuals who are seeking gender affirming medical care regardless of age or guardianship status. Treatment protocols for minors are found in a separate protocol entitled: Medical Care for Gender Diverse Youth and Adolescents.) Patients verbally consent to treatment when they feel they have a thorough understanding of the risks and benefits and are ready to move forward with medical treatment. Treatment for adults with legal guardians assigned will be arranged on an individual basis in consultation with all guardians and stakeholders necessary in the person’s care.

Hormone treatment results in partially reversible effects. The use of medications for GAHT is considered “off-label.” Prior to initiating GAHT, patients should be able to demonstrate understanding of the knowns and unknown of hormone therapy, realistic expectations, and the largely unpredictable responses of each individual to hormone therapy. The age at which therapy is started, body habitus, and genetics likely play a role in the degree and speed at which changes may occur. These aspects also tend to influence the potential for risk factors from GAHT. The clinician and patient should review the physical and behavioral changes that are expected, limitations of hormone therapy, and the general timeline of these changes to guide patient expectations. It is also necessary to discuss the potential risks of hormone therapy on the body that are known, as well as the unknowns that still exist in this field regarding these medications and their outcomes. This information should be discussed in the context of the individual’s goals and how these may, or may not, affirm their gender and meet their needs.

For some patients, assessment for appropriateness of hormone therapy is straightforward, while for others, more time may be needed to understand goals or to ensure support for ongoing medical, behavioral health, or social issues. Fenway follows WPATH’s considerations for assessing appropriateness of hormone therapy, which consisted of the following four criteria during the assessment:

1. Persistent, well-documented gender dysphoria (of at least 6 months as assessed by either a medical or behavioral health professional)
2. Capacity to make a fully informed decision and consent to treatment
3. Age of majority in a given country (if considered a minor, please refer to Medical Care of Gender Diverse Children and Adolescents for information specific to youth and adolescents)
4. If significant medical or mental health concerns are present, they should be reasonably well controlled.

We recognize that the presence of co-occurring medical or mental health conditions should not necessarily contraindicate or delay access to GAHT. If an underlying medical or mental health condition is both poorly controlled and presents a risk specifically in
the setting of GAHT, it is recommended that the condition is stabilized before initiating hormone therapy. This recommendation requires nuanced decision-making and an individualized approach, which should include assessment of the patient’s health history, baseline level of functioning, and current level of functioning. Finally, the role of the patient’s gender dysphoria or the impact of hormone therapy use on this health condition should be assessed to determine the potential positive or negative impact of starting or continuing hormone therapy.

Fenway clinicians realized that the decision to deny or delay care should not be taken lightly, as gender affirming hormones are considered medically necessary treatment. We recognize that in most cases, GAHT has significant positive protective mental health benefits, and denial of hormone therapy can worsen depression, anxiety, and suicidality. Additionally, blocking access to gender-affirming treatment can lead to procurement of non-medically supervised hormones and disengagement from medical care. Fenway clinicians are trained to practice gender-affirming care with a harm reduction philosophy to minimize adverse effects of denial of care and to promote patient retainment in medical care. Whenever possible, an attempt to stabilize a condition should be made while initiating GAHT.

3.2 Providers of GAHT

MEDICAL PROVIDER

The provision of gender affirming care is not a specialty service. Gender identity is an aspect of all humans that should be respected and acknowledged in any medical department, regardless of their focus. Competency in providing GAHT or supporting its use, is not a skill set specific to any one discipline, but rather should be integrated into all aspects of a patient’s care plan and care team. Access to gender affirming support, education, and hormones is specifically imperative within primary care. The aim of primary care is to improve the overall health and wellbeing of an individual through acute and preventive care over a life time. Providing gender affirming care within primary care is the ideal environment to build patient/provider trust and rapport, create a care plan, and provide a safe environment for self-affirmation, realization, and acceptance over the course of care. Additionally, primary care is often most equipped with supporting staff, such as patient advocates, behavioral health clinicians, case workers, and other care team members to best support the specific challenges and barriers that TGD populations experience.

At Fenway all medical providers are trained and expected to provide gender affirming care from initial hire and throughout their time at the health center. Medical providers are expected to maintain knowledge and competency over time, acknowledging the dynamic nature of this field. The Trans Health Program and the Medical Department hold regular trainings, CME activities, and internal consultation services to promote on-going education and the most up-to-date evidenced based care.
BEHAVIORAL HEALTH CLINICIANS

As stated above, gender affirming care and support is not a specialty service. All behavioral health clinicians may seek training and experience to best support their TGD patients. Behavioral health clinicians, like medical providers, can increase access to behavioral health services by building competency working with TGD patients and understanding the unique challenges that face this population and how to provide a supportive and affirming environment for all of their patients.

At Fenway, all behavioral health clinicians are trained in gender affirming care and are expected to care and support all patients within our medical community regardless of gender identity. Additionally, behavioral health clinicians are trained to assess for readiness of surgical gender affirming procedures and to write letters supporting these services, as often required by insurance for coverage.

Behavioral health services at Fenway are not used for gender assessments or clearance to start hormones. Our BH Department provides a patient-centered approach to supporting gender affirmation through individual therapy, therapeutic groups and peer support groups, as well as provision of supportive letters for other affirming services.

04. Medical Recommendations Prior to Initiation of GAHT

Prior to initiating GAHT, the clinician must attain a relevant medical, behavioral health, and social history, which is intended to guide the safe and effective care for each individual. This history taking can occur in the setting of a complete physical exam, or shorter consultative visits. If a medical provider outside of Fenway has already attained this information, this history can be requested with the patient’s consent and reviewed by the prescribing provider prior to the start of treatment.

Assessment for medical safety should occur in the setting of underlying medical issues and family health history. Prior to initiating GAHT, baseline laboratory tests and a physical exam may be warranted depending on the individual’s underlying medical conditions, age, and family medical history. A behavioral health history should also be performed to assess the patient’s need for supportive referrals, ensure mental health conditions are relatively stable, and to assess that the individual can consent to treatment. Additionally, a social history can illuminate safety concerns or supportive services that individual may need as they initiate treatment and beyond.

Obtaining a gender narrative or history of gender awareness is not required, but can help contextualize a patient’s experience and goals to help guide treatment and create a clearer understanding between the patient and clinician on how to provide the best individualized care.

Obtaining an anatomic inventory, or list of organs a patient retains or has had surgically removed, can be essential in providing appropriate ongoing preventive care services.
<table>
<thead>
<tr>
<th>Section</th>
<th>Information</th>
</tr>
</thead>
</table>
| Gender Narrative         | • History of experienced gender awareness and the development, exploration, acceptance/rejection, identification, and persistence of that gender  
                           • Any symptoms of gender dysphoria  
                           • Goals for non-medical affirmation of gender, GAHT, or other gender-affirming medical care |
| Medical History          | • Personal history of coronary artery or cerebrovascular disease, arterial or venous thromboembolism, hypertension, diabetes, hormone-sensitive cancer, polycythemia, pituitary adenoma, liver disease, HIV infection, and other sexually transmitted infections  
                           • Current specialists for any underlying medical issues  
                           • Use of current or past prescribed and unprescribed hormone use, as well as any history of surgical procedures, including body modifications or injectable silicone use |
| Behavioral Health History| • History of major depression or bipolar disorder, psychosis, suicidality, impulse control disorder, disordered eating patterns, and substance use and abuse  
                           • Current behavioral health providers and any past or present psychiatric medications  
                           • Psychiatric hospitalizations  
                           • Past or present sexual, physical, or emotional abuse or trauma (it may not be necessary or possible to explore this fully in the initial assessment)  
                           • Current or previous suicidality or self-injurious behavior |
| Family History           | • Family history of any cancer, cardiovascular disease, diabetes, or blood clotting disorders |
| Social History           | • Family, chosen family, friend support, rejection, acceptance  
                           • Cultural influences that may affect access to care or acceptance by community — religion, ethnicity, age, race, socioeconomic status, etc.  
                           • Supports at work or school  
                           • Community involvement, TGD peer support  
                           • Sexual history, sexual orientation, safety |
Capturing gender-affirming surgical procedures that include the removal of breasts or chest tissue, cervices, testicles, and other organs can guide the most accurate recommendations and communication with patients around cancer screening, fertility options, contraception needs, and other life-long considerations. Fenway has an Organ Inventory form in the electronic medical record (EMR), which should be utilized for each patient, regardless of their gender identity or use of GAHT.

A sexual history should be taken with a trauma-informed approach. Patients should first be asked if a discussion around sexual health is welcomed. If appropriate to proceed with this questioning, it is essential to be transparent about why these questions are being asked and to acknowledge that sexual health is an important aspect of an individual's overall health and wellbeing. Providers should be flexible with the timing of this history taking and follow the individual patient’s lead for when to proceed with questioning and when not appropriate or safe for the patient. Similarly, chest and genital exam screenings may be difficult for some patients who are dysphoric or who do not identify with certain parts of their bodies. Providers should be clear with patients on a plan for physical exam and assess appropriate timing, ensure the patient consents to the exam, and verbalize patient autonomy throughout the process. Declining a chest and/or genital exam should not be considered a reason to deny access to GAHT.

**SCREENING/BASELINE LABORATORY TESTING**

Baseline laboratory monitoring may be recommended based on patient age, underlying medical history, family history and the hormonal or ancillary medications being prescribed.

<table>
<thead>
<tr>
<th>LABS</th>
<th>BASELINE</th>
<th>ADDITIONAL COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total testosterone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Lipids</td>
<td>X</td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
<tr>
<td>Glucose or A1c</td>
<td>X</td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
</tbody>
</table>

- Urine HCG if patient is unsure of pregnancy status and pregnancy is possible
- Baseline serum total testosterone if history and exam suggest an androgenizing condition, and if this information would impact management
FOR THOSE INITIATING ESTROGEN AND ANTIANDROGEN TREATMENT

<table>
<thead>
<tr>
<th>LABS</th>
<th>BASELINE</th>
<th>ADDITIONAL COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total testosterone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BUN, Cr, Potassium</td>
<td>X</td>
<td>only necessary at baseline if initiating spironolactone</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
<tr>
<td>Glucose or A1c</td>
<td></td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
<tr>
<td>Prolactin</td>
<td></td>
<td>only if symptoms of hyperprolactinemia or on medications known to cause hyperprolactinemia (i.e. anti-psychotics)</td>
</tr>
</tbody>
</table>

- Consider liver function tests if patient will be taking oral estrogen and has a history or concern for underlying liver disease or dysfunction
- Consider liver function tests if patient will be using a GnRH agonist or bicalutamide as an androgen blocker
- Baseline testosterone level is generally not necessary and will not impact hormone treatment. However, consider in individuals if history and exam suggest hypogonadism, as this may allow for lower doses of anti-androgen

Evaluation by an endocrinologist is not necessary to begin GAHT. However, during the primary care assessment if the history or physical exam reveals the need for a specialist consult for further evaluation of an underlying or new medical condition, a referral may be recommended prior to initiation of GAHT. It can be important for the primary care team to collaborate with the specialist on safest and best options for long-term health and wellness, always centered on the patient’s goals and quality of life.

Patients should understand that monitoring laboratory tests will be recommended throughout the course of therapy, and that they will be expected to maintain regular follow up visits, especially during the first year of hormone treatment. Providers will discuss these expectations with their patients under a harm reduction perspective, understanding that some individuals may face significant barriers to care (financial, transportation, safety) by requiring lab testing or regular in-person visits. A safe but flexible patient-centered approach is recommended.

Finally, for research and quality assurance purposes at Fenway, providers in all departments throughout the clinic are expected to add the chart marker “THP” (for Trans
Health Program) to the EMR patient Problem List for anyone who identifies as gender diverse, regardless of GAHT use. This marker is not linked to an ICD10 code, but is used for internal purposes only to track our TGD population demographics, use of services, and quality assurance measures across our populations.

05. Hormone Treatment Regimens

Before starting GAHT, the patient and provider should have thoroughly completed the informed consent process to both parties’ satisfaction. The medical provider should create care options around the individual patient’s goals, risk factors, and needs to the extent that is safe and possible. It is also important for both the medical provider and patient to demonstrate flexibility in the care plan, as outcomes are not always predictable, goals can change, and barriers can arise (loss of insurance or denial of coverage, transportation, medication side effects, etc.).

In regards to discussion of hormone therapy, Fenway advocates to reject the rigid concepts of binary identities, and encourages clinicians to move away from classifying hormones as “masculinizing” or “feminizing” and instead refer to hormones themselves—testosterone, estrogen, androgen-blocker — and their known physical effects. In this way, clinicians can be specific about the effects of the hormones without tying physical traits or body characteristics to a gender.

TESTOSTERONE TREATMENT

Testosterone is the standard medication used to lower the pitch of the voice, increase facial and body hair, redistribute fat from the hips and buttocks to the abdomen, and increase muscle mass. Testosterone alone is effective at suppressing the body’s production of estrogen and thereby suppressing many of its effects on the body, one effect of this being the cessation of menses in many individuals. There are several options for administration of testosterone, including injectables, transdermal gels or patches, and implantable long-acting pellets. Choosing which formulation is best often depends on patient preference, ability to self-inject, risks of medication transfer to others (specific to transdermal gels), response to hormone therapy, insurance coverage, and cost.

Injectable Testosterone Formulations

The most common form of testosterone are injectables, due to their low cost and ability to increase testosterone quickly and efficiently. Testosterone can be injected subcutaneously (SC) or intramuscularly (IM).
### INJECTABLES

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Testosterone cypionate or Testosterone enanthate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Injected weekly or every two weeks, IM or SC</td>
</tr>
</tbody>
</table>

**Additional comments**

- Dose recommendations are the same whether using IM or SC injections. SC injections use smaller needles (both in length and gauge) than IM, and tend to be less painful. IM injections may be preferred or necessary for larger volumes.\textsuperscript{11,14}
- Biweekly dosing reduces the number of injections, but leads to wider fluctuations in testosterone levels which can be uncomfortable for some patients. Weekly dosing may be a better choice for those concerned about the impact of fluctuating hormone levels on mood or other medical conditions.
- Testosterone cypionate comes compounded in cottonseed oil, where testosterone enanthate is most commonly compounded in sesame oil. Dermatitis at the injection site as a result of a mild allergy to the compounding oil can occur and may dictate a need to change from one formulation to another. However, pre-dosing with Benadryl is sometimes enough to counter any mild reaction.

---

### Transdermal Testosterone Formulations

Transdermal testosterone is dosed daily and therefore may provide steadier serum (blood) testosterone levels, which is considered similar to physiologic fluctuations of testosterone. Consider starting on topical formulations especially if there are concerns about the effects of significant fluctuations in hormone levels. As opposed to injectable formulations transdermal testosterone does not lead to high peaks in serum levels and, as a result, physical changes can be slightly slower and more gradual to occur. Additionally, daily dosing can also allow for quick dose adjustments, discontinuation of therapy, and overall more autonomy over administration and dosing. These qualities of transdermal testosterone lend itself well to those who desire more gradual changes or control over their hormone therapy.

### PATCHES

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Androderm patch</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>New patch(es) applied daily</td>
</tr>
</tbody>
</table>

**Additional comments**

- Patches are known to commonly cause localized skin irritation. Not recommended for patients known to have sensitive skin.\textsuperscript{17}
## GELS

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Androgel packets, Androgel actuated pump, Testim tubes, testosterone underarm solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Applied daily</td>
</tr>
</tbody>
</table>

### Additional comments
- Patients must use caution in avoiding skin to skin contact at application area(s) with partners, children, or pets until the medication is completely absorbed. Hands should be washed immediately after application. If skin to skin contact is anticipated, the area should be washed with soap and water or covered. It is advised to wait at least 2 hours after application before bathing or showering.  
- Recommended application site is at upper arms and shoulders.

## Long-Acting Testosterone Formulations

Long-acting formulations can be good options for those who find regular injections difficult and who are not candidates for transdermal formulations. These injections and implantable pellets may provide more consistent levels of testosterone over longer periods of time. They tend to be higher cost and need to be administered by a medical professional in the clinic. Typically, long-acting formulations are recommended only after other methods have been tried.

### IMPLANTABLE PELLETS

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Testopel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Implanted every 3 to 4 months.</td>
</tr>
</tbody>
</table>

### Additional comments
- Requires a minor surgical procedure to implant pellets in the subdermal space at the upper, outer area of the buttock.
- It is recommended that individuals have been on another form of testosterone prior to initiating Testopel to ensure testosterone is tolerated and affirming.
LONG ACTING INJECTABLES

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Aveed (testosterone undecanoate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Initial injection, injection at 4 weeks, then injections every 10 weeks thereafter.</td>
</tr>
</tbody>
</table>
| Additional comments | • Rare, but potential adverse side effect of pulmonary oil microembolism and/or anaphylaxis following injection, therefore patients must remain in the clinic for 30min following injections for observation.  
  • Due to these unique risks, the FDA has approved this medication only under a restricted prescribing scheme. |

Oral testosterone formulations

An oral testosterone undecanoate option was FDA approved in the US in 2019. This option provides a nice alternative to injections, gels, or even the long-acting formulations which require administration by a medical professional. The downside of oral testosterone undecanoate is that it is newly FDA approved and without any efficacy or safety studies specifically with TGD individuals to date. This medication does show 87% efficacy in cisgender men with hypogonadism, but it is unclear if this medication will be as effective in trans and gender diverse individuals who inevitably will have lower, or no, baseline testosterone on which to build levels into the physiologic cisgender male range.  

ORAL

<table>
<thead>
<tr>
<th>Medication names</th>
<th>testosterone undecanoate capsules (Jatenzo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Twice daily dosing</td>
</tr>
</tbody>
</table>
| Additional comments | • Jatenzo has a black box warning for risk of elevated blood pressure while taking this medication. It is recommended to monitor blood pressure closely in the first several months of use  
  • There does not appear to be any specific or significant risk of hepatotoxicity or transaminitis with this oral formulation, as opposed to risks seen with oral methylated testosterone  
  • Based on the recent approval of this medication, no generic alternative, and little information of effectiveness in TGD populations, this medication may be expensive and difficult to obtain through prior authorization |
Suppression of Menses

Some patients may desire or are recommended additional medications to reduce symptoms of dysphoria, such as suppression of menses when testosterone and its effects are not desired. In these cases, hormonal medications — those in the contraceptive class — can be used to reduce or stop menstrual bleeding. Additionally, these medications may also be used as birth control when requested and warranted for any patient with reproductive potential, as testosterone itself does not reliably prevent pregnancy.(19)

ESTROGEN AND ANTI-ANDROGEN TREATMENT

Estrogen can result in softening of the skin, decreased muscle mass, breast growth, slowing of androgenic hair loss, and fat redistribution to the hips and buttocks. Estrogen can suppress testosterone and its effects, but estrogen alone may not be enough to suppress testosterone sufficiently for some individuals. Androgen blockers — or anti-androgen therapy — are medications that can further suppress the body’s production or response to testosterone and allow the effects of estrogen to be more apparent.

Estrogen Therapy

17ß-estradiol, more commonly known as estradiol, is the recommended medication for GAHT, as this is the bio-identical form of estrogen and observed to have the lowest risk profile, while also being quite effective.20,21 Much like testosterone, there are several options for administration, and the choice is typically based on patient preference, accessibility, effectiveness, cost, and individual safety considerations.

Oral Estrogen Formulations

Oral estradiol is dosed daily and therefore provides steady levels of estrogen in the body. This formulation is relatively cheap, accessible, and easy to administer.
**ORAL**

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Estradiol tablets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>By mouth daily</td>
</tr>
</tbody>
</table>

**Additional comments**

- Some dissolve these tablets under the tongue, called sublingual (SL) dosing. The theory is that SL dosing would allow estradiol to bypass the liver and avoid the metabolism of the medication in this way. However, this is not evidence-based and there is no data to support that SL dosing is any safer or more beneficial than swallowing the tablets. The amount absorbed under the tongue is likely to be variable and unpredictable. The benefits versus risks of this dosing method are largely unknown.
- There may be pharmacokinetic differences in serum levels produced by oral vs sublingual dosing of the estradiol, but the average serum levels throughout the day are likely the same.\(^{22}\)

**Transdermal Estrogen Formulations**

Transdermal estradiol appears to be the safest formulation from a thromboembolic standpoint, with documented decreased risk of blood clots, strokes when compared to other formulations. (Additionally, estradiol patches and gels show little impact on lipids (cholesterol), which makes transdermal formulations ideal for those with higher-than-average cardiovascular risk, such as patients who are hypertensive, diabetic, or smokers.\(^{23-26}\) Transdermal formulations are also dosed daily, thereby providing the benefit of steady levels, as well as ease of use.

**PATCHES**

<table>
<thead>
<tr>
<th>Medication names</th>
<th>estradiol patches</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Patch(es) applied once or twice a week, depending on the brand.</td>
</tr>
</tbody>
</table>

**Additional comments**

- Patches formulated for twice weekly use may be preferable for patients for whom adhesiveness is an issue.

**GELS**

<table>
<thead>
<tr>
<th>Medication names</th>
<th>estradiol gel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Applied daily</td>
</tr>
</tbody>
</table>

**Additional comments**

- May be more expensive than other formulations.
- Less likely to cause a skin reaction (no adhesive as with the patch).
Injectable Estrogen Formulations

Injectable estradiol is typically dosed intramuscularly (IM) every 2 weeks, though dosing weekly with smaller amounts is possible, with the benefit of decreasing the fluctuations between doses. The peak levels that occur just after dosing can feel affirming for some, and others have felt these may also produce more rapid physical changes. However, there is no evidence to suggest that higher levels produce better or quicker results. Some avoid injectable formulations due to needlephobia, the inconvenience and time of injections (whether self-injecting or by a medical professional), and the wider fluctuations in hormone levels from dose to dose.

### Injectables

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Frequency</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>estradiol valerate</td>
<td>Injected every week or every 2 weeks IM.</td>
<td>Injectable estrogens have few applications outside of their use in gender affirmation, resulting in periodic shortages from the manufacturer and/or difficulty obtaining injectable estradiol. These shortages are likely to continue, and those with concerns about this may consider topical or oral formulations instead.</td>
</tr>
<tr>
<td>estradiol cypionate</td>
<td>Injected every 2 weeks IM.</td>
<td>If switching from the valerate to the cypionate formulation, there is a dose adjustment necessary. The dosing of estradiol cypionate should be lowered to about 1/3-1/4 of the valerate dose. Estradiol cypionate tends to produce a lower, later, and longer peak level when compared to estradiol valerate, but the average levels in the blood, and effects on the body, should be the same.</td>
</tr>
</tbody>
</table>

Anti-Androgen Therapy

Androgen blockers are medications used to suppress the production or response of the body to one’s own, or endogenous, testosterone. By suppressing endogenous testosterone, androgen blockers allow the effects of estrogen to be more apparent. Estrogen alone can suppress testosterone, but for some estrogen alone may not be enough to suppress testosterone sufficiently. In these cases individuals may request or be recommended these additional medication options.
<table>
<thead>
<tr>
<th>Medication name</th>
<th>spironolactone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>By mouth once or twice daily</td>
</tr>
</tbody>
</table>
| Additional comments | • A potassium-sparing diuretic that can directly inhibit testosterone production and its effects, as well as potentially having its own small estrogenic effect.  
• Those who are smaller and thinner, have lower blood pressure, are on certain blood pressure medications, and/or have underlying kidney disease may be at increased risk of experiencing adverse side effects.  
• This is currently the anti-androgen of choice in the United States |

<table>
<thead>
<tr>
<th>Medication names</th>
<th>finasteride, dutasteride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>By mouth once daily</td>
</tr>
</tbody>
</table>
| Additional comments | • Blocks the conversion of testosterone to its more potent form, DHT. It does not inhibit the production of testosterone and therefore will not lower serum testosterone levels.  
• May be most effective for those experiencing unwanted hair loss, significant facial hair, or those who are unable to tolerate higher doses of spironolactone |

<table>
<thead>
<tr>
<th>Medication name</th>
<th>bicalutamide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>By mouth once daily</td>
</tr>
</tbody>
</table>
| Additional comments | • A nonsteroidal androgen blocker that works by competitively blocking the androgen receptor. Bicalutamide does not suppress testosterone itself, but blocks its ability to bind to the receptor, and therefore its effects on the body  
• Bicalutamide can have indirect estrogenic effects, such as increased breast growth, due to increased serum testosterone levels resulting in aromatization to estrogen, which would be a desired effect when used for gender affirming care.  
• Bicalutamide has a rare, but severe potential side effect of fulminant hepatitis. There are only several documented cases worldwide. Though uncommon, fulminant hepatitis can result in death  
• Bicalutamide can be used for GAHT, but there are very few studies examining its use and the relative risk/benefit for this purpose. Because of reported cases of fulminant hepatitis, consensus is that its use in gender affirming hormonal regimen should be carefully considered, used only after alternative options have been trialed or offered, and an in-depth discussion of these potential risks have been had. |
**Progesterone Therapy**

The benefit of progestins for gender affirmation is not well studied. Some patients and medical providers report progesterone may help improve breast development, promote improvement in mood and libido, and have other positive benefits. However, progesterone has also been known to cause weight gain, fatigue, irritability and negative mood changes.\(^{29-31}\) Progesterone is part of a cisgender female’s hormonal makeup, and may be desired on this basis as part of a patient’s gender affirming hormone therapy. It is important to weigh the benefits vs potential risks of starting progesterone or staying on progesterone long-term.

Additionally, progesterone has been shown to play a role in suppressing testosterone production, which supports its use as another, or alternative, anti-androgen when needed.\(^{32}\) Estrogen alone or estrogen and spironolactone are not effective in adequately suppressing testosterone.

There is no evidence to suggest that using progesterone in the context of GAHT is harmful, however there is little safety data available for its role in this care. General concerns with prescribing progesterone with estrogen arose out of the Women’s Health Initiative (WHI) studies, which showed a modest increased incidence of cardiovascular events and breast cancer when taking these hormones.\(^{33}\) However, these results should not necessarily be extrapolated to assume the same risk when used for gender affirming care. The WHI studies were done with older cisgender females, some more than 10 years post-menopausal, who were taking conjugated equine estrogen and medroxyprogesterone – both of these medications now known to be associated with elevated rates of venous thromboembolic events over bioidentical hormone replacement options.\(^{34,35}\) Additionally, in the setting of gender affirming care, patients tend to be younger overall and it is recommended to use micronized progesterone and 17-b estradiol. Therefore, for use in gender affirming care, it seems that the benefits may outweigh any perceived risks.

### INJECTABLES

<table>
<thead>
<tr>
<th>Medication names</th>
<th>GnRH agonists (leuprolide, triptorelin)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Injected monthly, every 3 months, or every 6 months depending on the medication and formulation. In most cases, this injection is done by a medical provider.</td>
</tr>
</tbody>
</table>
| **Additional comments** | • Decreases one’s own production of sex hormones, and is used for the purpose of blocking gonadal (testicular or ovarian) function. In youth, this can also reversibly block pubertal development prior to starting on gender-affirming hormone therapy.  
  • GnRH agonists can and should be an option for some adults as part of a hormone therapy regimen, but it may be cost prohibitive. |
Micronized progesterone (Prometrium) is the bio-identical formulation and appears to be the safest option in terms of cardiovascular health risks. In older individuals and those with higher than average cardiovascular risk, it is recommended to counsel patients on potential risks and lack of safety data.

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Frequency</th>
<th>Additional comments</th>
</tr>
</thead>
</table>
| Micronized Progesterone | By mouth once daily, or cyclical dosing (10 days every month) | • Some patients may prefer cyclic dosing as its effects may mimic a menstrual cycle, which can be affirming for some. However, others may find the hormonal fluctuations with cyclic dosing troubling and may prefer to take this medication daily.  
• Progesterone’s role in breast development has yet to be proven. Reported increases in breast size seem most likely due to general weight gain and fat deposition in the breasts, and not the direct effect of progesterone on the breast tissue itself. So far, there is no evidence to show any specific benefit (or lack of benefit) regarding progesterone’s effect on breast development. |

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Frequency</th>
<th>Additional comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medroxyprogesterone Acetate, MPA</td>
<td>By mouth once daily or injected every 3 months (Depo Provera)</td>
<td>• Medroxyprogesterone has been shown to have a slightly higher risk of side effects than micronized progesterone — MPA is associated with bone loss in cisgender women, as well as mood changes (irritability, depression). There is also suggestion that MPA may pose in increased risk of blood clotting events as compared to the bio-identical micronized progesterone, but this needs to be studied further. The 3-month injectable dosing may be beneficial given its ease, but the risks may outweigh the benefits in many individuals.</td>
</tr>
</tbody>
</table>

**Dosing Options**

Please note that these dosing recommendations reflect a more binary approach to care and treatment goals. Consider alternative, flexible dosing based on patient goals through safe and informed decision making with the patient.
### Dosage for Testosterone

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Medication Name</th>
<th>Dose Frequency</th>
<th>Low Dose</th>
<th>Common Dose</th>
<th>Max Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injectable</td>
<td>Testosterone cypionate or enanthate</td>
<td>Weekly or every 2 weeks</td>
<td>25-50mg</td>
<td>80-100mg</td>
<td>100-125mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*If dosing every 2 weeks, double the dose as listed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transdermal</td>
<td>Testosterone patch</td>
<td>Daily application</td>
<td>2mg</td>
<td>4mg</td>
<td>8mg</td>
</tr>
<tr>
<td></td>
<td>Testosterone gel 1%</td>
<td>Daily application</td>
<td>12.5-25mg</td>
<td>50mg</td>
<td>100mg</td>
</tr>
<tr>
<td></td>
<td>Testosterone gel 1.62%</td>
<td>Daily application</td>
<td>20.25mg</td>
<td>40.5-60.75mg</td>
<td>81-101.25mg</td>
</tr>
<tr>
<td></td>
<td>Testosterone axillary gel</td>
<td>Daily application</td>
<td>30mg</td>
<td>60-90mg</td>
<td>120mg</td>
</tr>
<tr>
<td>Long-Acting</td>
<td>Testopel</td>
<td>Every 3 months</td>
<td>6 pellets</td>
<td>8-10 pellets(^{28})</td>
<td>14 pellets</td>
</tr>
<tr>
<td></td>
<td>Aveed</td>
<td>Loading dose at 4wks, then every 10wks thereafter</td>
<td>n/a</td>
<td>750mg single dose formulations</td>
<td>n/a</td>
</tr>
<tr>
<td>Oral</td>
<td>Jatenzo</td>
<td>Twice daily</td>
<td>158mg</td>
<td>237mg</td>
<td>396mg</td>
</tr>
</tbody>
</table>

### Additional Medications

<table>
<thead>
<tr>
<th>Use</th>
<th>Medications</th>
<th>Typical Dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraceptive medications</td>
<td>Consider use for decreasing uterine bleeding and/or contraceptive purposes</td>
<td>Please see Krempasky C, Harris M, Abern L, Grimstad F. Contraception across the transmasculine spectrum(^{19})</td>
</tr>
<tr>
<td>5α-reductase inhibitors</td>
<td>Reduce androgenic hair loss</td>
<td>finasteride</td>
</tr>
<tr>
<td></td>
<td></td>
<td>dutasteride</td>
</tr>
<tr>
<td>Topical testosterone to genitals</td>
<td>Enlargement of clitoris/phallus(^{**})</td>
<td>testosterone compounded in petrolatum base</td>
</tr>
</tbody>
</table>
At this time there is only limited anecdotal data to suggest improved efficacy for clitoral/phallus enlargement in TGD individuals using testosterone or DHT cream/gel applied directly to genitals, in addition to other forms of testosterone. DHT cream/gel is not currently FDA approved or otherwise available in the US.

The limited research that may provide guidance on dosing and benefit of topical testosterone for genital growth comes from studies with cisgender males with microphallus. Studies showed some positive penile growth in prepubertal and pubertal individuals with microphallus using a genital application of testosterone cream or gels with varied concentrations; however, the effects in many studies appear to be due to systemic serum level testosterone increase — not necessarily due to specific genital application. Also, despite some positive results in prepubertal and pubertal cisgender males, there is currently no data to indicate response in penile growth in post-pubertal adults with microphallus.

If prescribing transdermal testosterone for direct genital application, it is recommended to discuss realistic expectations of this treatment. Additionally, it is encouraged to use testosterone compounded in a petrolatum base to reduce complications of skin and genital irritation from the commercially available transdermal options, which are compounded in an alcohol base. Finally, transdermal application of testosterone to the genitals will be systemically absorbed, which should be taken into account if other formulations are also being used in conjunction.39-42

See Appendix 8 for a timeline of testosterone’s effects.
### DOSING FOR ESTRADIOL

<table>
<thead>
<tr>
<th>FORMULATION</th>
<th>MEDICATION NAME</th>
<th>DOSE FREQUENCY</th>
<th>LOW DOSE</th>
<th>COMMON DOSE</th>
<th>MAX DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Injectable</td>
<td>Estradiol valerate</td>
<td>Every 2 weeks (can also be given weekly)</td>
<td>5mg</td>
<td>10-15mg</td>
<td>30mg</td>
</tr>
<tr>
<td>Injectable</td>
<td>Estradiol cypionate</td>
<td>*If dosing every week, half the dose that is listed</td>
<td>1.5mg</td>
<td>3-6mg</td>
<td>10mg</td>
</tr>
<tr>
<td>Transdermal</td>
<td>estradiol patch (Climera)</td>
<td>Weekly</td>
<td>0.05mg</td>
<td>0.1-0.2mg</td>
<td>0.4mg</td>
</tr>
<tr>
<td>Transdermal</td>
<td>estradiol patch (Vivelle dot)</td>
<td>Twice weekly</td>
<td>0.05mg</td>
<td>0.1-0.2mg</td>
<td>0.4mg</td>
</tr>
<tr>
<td>Transdermal</td>
<td>estradiol gel (0.06%)</td>
<td>Daily</td>
<td>0.75mg</td>
<td>1.25-2mg</td>
<td>3mg</td>
</tr>
<tr>
<td>Oral</td>
<td>estradiol tablet</td>
<td>Daily or twice daily</td>
<td>1mg</td>
<td>4-6mg</td>
<td>8mg</td>
</tr>
</tbody>
</table>

### DOSING FOR ANDROGEN-BLOCKING MEDICATION

<table>
<thead>
<tr>
<th>MEDICATION NAME</th>
<th>DOSE FREQUENCY</th>
<th>LOW DOSE</th>
<th>COMMON DOSE</th>
<th>MAX DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone</td>
<td>Spironolactone</td>
<td>Daily or twice daily</td>
<td>25mg twice daily</td>
<td>50-100mg twice daily</td>
</tr>
<tr>
<td>5 alpha-reductase inhibitors</td>
<td>finasteride</td>
<td>Daily</td>
<td>1mg</td>
<td>1.25-5mg</td>
</tr>
<tr>
<td>5 alpha-reductase inhibitors</td>
<td>dutasteride</td>
<td>Daily</td>
<td>n/a</td>
<td>0.5mg</td>
</tr>
<tr>
<td>Progesterone</td>
<td>micronized progesterone</td>
<td>Daily, or may dose cyclically (10d/month)</td>
<td>n/a</td>
<td>100mg</td>
</tr>
<tr>
<td>Progesterone</td>
<td>medroxyprogesterone</td>
<td></td>
<td>5mg</td>
<td>5mg</td>
</tr>
<tr>
<td>Progesterone</td>
<td>Depo Provera</td>
<td>Every 3 months IM or SC</td>
<td>n/a</td>
<td>104mg</td>
</tr>
<tr>
<td>GnRH Agonist</td>
<td>leuprolide</td>
<td>Monthly or every 3 months depending on formulation</td>
<td>n/a</td>
<td>11.25mg-22.5mg</td>
</tr>
<tr>
<td>GnRH Agonist</td>
<td>triptorelin</td>
<td>Every 6 months</td>
<td>n/a</td>
<td>22.5mg</td>
</tr>
<tr>
<td>Non-steroidal androgen receptor antagonist</td>
<td>bicalutamide</td>
<td>Daily</td>
<td>25mg</td>
<td>n/a</td>
</tr>
</tbody>
</table>
Patients on Preexisting GAHT When Entering Care

**PROVIDER-PRESCRIBED GAHT:**

For patients who have begun hormone treatment prescribed by a previous health care provider or licensed medical facility, and who are transferring care to Fenway Health, the provider will work to avoid disruption of ongoing treatment and ensure responsible and medically sound treatment and management. Patients transferring preexisting care to Fenway will be asked to provide documentation of their previous treatment or sign a release form granting Fenway Health access to that documentation and record in order to provide the best continuity of care.

Hormone therapy should be continued without interruption, unless there are specific serious medical or mental health contraindications and concerns. The medical provider will review and ensure that the doses and formulations of hormonal medications are appropriate and safe for each individual patient as part of the initial medical evaluation and discussion with the patient. The medical provider will assess the need for appropriate monitoring examination and laboratory evaluation.

**SELF-PRESCRIBED GAHT:**

Some patients may be self-medicating with hormonal medications gained through informal sources (e.g., internet, friends), and request the provider take over care. In this case, the provider will assess the safety and appropriateness of the medications the patient is currently using. In the interest of harm reduction, the provider may choose to continue the patient on an appropriate course of gender-affirming hormone therapy without interruption (“bridging therapy”) while working with the patient to monitor labs if warranted, and move toward assuming responsibility for prescribing GAHT. The transferring patient should be assessed as above, with a complete history, physical examination and laboratory evaluation as determined necessary, and be provided with informed consent.

**GAHT FOR NONBINARY/GENDERQUEER INDIVIDUALS**

Some nonbinary or genderqueer individuals may desire sex hormone levels in a range mid-way between the physiologic cisgender male and female ranges, or to use gender-affirming hormones for a limited amount of time. As with all individuals, prescribing GAHT and dose decision-making should be based on a discussion with the patient. A clear understanding of goals and ensuring realistic expectations is necessary given the unique and largely unpredictable responses of each individual to hormone therapy.
Microdosing is a term that is sometimes used to describe using low doses or limited doses of testosterone or estrogen to affirm a gender identity. Most often microdosing is requested by individuals identifying as nonbinary or genderqueer, but may be requested by anyone for whom these alternative dosing options affirm their nuanced identity.

There is not one way to “microdose,” but rather it is another example of an individualized approach to prescribing hormone therapy. Doses are often started low and monitored closely by the patient and provider to ensure that the medication continues to affirm their identity and that changes that are not desired do not occur. Pre-prescription counseling is strongly recommended to discuss that it is not possible to predict which changes may occur on hormone therapy for every individual, or how fast they may occur. It is imperative to discuss changes which may be permanent and that it may not be possible to tailor hormone regimens to allow for some changes and not others. Patients should be given the option to stop hormone therapy whenever they feel the medication is no longer affirming or desired.

Some patients may wish to start on lower than usual doses and slowly increase over time. Giving the option to more slowly experience the effects of hormones may provide some relief, decreased anxiety, and autonomy over the process. A safe, but flexible approach to dosing should be presented during the informed consent process for all patients when initiating hormone therapy.

06. Follow-up Care and Monitoring

FOLLOW UP VISITS

Monitoring the use of GAHT most often centers on ensuring treatment continues to be affirming and safety. Despite the initial assessment and expectation setting, it is not until an individual starts on GAHT that it can be truly known if the medications and their effects will feel affirming to their gender. It is important to follow up with patients to assess their experience and satisfaction with treatment. Additionally, goals, gender, safety, and supports can all change over time, which may require individualized adjustments in medication or supportive referrals. Follow up office visits are recommended regularly within the first year, and semi-regularly thereafter to ensure that GAHT is meeting their needs and expectations over time, and to reassess behavioral health, social supports, stability, and to provide overall comprehensive and preventive care for general health and well-being.

Another aspect of follow up care may include lab monitoring to determine if hormone levels are within expected or therapeutic, safe ranges. It may also be important to
monitor underlying medical conditions, organ systems, or other aspects of the body that may be affected by GAHT and pose a potential health risk to the patient. As with other aspects of gender-affirming care, these recommendations can be individualized to patient-specific risk and a patient’s ability to access care (i.e. insurance coverage, distance from clinic). A patient-centered, harm-reduction approach is encouraged. Requiring regular lab screening in order to continue on GAHT can pose unnecessary risk and harm to certain patients who require lower barriers to care to remain engaged. Medical providers should thoughtfully assess risks versus benefits of the lab studies and work with the patient to best assess safety through a patient-centered approach.

Consider the following assessments at follow up visits:

- Appropriate use and dosing of medication (i.e. assess injection technique and inquire if issues with self-injecting medication).
- Use of non-prescribed hormones, including herbal/naturopathic formulas, OTC medications, and any new drugs, vitamins, or supplements.
- Objective and subjective physical changes and patient satisfaction with anatomic changes toward their stated goals. May provide realistic expectations and re-education on the course and timing of changes (see Appendix C for onset and timing of effects of hormone therapy).
- Mental health and any mood changes whether related to gender-affirming treatment(s) or other causes. Consider referral to counseling and/or other supportive services as necessary.
- Potential stressors and impact of stigma and minority stress on the patient as part of gender affirmation or expression, effects of both medical and social gender affirmation as applicable. Check in on relationships and review sexual history of current or ongoing sexual behaviors and/or desires. Inquire about changes in sexual experience, behaviors, pleasures, and risks. Assess for intimate partner violence and/or any other sources of violence and discrimination, sex work, survival sex, non-consensual sex, appropriateness for PrEP, and pregnancy risks/need for contraception. Discuss family planning goals/reproductive rights and protection. Refer for reproductive preservation and family planning supports as necessary.
- The need/desire for legal document changes. Patients may seek support and assistance through online resources, medical case management, and the THP Patient Advocate. The primary care provider may also need to assist patients to complete letters and forms as needed or required.
- Plans/desire for gender affirming surgery(ies).
# Laboratory Monitoring by Visit Timelines

## Testosterone Use

<table>
<thead>
<tr>
<th>Labs</th>
<th>Baseline</th>
<th>3mo</th>
<th>6mo</th>
<th>12mo</th>
<th>Yearly</th>
<th>PRN</th>
<th>Additional Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Testosterone</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td>X</td>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipids</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>only as recommended by USPSTF guidelines</td>
</tr>
<tr>
<td>Glucose or A1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>only as recommended by USPSTF guidelines</td>
</tr>
</tbody>
</table>

### Timing of Testosterone Monitoring:

**Injections:** Check level mid-way between injections.

**Topicals:** Check levels any time. May consider checking total testosterone level sooner (at 3mo after initiation) if physical changes are slower or less than expected and/or persistence of menses.

**Long-acting medications:** After initiating medication it is recommended to check testosterone levels at 1mo and again at trough (just before next dose). Then can check periodically at mid-dose once stabilized on the medication.

**Oral:** At least 4-6 hours after dosing.
• If the patient is interested in full effects of the medication, target levels for testosterone should fall within the cisgender male range for the laboratory used. If lower testosterone levels are desired, then these should be tailored to individual needs and goals.

• For most patients, serum total testosterone should reflect the adequacy of dosing. However, for patients who are not achieving expected physical changes, or who are experiencing testosterone side effects, it may be warranted to check levels of bioavailable/free testosterone or estradiol levels, as testosterone may be aromatizing more readily in these patients.

• Cessation of menses is expected for most individuals within 3-6 months of starting testosterone and with serum levels in the cisgender male physiologic range. If bleeding persists, it is warranted to check serum total testosterone levels to assess for appropriate range.

  ○ Research does show that up to 25% of individuals may still have persistent uterine bleeding after 6 mo despite adequate serum testosterone levels. Though the endometrium tends to be thin while on testosterone, it appears that individuals continue to have histologic findings to suggest proliferative endometrium and pathology at the same rates as those not on testosterone (fibroids, adenomyosis, atypia, etc).\textsuperscript{44,45}

  ○ Importantly, there does not appear to be any increased rates of endometrial carcinomas seen in those on testosterone compared to the general population, but there is also no evidence to suggest that testosterone provides any additional benefit or risk reduction. If bleeding does persist, or recurs after many months or years of being on testosterone, it is important to evaluate this based on individual risk and assessment. Considerations should include:

    • Testosterone dose and serum levels
    • STD risk and testing
    • Sexual activity — consider bleeding associated with sex and/or masturbation due to atrophy of the vaginal canal and cervix
    • Pelvic ultrasound to assess for abnormalities of the uterus, fallopian tubes, and ovaries — whenever possible, assessment with trans abdominal ultrasound is recommend to avoid any unnecessary stress on the patient
      • Those aged 35 or older may be at increased risk for endometrial cancer, and therefore lower threshold for pelvic ultrasound may be considered\textsuperscript{44}
ESTROGEN AND/OR ANTI-ANDROGEN USE:

<table>
<thead>
<tr>
<th>LABS</th>
<th>BASELINE</th>
<th>3mo</th>
<th>6mo</th>
<th>12mo</th>
<th>YEARLY</th>
<th>PRN</th>
<th>ADDITIONAL COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total testosterone</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>monitoring no longer necessary following gonadectomy</td>
</tr>
<tr>
<td>BUN, Cr, Potassium</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>only necessary if taking spironolactone</td>
</tr>
<tr>
<td>Transaminases</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
<td>only necessary if taking a GnRH agonist or bicalutamide</td>
</tr>
<tr>
<td>Lipids</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
<tr>
<td>Glucose or A1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td>only as recommended by current USPSTF guidelines</td>
</tr>
<tr>
<td>Prolactin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>only if symptoms of prolactinemia or on medications known to cause prolactinemia (i.e. anti-psychotics)</td>
</tr>
</tbody>
</table>

TIMING OF ESTRADIOL MONITORING:

**Injections:** Check level mid-way between dosing.

**Sublingual:** There is suggestion that sublingual dosing of tablets may lead to rapid, high peaks of serum estradiol levels 2-6hrs after taking, which should be considered when interpreting lab values. Suggest checking levels at least 6 hours after dosing medication.46,47

**Topical (patches, gel):** Levels may be checked at any time.
• If the patient is interested in the full effects of both estradiol and androgen suppression, typical goals would be the psychologic ranges for a cisgender female: testosterone 5-55 ng/dL and estradiol 100-200 pg/mL. The estradiol goal of 100-250 pg/mL is based off of the average level for a healthy, menstruating cisgender female.

• There is currently no evidence-based specific range for estrogen levels for those taking exogenous estrogen, however most health care facilities follow the 2009 Endocrine Society Guidelines that recommend maintaining levels at the mid-cycle range for non-transgender/cisgender, menstruating women. This recommendation has been commonly adopted by many health care providers.\(^3\)

  - Some patients may expect or desire to maintain serum estradiol levels in the higher end of a menstruating cisgender female range (300-400 pg/mL). There is not a clearly established association between specific serum estradiol levels and causative physical effects, and higher levels do not necessarily promote faster, more significant physical changes. In younger patients, with low cardiovascular risk, levels in the upper end of the physiologic range may be reasonably safe. Titration upwards of dosing should be dictated by patient goals in the context of clinical response, hormone level monitoring, and safety monitoring (e.g. presence of risk factors such as smoking, CVD, renal function, and potassium levels in patients using spironolactone).\(^3\)

• A general approach for titration if initial doses do not achieve therapeutic levels would include increasing estrogen until the serum estrogen level is in the female physiologic range. If this cannot be achieved with one form of administration at the max dose, it typically is best to trial a different formulation

  - e.g. subtherapeutic levels still at 8mg of oral estradiol daily, then recommendation would be to switch to injectable or transdermal formulations to see if patient achieves a better response

• Once therapeutic serum estradiol levels have been achieved, titration efforts can focus on increasing androgen blockade. There can be several approaches to titration of androgens:

  - Continue increasing estrogen until it reaches the upper physiologic cisgender female range, as estradiol alone will suppress endogenous testosterone to some extent. The drawback for this approach is that higher levels of estrogen may be prove too risky for some patients with high CVD risk.

  - Maintain current estrogen dosing and titrate upward on antiandrogens (spironolactone and/or progesterone, or GnRH agonist)
Transient elevation of serum prolactin levels shortly after starting exogenous estradiol is occasionally observed, but the clinical significance of this remains unclear.\textsuperscript{48-50} Based on the paucity of consistent or compelling information on increased incidence of prolactinomas or clinical relevance of hyperprolactinemia, we do not recommend routine monitoring of serum prolactin levels. However, patients should be routinely screened for signs and symptoms of prolactinoma (e.g., unusual headaches, visual disturbances, galactorrhea) at each visit through the review of systems (ROS).

07. Health Maintenance Care

7.1 Mental Health

The TGD community has significant disparities in mental health and wellbeing compared to the general population, much in part due to discrimination, stigma, and minority stress related to gender and/or other intersecting marginalized identities. Despite access to gender affirming care and services, these daily overwhelming stressors can continue to be negatively impactful for many individuals.\textsuperscript{51,52} Reports show increased incidences of depression and anxiety, as well as high rates of violence victimization, suicidal ideation (81.7%), suicide attempts (range 30-69%), and lower rates of social and familial supports compared to the general population.\textsuperscript{43,53-55} Therefore, continuing to screen for and be sensitive to mental health issues, even after accessing gender-affirming care is strongly encouraged in order to provide support and services when needed.\textsuperscript{56} This includes assessing the process, progress, and support for gender affirmation and possible impact this may have on mental health, as well as screening for intimate partner violence and/or any abuse, violence occurring in the community, isolation, and access to social supports. Referring to mental health clinicians, peer support, and other community engagement programs can provide support, validation, and skills to navigate on-going struggles.

Research corroborates many patient reports of significant improvement in mental health, functioning, and quality of life after receiving appropriate and adequate gender affirming treatments including GAHT and surgery(ies).\textsuperscript{73,74,63} While hormone treatment has been anecdotally associated with destabilization of serious psychiatric disorders, there is no evidence in the literature to link worsening of severe mental illness with use of GAHT. Thus, there is no absolute contraindication to initiating or continuing GAHT within the context of serious mental illness when other readiness and eligibility criteria have also been met.\textsuperscript{2} Collaboration with the patient’s behavioral health provider(s) is encouraged in the case of severe mental illness whenever possible to improve continuity of care.
7.2 Sexual Health and Safety

Sexual health should be discussed with all patients when appropriate and welcomed by the individual. Approaching these conversations through a trauma informed lens allows the patient to have autonomy over the questions, timing, and rate of disclosure of this interview. The provider is encouraged to be transparent about why specific questions are being asked, and it is important to keep the interview individualized and free of assumptions. Once a conversation around sexual health is welcomed, ask open-ended questions – these are more likely to capture the diversity of possible answers -- and then follow up questions can be narrowed down as appropriate. Validate all sexual practices and assess for pleasure, not just perceived risk.

Finally, focusing sexual health questions on the anatomy of the patient and their partners, and not on gender, will keep the questions relevant, free of assumptions, and specific to that individual. Taking an anatomic inventory, or organ inventory, is essential to performing an anatomy-based sexual history. An organ inventory means asking patients if they have any gender affirming surgeries, body modification surgeries, or any other surgical procedures during which organs were removed. This information is important when talking about genitals, types of sex and pleasure, STD testing sites, and routine preventive screening recommendations.

Examples of possible questions may include:

- Have you had any gender-affirming surgeries?
- When referring to your genitals, are there specific terms that you use or that you would feel more comfortable with me using?
- Who are you sexually active with?
- What kinds of sex do you engage in? What body parts of yours touch body parts of your partner(s)?
- Are you using toys or prosthesis for sex? Are you sharing these?
- Are you or your partner(s) using any form of protection from STDs (or pregnancy if appropriate)? Do you feel empowered to ask your partner(s) to use these protections?
- Are you engaging in sex for pleasure or do you feel forced in any way?
- Are you engaging in sex for money, housing, drugs, or any other services?

GAHT can alter libido, while genital surgeries can change the way an individual accesses and experiences pleasure. Additionally, it is not uncommon for individuals to explore new sexual desires, practices, and partners after gender affirming medical treatment. After initiation of GAHT, assess for changes in libido, sexual desires, practices, partners, and risks.64,65 In individuals with a uterus and ovaries and with exposure to sperm, it is also encouraged to discuss desire for contraception and future reproductive goals. Regular screening for HIV and STDs may be indicated, as would be appropriate for all
patients. Sexual history and the anatomy present should guide testing sites – genital and extragenital. Education on access and safety of PrEP and PEP should be given to all TGD individuals who are interested and those at particular risk. Finally, vaccination for HPV, Hepatitis A, and Hepatitis B can be offered if not already done.

In repeated observational studies, individuals identifying as transfeminine have disproportionately high rates of HIV infection and high-risk sexual behavior. Transgender women who have sex with cisgender men, particularly Black trans women, experience the highest vulnerability for HIV infection in any key population. Higher vulnerabilities are also reported in other transfeminine people of color. These increased risks are often associated with discrimination seen in an additive effect as the result of the intersection of transphobia, racism, socioeconomic disparities, and other social stigmas based on other identities that may be present. Patients at high risk of HIV should be encouraged to consider PrEP and be provided low-barrier access to regular HIV and STD testing, PEP, and engagement in primary medical services. Discussing PrEP safety, the lack of drug interactions of PrEP medications with GAHT, and programs for medication cost assistance can be essential in reducing barriers and increasing medication up-take.

Fewer studies have looked at rates of STDs and HIV with trans and gender diverse individuals on testosterone, although the limited data that does exist reports significant rates of high-risk sexual behavior in this population. Unprotected vaginal/frontal canal intercourse and receptive anal intercourse are reported as significant risk factors for AFAB persons. Transmasculine and nonbinary individuals should be equally assessed for HIV risk and offered PrEP whenever a sexual history reveals a recommendation.

7.3 Cancer Screening

To date there is no conclusive evidence that GAHT or other medical gender affirming treatments have a direct relationship to increased incidence of breast or reproductive cancers in TGD populations. However, there continue to be limited long-term studies which confirm or refute the impact of gender affirming medical treatment on cancer risk factors.

7.3.1 Breast/Chest Health

The specific impact of gender-affirming hormones in the pathogenesis of breast cancer in transgender individuals is unknown. To date there does not appear to be any increased incidence of breast cancer overall in individuals taking GAHT compared to the general population. However, it appears GAHT may impact the risk of developing breast cancer as compared with an initial risk based on the individual’s sex assigned at birth.

The largest trans-identified cohort study assessing and reporting on breast cancer
incidence is a population-based longitudinal study in The Netherlands, beginning in 1972 and continuing through the present. A 2019 review of this Dutch cohort data found breast cancer risks most comparable to the cisgender male population for both trans women and trans men receiving GAHT, and the rates much lower when compared to those seen in cisgender women. This study does indicate an increased incidence of breast cancer in trans women on GAHT compared to cisgender men, though again, the rates are still much lower than those seen in cisgender women. This study concluded that the recommendations for breast cancer screening for cisgender people are sufficient for monitoring TGD individuals on GAHT as well. In the US, a retrospective chart review of 5,135 trans-identified veterans receiving care within the VA system showed a similar incidence of breast cancer as noted in the Dutch cohort studies. The study concluded that breast cancer is uncommon in gender diverse populations regardless of GAHT use, and GAHT appears not to be connected to an increased risk of breast cancer compared to cisgender women.

Nonetheless, a commonality that these retrospective studies observed was a younger age at time of breast cancer diagnosis in TGD people compared with cisgender women. The exposure to hormone treatment prior to diagnosis of breast cancer was also relatively short in all TGD individuals on GAHT suggesting a rapid development of breast tumors in a subset of people for unknown reasons. De Blok et. al. hypothesized this may be due to underlying genetic susceptibility (BRCA1 mutation) or the presence of undiagnosed hormone sensitive cancer. Additionally, Brown observed that nearly all of the diagnoses in transfeminine-identified individuals were made late and the outcomes were poor. These observations support routine screening and suggest their importance in finding these cancers as early as possible.

Breast implants have not been associated with higher rates of breast cancer or delayed diagnoses of breast cancer in TGD individuals, however implants may decrease sensitivity of screening mammography. Additionally, studies have shown that TGD individuals on estradiol and those on testosterone (who have not undergone chest reconstruction surgery) have increased breast tissue density. Based on these observations, TGD individuals on either estradiol or testosterone may have a higher incidence of false negative results from mammogram screening procedures. Finally, any TGD individual who have BRCA1 variants should receive guidance on their unique risks for developing cancer, especially in the setting of GAHT. It is important to discuss options for genetic testing and counseling. Having a known BRCA1 variant is not a contraindication for GAHT, but appropriate genetic and oncologic consultations may be needed for appropriate care planning and management.

**RECOMMENDATIONS:**

In patients assigned female at birth (AFAB) who have not undergone chest reconstruction (including those who have had breast reduction), breast/chest screening recommendations are the same as for cisgender women of a similar age and medical history.
In patients who have had chest reconstruction surgery, no conclusive evidence exists to guide screening. Some residual breast tissue may remain after top surgery and therefore the risk of breast cancer is still possible. It is recommended to take a thorough family history and breast cancer risk assessment, and inquire about any new or unusual masses in the chest area. Yearly clinical chest and axillary exams can be considered, but it must be noted that there is no evidence of their clinical significance and many national guidelines have moved away from recommending clinic breast and chest exams. It is important to inform patients of their probable risks based on their history and that there are no evidence-based guidelines currently for breast cancer screening recommendations for individuals post-top surgery.

In TGD patients on estrogen, consider initial screening mammography starting at age 50, and only once on estrogen therapy for greater than 5 years. Thereafter mammograms are recommended every two years, following screening guidelines for cisgender women.

### 7.3.4 Prostate Cancer

The incidence of prostate cancer in TGD individuals who have been on estrogen and/or androgen blockers is extremely rare, and there are no clear guidelines for screening or managing prostate cancer in individuals on GAHT, other than those established for the general population. Individuals who have undergone gender affirming vaginoplasty typically retain the prostate gland and should continue to be screened for prostate cancer as recommended by the current USPSTF guidelines.

As of 2017 there have been only 10 reported cases of prostate cancer in TGD people on GAHT; these numbers do not suggest an increased incidence compared to the general population. It remains unknown what the effect of long-term low testosterone and/or estrogen exposure may have on the prostate tissue. There is some evidence to suggest that anti-androgen therapy may be protective, especially if this therapy is initiated before the age of 40 years old, however, these studies are based in cisgender men. On the other hand, a 2017 review of the incidence and pathogenesis of prostate cancer challenged the protective effect of low testosterone on the prostate. This review sited possible negative effects of low testosterone and estrogen in the development or progression of prostate cancer.

### RECOMMENDATIONS:

There is limited evidence to suggest protective or harmful effects of GAHT, and therefore the recommendation is to screen for prostate cancer as recommended by updated national guidelines as it pertains to anyone with a prostate and their individual and family medical history. If screening is determined to be the preference of the patient...
after weighing risks and benefits, the USPFTF guidelines recommend screening via PSA testing. Based on lack of any evidence on its benefits, a digital rectal exam is not recommended.\textsuperscript{97} If PSA testing is provided, the medical provider should take into consideration that estrogen and anti-androgen treatment can lower PSA levels and may result in unreliable monitoring.

\textbf{7.3.5 Cervical Cancer}

Estimates indicate about 91\% of cervical cancers are attributable to HPV.\textsuperscript{98} The action of co-factors in the progression of HPV infection to precancer to cancer are not well known, including any impact that hormonal factors may have.\textsuperscript{99–102} To date, there is no evidence to suggest that the incidence of cervical cancer is higher or lower in individuals on GAHT than in a general cisgender female population. Establishing a clear and accurate sexual history with patients who have cervices is a crucial step in assessing HPV-related cervical cancer risks.

Evidence does suggest that individuals with cervices on testosterone appear to have a higher incidence of unsatisfactory pap tests.\textsuperscript{103,104} The specific cause for this is unclear, but likely attributable to a combination of cervical atrophy, the transformation zone localizing more internally, and patient and provider discomfort that together lead to difficulty obtaining a sample and/or having a rushed exam.\textsuperscript{105–108} The hypothesis that vaginal and cervical atrophy due to testosterone therapy and suppression of estrogen is an associated factor in obtaining poor pap samples is further supported by research that finds a negative predictive relationship between time on testosterone and unsatisfactory pap tests.\textsuperscript{104}

In addition to an increased incidence of unsatisfactory pap tests, TGD people may have a longer latency to follow up for screening.\textsuperscript{105,106} It is hypothesized that this may be secondary to gender dysphoria of the genital area and/or vulnerability as part of the invasive nature of this exam. Furthermore, genital and pelvic exams may trigger past experiences of sexual trauma leading to heightened anxiety and avoidance of care. This exam should be performed with sensitivity and with a trauma-informed approach. Patients should always be given the option to defer screening, to have trusted personal advocates in the exam room with them, or be offered other means to desensitize the process such as having several appointments prior to the exam, limiting the number of people in the room, putting feet on the table instead of stirrups, and inserting a speculum on their own, etc. It is important to provide sensitive and responsive education as to why the exam is recommended for the patient based on their personal situation and risks, how it is usually performed, and associated risks. Offering assurances that the patient has the right to stop the exam at any point in the process, gives patients autonomy over the procedure and their body. Providers may significantly improve collaboration with the patient by using non-gendered, sensitive language, and a patient-centered approach.
Initiating or continuing GAHT is not ever predicated on completing cancer screening exams such as a pap test and providers must not imply or make GAHT contingent on the patient receiving this exam.

TGD individuals who have undergone vaginoplasty do not require cervical or blind vaginal HPV screening via a pap test, as there is no cervix or transformation zone present. However, all sexually active TGD individuals are still at risk for HPV infection. Therefore, assessing for symptoms and an annual visual evaluation of the neovaginal tissue is generally sufficient to screen for condyloma or squamous cell carcinoma (in the case of penile inversion vaginoplasty).

**RECOMMENDATIONS:**

TGD patients who have a cervix are recommended to have regular cervical pap tests as per the published guidelines for cisgender women. It is encouraged to discuss the possibility of unsatisfactory pap tests with patients on testosterone prior to performing the exam in order to set expectations and provide anticipatory guidance. Whenever possible, collecting the sample using several collection tools (i.e. collect with the brush, broom, and spatula) can help reduce the chances of unsatisfactory pap tests.

For those patients who cannot tolerate a clinician-performed speculum examination, HPV testing alone may be appropriate via a self-performed swab of the frontal canal (vagina). A study of 150 transmasculine-identified individuals showed that self-swabbing detected high-risk HPV (hrHPV) with a concordance of 71.4% to hrHPV detected by provider-collected specimens, and a 90% preference for this collection method by the participants. Therefore, this may be considered a reasonable and patient-centered alternative to provider-collected pap testing. It should be noted that those whose tests reveal the presence of HPV will be referred for cytology testing or colposcopy as dictated by the ASCCP guidelines.

Patients who have had penile inversion vaginoplasty are recommended to have annual vaginal exams to evaluate for condyloma, skin cancers, or other concerns the patient may have.

For individuals who have had sigmoid colon vaginoplasty, the provider should be aware that this tissue is subject to all the same functions, diseases, and irritants as any colon tissue, and may develop related issues. Screening with colonoscopy may be indicated.
7.3.6 Endometrial Cancer

Endometrial cancer is one of the most common gynecologic cancers in those born with a uterus.\textsuperscript{115,116} There are several known risk factors for endometrial cancer related to unopposed estrogen therapy, including PCOS, early menarche, nulliparity, and infertility. Additional risk factors are related to older age (>45), obesity, hypertension, diabetes, and hereditary colorectal cancer.\textsuperscript{116} All of these factors may lead to proliferation of the endometrial tissue without control from progesterone to counterbalance proliferation and control growth.

For TGD individuals on testosterone, a similar hormone milieu of unopposed estrogen on the uterus may be created. Testosterone aromatizes to estrogen in certain tissues of the body, including the uterus, and at the same time leads to amenorrhea. Despite this scenario, in the published studies to date there does not appear to be increased risk of endometrial cancer in TGD people on testosterone compared to the general cisgender female population.\textsuperscript{117} In fact, the endometrium of TGD people on testosterone may appear thinner and more similar to that of post-menopausal cisgender women.\textsuperscript{117,118} Despite the possibility of a thinner endometrium and amenorrhea, there is evidence that the endometrium in reproductive-age TGD people on GAHT may continue to be active at a low level of proliferation. Additionally, the endometrium appears to have the same variance of pathology (fibroids, adenomyosis, hyperplasia without atypia, etc) as found in cisgender females with a uterus.\textsuperscript{119,120} The clinical significance of this continued activity of the endometrium is unknown, and there is not currently enough evidence to suggest a decreased or increased incidence of endometrial cancer in this population.\textsuperscript{119}

**RECOMMENDATIONS:**

Routine screening of TGD individuals for endometrial cancer is not recommended, given the lack of evidence for any increased incidence over the general population.\textsuperscript{30} Preemptive hysterectomy to prevent endometrial cancer is also not recommended; however, hysterectomy for gender affirmation, or specifically to reduce gender dysphoria, is considered medically necessary. The impact of hysterectomy and/or oophorectomy on fertility and fertility preservation options must be discussed with any patient considering these procedures. Patients should also be counseled that a total hysterectomy can be performed with the option to retain one or both ovaries. This may allow for more options around fertility, as well as dependence on exogenous hormones.

Any TGD individual with an endometrium with unexplained vaginal bleeding, especially if they are over the age of 35, should be evaluated for endometrial hyperplasia and malignancy. This includes a detailed history of symptoms, hormone dosing, and serum levels, and then pelvic exam, pelvic ultrasound, and possible endometrial biopsy as warranted. Requesting trans abdominal pelvic ultrasounds are usually appreciated by patients and are appropriate for assessment of endometrial abnormalities.\textsuperscript{119}
7.3.7 Ovarian Cancer

Symptoms of ovarian cancer are often vague and late to occur, which can lead to poor diagnosis and poor prognosis for treatment when it is discovered. There are no conclusive data about what effect testosterone therapy may have on the development of ovarian cancer. There are few documented cases of ovarian cancer in TGD individuals on testosterone, and no data to indicate a higher incidence or a relationship to GAHT. In the cases of ovarian cancer reported in TGD people, neither the incidence nor the disease course appears different than observed in the cisgender female population. Therefore, it is not clear that testosterone treatment affects the risks of developing ovarian cancer.

It is important to take an anatomic inventory with all patients to determine if ovaries are intact. These organs are commonly retained even with hysterectomy and genital reconstructive surgery, including closing of the vaginal vault (e.g., colpocleisis). Some patients may neglect to disclose their presence, forget they are retained, or may even be generally unaware that they were never removed with a prior surgery. Taking an anatomic inventory may help with disclosure or discovery of this information. It is important to discuss any risk factors with TGD patients for ovarian and gynecologic cancers in order to offer recommendations and weigh risks and benefits based on their individual risk and family history.

RECOMMENDATIONS:

There are currently no evidence-based guidelines to support the asymptomatic screening for ovarian cancer in anyone with ovaries. Bimanual pelvic exams do not reliably detect ovarian cancer at an early stage. Individuals with retained ovaries with symptoms of pelvic pain, fullness, or detection of a lower abdominal or pelvic mass, should be referred for evaluation of possible ovarian cancer.

7.4 Unexplained Pelvic Pain

There are many anecdotal reports from TGD people on testosterone who experience cramping of the lower abdomen/pelvic pain — sometimes quite severe — beginning typically 6 months to 2 years following initiation of testosterone treatment. In many cases symptoms are associated with sexual activity and triggered by orgasm specifically. The cause for this syndrome is not clear, as evaluation is often unremarkable. Most cases are self-limited and may respond, at least somewhat, to NSAID therapy prior to sexual activity. Some patients may have pain that is persistent or severe enough to warrant referral to pelvic floor physical therapy, or even a gynecologic surgeon for possible hysterectomy after a complete work up of possible causes has been addressed. Because the etiology is often unknown, it is important to discuss the possibility that hysterectomy may not result in the resolution of these symptoms.
7.5 Cardiovascular Health

The role of sex hormones on cardiovascular health remains obscure, despite there being clear indicators that endogenous hormones are an independent predictor of cardiovascular health outcomes. Studies evaluating the effects of hormone replacement therapies in menopausal cisgender women have mixed results from a low rise in the risk of stroke, to no increased risks.\cite{117,122} Studying cardiovascular outcomes in TGD individuals, specifically at it relates to GAHT use has proven difficult over time given the complexity of variables and risk factors that may also contribute to risk: age, family history, individual risk (tobacco use, obesity, lipid profile, peri-operative care, etc), and the various hormone formulations and levels, to name just a few.\cite{123}

Two large cohort studies analyzed in 2018 give a fairly cohesive overview of the incidence of cardiovascular events in TGD individuals on both estradiol and testosterone in Europe and the US. These studies indicate that estrogen therapy (with or without an androgen blocker) does appear to increase the incidence of venous thromboembolism (VTE) and ischemic stroke in trans-identified individuals compared to both cisgender women and men. The rates of myocardial infarction (MI) are elevated in TGD people on estradiol compared to cisgender female controls, but rates are on par with the expected incidence seen in cisgender men. On the other hand, TGD individuals on testosterone do not appear to have increased rates of stroke, VTE, or MI compared to cisgender men, but do show an increased risk of MI when compared to cisgender women.\cite{124,125} Despite the apparent increased cardiovascular risk in TGD individuals on estrogen, these data fail to take into account the numbers needed to harm versus the numbers needed to treat. With treatment assumed to be a reduction in gender dysphoria, then this number needed to treat would be extremely low. Considerations around benefits of hormone therapy and quality of life, compared to their associated risks, are an important and human component to these statistics that often go overlooked.\cite{126} Therefore, taking a harm reduction approach to prescribing gender affirming care is essential in this work.

It is recommended to calculate and reduce cardiovascular risk whenever possible, especially in the setting of GAHT. This can be done by reviewing the medical history and risks prior to initiating hormone therapy, and assessing these continually throughout the time in care. These considerations should include co-morbidities, family history, and tobacco use. Reduction of risk would be the same as for all patients – education around modifiable interventions, such as exercise, healthy diet, and management of co-morbid conditions, such as sleep apnea, substance use, or hyperlipidemia. Additionally, it is important to review and provide options to access the safest hormone regimens. Transdermal estradiol is recommended for TGD individuals with higher-than-average cardiovascular risk. While there is currently little evidence to show transdermal estradiol reduces overall cardiovascular risk, studies do show that those on transdermal estradiol have significantly lower rates of VTE, and transdermal formulations have less impact on coagulation markers and lipid profile when compared to oral formulations.\cite{24,30,127-131}
Further research is needed to inform how specific hormone therapy regimens impact long-term outcomes, especially as individuals are able to access GAHT at younger ages. Determining the role hormones play in cardiovascular health may better guide patient safety and decision-making. In the meantime, cardiovascular risk reduction through lifestyle changes and other medical management is imperative over the course of care.

**RECOMMENDATIONS:**

Patients should be screened and managed based on their cardiac risk factors and known personal and family history of cardiac and thromboembolic disease. Throughout the time in care, it is recommended to assess weight, blood pressure, smoking status, review for disordered sleep, and screen lipids and glucose based on current USPSTF guidelines. Providers should encourage smoking cessation, and healthy lifestyle with physical activity and appropriate diet.

During the informed consent process, providers must discuss thromboembolic and cardiovascular risks when starting on estrogen therapy. Transdermal administration of estrogen is preferred treatment in patients at high risk for or with known CAD or history of thromboembolic disease.

### 7.6 Diabetes

TGD individuals appear to have increased rates of diabetes over the general population, however the direct impact of GAHT on the risk of developing diabetes is unclear. Current studies remain mixed as to the effects of exogenous estrogen and testosterone and the development of diabetes, however there is no data showing an increased incidence of diabetes specifically after initiation of GAHT. Testosterone treatment in cisgender men is associated with increased body weight, visceral fat, and some increase in insulin resistance (IR), while other studies in show decreased IR. Patients taking estrogen appear to develop increased subcutaneous body fat, with evidence for increased IR and higher levels of circulating insulin. Despite the lack of clarity in our current literature, it is important to note that the majority of diabetes diagnoses in TGD individuals were made prior to starting on gender-affirming hormone therapy. It is likely then that these higher rates of diabetes could, at least in part, be attributed to screening bias, with increased endocrine screening in these populations, as well as the impact of health inequities, minority stress outcomes, and generally poorer socioeconomic wellbeing over the general population.
RECOMMENDATIONS:

Screening for diabetes should be based upon current USPFTF guidelines, or sooner if indicated by symptoms, patient risk factors, and/or family history of DM. Patients with a history of PCOS, or symptoms suggestive of PCOS, may be considered for earlier or more frequent diabetes screening, as PCOS is associated with a higher likelihood of insulin resistance. However, there is no data to indicate increased risk of diabetes in TGD people with PCOS once they are being treated with testosterone. Any direct link between elevated serum testosterone levels and diabetes remains unclear.

Counsel all patients on lifestyle changes that may reduce risks for developing diabetes or assist to manage glycemic control through weight reduction, exercise, and glucose-lowering agents as required.

7.7 Bone Health

Both estrogen and testosterone are crucial for bone formation during puberty and bone turnover during adulthood. Testosterone plays a role in periosteal formation and estrogen plays a vital role in the acquisition and maintenance of healthy bone in all people regardless of sex or gender. While bone density appears to generally start low and improve over time in TGD people on estrogen, bone density in TGD people on testosterone appears to remain largely unchanged over time. There remains limited knowledge on best practices to optimize bone health and reduce risks of fractures in TGD populations. Despite some longer term observed changes in bone density and muscle mass in TGD individuals treated with GAHT, there are currently no data indicating an increase in pathological fractures in these populations.

Studies suggest that transfeminine individuals have a lower bone mass density (BMD) than their cisgender male peers even prior to starting on hormone therapy. This may be attributable to lower physical activity and muscle mass, higher rates of smoking, and lower vitamin D levels. Once estradiol is initiated, estrogen therapy is associated with increases in BMD early in treatment and a potential increase in endosteal bone formation. However, these positive affects seem to plateau after about 10 years, at which time a slight decrease in periosteal bone has been observed, possibly due to decreased muscle mass and an increase in fatty tissue, leading to less mechanical loading on the bone. Overtime, studies show an overall increase in osteopenia and osteoporosis compared to cisgender men, but BMD generally preserved compared to cisgender women. A recent study found that the addition of progesterone to GAHT in TGD individuals on estradiol caused a significant annual gain in spinal BMD when compared to GAHT without progesterone, but it is unclear if this is clinically significant. Importantly, there does not appear to be an increased fracture risk overtime TGD individuals on estradiol therapy compared to cisgender women over the age of 50.
In contrast, individuals identifying as transmasculine in these studies do not appear to have lower baseline bone density prior to starting on gender-affirming testosterone therapy, despite low levels of vitamin D and high levels of tobacco use observed. Testosterone does appear to be overall protective, with studies showing larger cortical bone size just 1 year after starting testosterone therapy. The protective effects of testosterone could be due to increased muscle mass, as well as the protective effects of testosterone aromatizing to estrogen, as seen in cisgender men. Fracture risk in TGD individuals on testosterone appears lower when compared to both cisgender men and women.

Sex hormones alone are not solely responsible for bone health or fracture risks. Any patient with a strong family history of osteoporosis or those with individual histories of disordered, restrictive eating should be closely monitored for bone health issues. Additionally, other factors that are modifiable and that negatively affect bone health should be addressed - smoking, low vitamin D levels, poor calcium intake, and lack of exercise. Finally, hypogonadal states may also present a risk of decreased BMD over time. In those individuals who have been off of GAHT for more than 5 years, and are without the ability to produce endogenous sex hormones, it is recommended to screen for BMD. The minimal amount of estrogen or testosterone needed to protect bone health is unknown at this time, so those on low dose or intermittent dosing of GAHT should be counseled on risks to bone health, and screening of BMD should be considered on an individual basis.

**RECOMMENDATIONS:**

There is insufficient evidence to guide general bone density screening recommendations in TGD populations. The USPSTF guidelines recommend cisgender women aged 65 and older be routinely screened for osteoporosis with bone measurement testing, and conclude there is no evidence to assess the benefits versus risks of screening in cisgender men. The USPSTF does not comment on recommendations for TGD individuals on gender affirming hormone therapy. Furthermore, guidelines on the frequency of screening are inconsistent.

Based on the current evidence that TGD populations over the age of 50 have not shown increased fracture rates above the general population, it is generally concluded that following recommendations from the USPSTF guidelines is sufficient and safe. Therefore, TGD people should begin bone density screening at age 65. Screening between ages 50 and 64 should be considered for those with established risk factors for osteoporosis. Finally, because hypogonadal states increase risk of low BMD, TGD people who have undergone gonadectomy and have a history of at least 5 years without hormone therapy should also be considered for bone density testing, regardless of age.
08. Pre, Peri, and Post-Operative Care

Medical providers should have knowledge about surgical options, insurance coverage and the general process of approval, and pre- and post-procedural supports. While it may not be feasible for providers to know the details of all surgical procedures available, they should remain generally aware of the various gender affirming surgeries offered and those surgeons providing the services in their area. If possible, reaching out to referring institutions and their teams can help facilitate coordination of care, communication, and a team approach to caring for patients around their surgeries. Attending conferences or searching professional provider websites (e.g. WPATH) are other ways to identify surgeons from around the country and the services they provide. Medical providers, and even behavioral health clinicians, should feel comfortable with general education and expectation setting for their patients regarding the most common surgeries. Once a patient is referred for surgery, providers are expected to communicate with the surgeon as needed throughout the surgical process in order to optimize coordination of care and reduce or manage complications during healing.

Some patients may benefit from pre-operative care to obtain the most ideal results from the upcoming surgery. This may include maximizing control of underlying medical, mental health, or social issues, such as optimizing A1c, blood pressure, reducing substance use, or by stabilizing mental health conditions, housing, finances, and job security. Some may also benefit from pre-operative physical therapy prior to chest surgeries and genital surgeries to maximize functioning and decrease pain prior to undergoing a major surgery.

Post-operative support in the setting of primary care is equally as important. Medical providers should feel comfortable with post-operative anatomy in order to assess and triage for post-operative symptoms that are expected, minor complications that can be treated in the office, or more major complications that may require a return to the original surgeon or an appropriate specialist. Cultivating relationships and referral sources with various local specialists trained in gender affirming care can significantly benefit patients who may experience complications and require these referrals. Many patients continue to seek surgical care out of state, or even out of the country, therefore, reliance on their local primary care provider and specialists for post-operative management of minor to severe complications can be essential. The primary care team should feel comfortable communicating with the surgeon to understand their particular protocols and recommendations for post-operative management. Finally, post-operative physical therapy can also play an essential role in building back muscle tone and flexibility, reducing scar burden, increasing mobility, and improving confidence in functioning following surgery.

Procedures involving genital reconstruction and urology (particularly urethral lengthening), are major surgeries that often require rigorous post-operative care plans and may take years to complete and fully heal depending on procedures chosen and any complications. These surgeries are often emotionally, psychologically, and physically challenging even for people in excellent health. Post-operative care may put a large
burden on the patient in terms of dressing changes, monitoring incisions, regular dilation in the case of the neovagina, and drain maintenance to name a few. It is important to discuss these expectations with patients prior to surgery, and assess their ability to follow through post-surgery.

Prior to surgery, the primary care provider and/or behavioral health clinician should collaborate with the patient to devise an aftercare plan, as well as help to prepare emotionally and psychologically. Preparation includes discussing realistic expectations for surgery, including the post-operative care that may be necessary and planning for any potential complications. It may be important to discuss concrete stressors, such as the financial burden in regards to insurance coverage, travel, and time off of work. Finally, assessing for supports and a safe, stable, clean environment in which to heal during recovery may be vital to safety and achieving desired outcomes. Some patients may need a referral to access post-surgical recovery care facilities during the acute healing process depending on their life situation and access to safe and hygienic housing.

Common procedures that can be done in the primary care setting to support and manage minor complications may include wound assessment and dressing, changing suprapubic Foley catheters, treatment of granulation tissue with silver nitrate, and treating minor to moderate infections (UTIs, cellulitis, abscesses). The ability to assess for infection, granulation tissue, urethral strictures, wound dehiscence, tissue congestion, inadequate neovaginal dilation, and fistulas can be very helpful in quick detection and immediate management of conditions to reduce major complications later on.

**SPECIFIC CONSIDERATIONS REGARDING BREAST AUGMENTATION, ORCHIECTOMY, AND VAGINOPLASTY SURGERIES:**

Patients may be counseled to wait for at least 1 year, but often two, after initiating estradiol therapy before undergoing breast augmentation. 1-2 years on consistent estradiol therapy should produce close to the maximal expected breast growth and sizing. Performing breast augmentation prior to this maximal grow could potentially lead to undesired size or shape in the years following surgery. Surgeons and insurance carriers have differing guidelines for breast augmentation and individual surgeons and insurances must be consulted for their requirements prior to initiating evaluations and referrals for surgery.

Patients who undergo orchiectomy will no longer require androgen blocking agents. Some patients may be able to decrease their estrogen dose, as the estrogen will no longer be opposing endogenous testosterone. It is recommended that patients continue estrogen indefinitely, or at least through the typical premenopausal age, in order to preserve bone health.

If testosterone was not fully suppressed on GAHT prior to orchiectomy, patients may experience symptoms related to the near total and sudden loss of testosterone brought on by gonadectomy (e.g., fatigue, decreased libido, etc.). Serum testosterone levels
are generally undetectable in post gonadectomy patients. Some patients may find that supplementation with very small doses of testosterone, even for a short period of time, provides relief or reduction in these symptoms. Testosterone supplementation can be done with application of transdermal testosterone gel, which allows for low dosing, easy ability to stop use, and patient autonomy over dosing. Providers must discuss benefits versus potential risks with this supplementation and remind patients they can stop use at any time.

The neovagina is most often constructed from the skin of the penis, which means the lining of the vagina is squamous epithelium rather than mucosa. The pH and flora of the neovagina differs greatly from that of the mucosal vagina. Yeast infections are rare. Symptoms of bacterial vaginosis may occur, and this tends to be comprised of more complex flora. Because of this, when treatment is warranted, it is recommended to treat bacterial vaginitis with clindamycin.

A yellow or brownish vaginal discharge may be expected for up to 4 weeks postoperatively after vaginoplasty. Thereafter, brownish discharge or bleeding is usually due to granulation tissue along the incision lines. The medical provider may use a speculum or anoscope to visualize residual granulation tissue. Silver nitrate can be used to gently cauterize the granulation tissue, usually with good effect. Rarely granulation tissue can be excessive and silver nitrate alone may not be adequate; in these cases, referral to a local gynecologist or to the original surgeon may be necessary for excision of this tissue.

The neovagina requires regular self-dilation in order to maintain its depth and patency. Beginning three to four weeks post-operatively, patients will be asked to dilate two to four times a day for the first several weeks, and then gradually reduce to once daily throughout the first few months postoperatively. Most surgeons recommend continuing regular dilation once or twice a week indefinitely, even if the patient engages in regular penetrative vaginal sex with the neovagina. Each surgeon should provide the patient with instructions for dilation. The primary care provider should verify the patient has instructions and is following them as recommended or has the supports needed to be able to do so.

Wound infections or fistulas, which cause urine or fecal drainage into the neovagina from the bladder or intestines, may occur at any time, including as distant complications of surgery. Patients with these complications should be referred to their surgeons or local specialists with trans competence as appropriate. Partial wound dehiscence is not uncommon and generally heals in by secondary intent with acceptable aesthetic results.

**SPECIFIC CONSIDERATIONS REGARDING CHEST RECONSTRUCTION, METOIDIOPLASTY, AND PHALLOPLASTY**

Chest reconstruction surgery does not require any set time on GAHT, or being on hormone therapy at all prior to surgery for most insurance companies. When referring a
patient for chest reconstruction without concomitant testosterone therapy, the PCP may simply state that hormone therapy does not affirm the patient’s gender, the breasts are the specific cause of dysphoria, and therefore GAHT is not medically indicated.

The majority of chest reconstruction surgeries are double incision mastectomies, which is done with bilateral, horizontal pectoral incisions with removal of the nipple-areola complex for resizing and re-grafting back onto the chest with a size and location more consistent with that seen on the average cisgender male body. Grafting the nipple-areola complex back onto the reconstructed chest severs all nerves to the nipples and therefore individuals lose erotic sensation. Some patients report having protective sensations return, however, some also report experiencing lifelong significant numbness in their nipples and even entire pectoral chest region after surgery. Alternative procedures for chest masculinization surgery are less common and typically only an option for those with very minimal breast tissue, such as peri-areolar incision with liposuction, or “keyhole procedure.” This procedure often preserves the nerve supply to the nipple and erotic sensation, as well as minimizes scarring.153,154

Post-operative seromas and hematomas are not uncommon with chest reconstruction surgeries. Some surgeons use post-operative compression vests, while others use drains at the lateral aspects of the incisions to reduce fluid collection and swelling. Drains are generally removed within 14 days, though occasionally a patient may require that a drain be left in place longer and be removed at the primary care provider’s office. This is generally a very simple procedure. It is helpful and good practice for the PCP to be aware of the surgeon’s technique and post-operative plan in order to best coordinate and manage postsurgical care. Some patients receiving a double incision procedure will require a revision and resection of “dog ears,” or protruding pouches of skin, at the lateral aspects of the incisions on the sides of the chest.153,154

With phalloplasty or metoidioplasty, complications are quite common and are often quoted as occurring more than 80% of the time. The vast majority of these complications arise from urethral lengthening, specifically at the anastomosis of the original urethra to the neourethra. Complications include urinary tract infections, urethral strictures, and urethral fistulas. Strictures are sometimes resolved with dilatation or surgical revision. Fistulas can heal on their own after diversion of urine with a suprapubic catheter, however these may also require surgical revision. Resolution of these complications may require minor office procedures, or many surgeries and years to fully resolve. Some patients with a stricture or a fistula may opt to reroute the urethra, by way of a urethrotomy, from the neophallus to perineum, behind the constructed scrotum. The location of the urethra at the perineum no longer requires the extension of the urethra, and therefore allows for quicker, less complicated healing.155,156

The primary care provider can assist the patient by helping guide questions to ask their surgeon and setting realistic expectations for the short-term and long-term post-operative phase. If the operating surgeon is not local, a consultation with a more accessible reconstructive urologist prior to undergoing genital surgery may be recommended.
09. Other Considerations

AGING

Currently there is an absence of high-quality data documenting and assessing the long-term health outcomes of GAHT and/or gender affirming surgeries in trans and gender diverse populations. This may add complexity to decision-making regarding dosing and formulation of hormone therapies, decisions around surgical treatments, and when or if to decrease or stop GAHT at any time based on age (e.g. decrease or stop estrogen therapy around 50-60 years old to mimic menopause). There is a paucity of evidence-based recommendations to guide these decisions, and therefore decision-making relies largely on anecdotal evidence, the effects of these hormones on cisgender populations, and considering patient preference and a harm-reduction approach. As cohort populations continue to age, there will be more and more information to build stronger recommendations. Taking a patient-centered approach and considering the individual’s quality of life should be forefront in this decision-making process.

It is common for elderly or seriously ill TGD people to experience significant challenges or barriers to receiving long-term nursing care, retirement housing and services, or even safe and respectful personal care supports. Discrimination and stigma are unfortunate issues at any time, but can prove even more harmful and stressful at a time when a person is at their most vulnerable. As TGD people age, coordination of care may result in reliance on family members who have never been supportive or organizations incompetent in gender-affirming care. Primary care providers, behavioral health clinicians, and support staff should be aware of LGBTQIA+ elder support groups and organizations in their area, and work with TGD patients to identify trusted advocates, personal care providers, or health care proxies. End of life discussions are important for all people; but, for TGD individuals, creating plans for safe and respectful care and end of life choices can help to ensure that an individual’s identity and wishes will be respected even after they can no longer advocate for themselves. Advanced care directives, durable powers of attorney for health decisions, health care proxies, prepaid funeral and burial planning are all important discussions to have with patients.
References


36. Mueck AO. Postmenopausal hormone replacement therapy and cardiovascular disease: the


54. Ross-Reed DE, Reno J, Peñaloza L, Green D, FitzGerald C. Family, School, and Peer Support Are


71. Becasen JS, Denard CL, Mullins MM, Higa DH, Sipe TA. Estimating the Prevalence of HIV and


56 MEDICAL CARE OF TRANS AND GENDER DIVERSE ADULTS


111. Dermatologic Care for lesbian, gay, bisexual, and transgender persons. Partll. Epidem... Yeung, Luk, Katz. *J of Amer Acad of Derm* 2019 Mar 80(3) 591-602


The goal of this form is to provide the most up to date information about the expected effects of hormone therapy, including both the desired effects as well as possible unwanted side effects. You should have the information you need to make decisions about your care. Please do not hesitate to ask questions and talk about any concerns you have at any time.

Testosterone treatment results in certain changes to the body that some people find affirming, including lowering the pitch of the voice, possible increased facial and body hair, fat redistribution, and increased muscle mass. Each person responds to hormones differently, and it is difficult to predict some aspects of how your body might change.

Hormone therapy will not change some body features. A person’s bone structure or height will not change. Breast/chest size will not decrease or go away. Hormone therapy is not the only way to achieve your goals - we can always talk about other options (such as non-medical affirming products, other medications, and/or surgeries) that might be right for you.

Your medical provider will help decide which formulation and dose of testosterone (injections, topical gels or creams, patches) may be best for you based on your gender affirmation goals, personal needs, and any medical or mental health conditions you might have. As part of this treatment, you agree to take the medications only as prescribed and to talk with your medical provider before making any changes in your medication. You and your medical provider can work together to best support your goals for care as safely as possible.

Fenway has worked with gender diverse people for many years. Our approach to gender affirming care is based on scientific evidence whenever possible, national and international guidelines, and the feedback and experience we get from our own gender diverse community. Research on gender affirming hormone therapy provides us with information on the safety and effectiveness of these medications in helping you to achieve your goals. Despite the available research, the long-term effects of hormone therapy across the lifespan are not yet fully understood. This document outlines what we currently know about these medications. We will pass along any new information or research we learn, especially as it affects your health and wellbeing.
Expected Physical and Emotional Effects of Testosterone Therapy

The changes in your body may take several months to become noticeable and may take 3 to 5 years to progress fully.

Some changes are **PERMANENT** and will not go away, even if you decide to stop taking testosterone or take a lower amount:

- Deepening of the pitch (sound) of your voice.
- Growth, thickening, and darkening of hair on the body.
- Growth of facial hair, including beard and mustache. The ability to grow facial hair is not unlike a cisgender male, some will have the ability to grow a thick beard and in a short time, whereas others may have scant growth or facial hair that takes years to come in.
- Possible hair loss at the temples and crown/top of the head (androgenic alopecia) with the possibility of complete baldness. This may resemble and be affected by the hair patterns of cisgender men in your family. However, some do note that this form of hair loss is seen more commonly in those taking testosterone.
- Growth in the size of the phallus/clitoris. Some may also experience increased sensitivity of the phallus/clitoris as this early growth occurs.

Some changes are **NOT PERMANENT** and will likely return to how your body looked or worked before treatment if you stop taking testosterone. This may take a few weeks to months or longer depending on the change:

- Menstrual/monthly bleeding stopping, usually within a few months.
- There may be changes to the inside lining of the frontal canal/vagina (thinning, dryness). For some, this dryness can cause symptoms of discomfort with sex, can lead to increased risks of injury or infections if you are sexually active, and may make routine genital screening exams more challenging.
- Changes in where fat is stored in the body; If you gain weight, the fat will tend to localize to the abdomen and mid-section, rather than the buttocks, hips and thighs. You may lose fat from chest/breasts, buttocks, and thighs if you lose weight.
- Muscle mass and upper body strength increase.
- Some people feel more energy, more active, or more short-tempered and angry. Some people experience improvement in their mental health; feeling better or calmer and more focused.
- Many people experience skin changes including acne on the face and back that may need medical treatment to manage. This may last months to a few years, like in puberty.
- Most people experience a significant increase in their sex drive or interest in sexual activity. Some people experience changes in who they are attracted to physically.
Possible Fertility Effects of Testosterone Therapy

- Possible loss of fertility; you may not be able to get pregnant after being on testosterone therapy for some time. How long this might take is unknown. Some people choose to harvest and bank eggs before starting testosterone.
- Testosterone is not reliable birth control. Even if menstrual periods (bleeding) stop, you could get pregnant; if you are having genital sex with a partner who produces sperm, discuss using some form of birth control with your medical provider.
- If you get pregnant while taking testosterone, the high levels of testosterone in your system may cause harm and even death to the developing fetus.
- Other effects of testosterone on the ovaries and on ova (eggs) are not fully known.

Possible Side Effects and Risks of Testosterone Therapy

- After being on testosterone for a number of months, some people may develop pelvic pain. Some experience this pain with sexual arousal/orgasm and some for no apparent reason. The level of pain varies in the people who experience this effect. For some the pain resolves on its own after several months. For others the pain may persist. For a few the pain seems to go away only with removal of the uterus (hysterectomy). The cause of this pain is unknown.
- The cervix and walls of the frontal canal may become drier and more fragile (thinner). This may cause irritation and discomfort. It also may make you more vulnerable to sexually transmitted infections and HIV if you have unprotected sex using the frontal canal/vaginal opening.
Testosterone will not protect against cervical, ovarian, uterine, or chest/breast cancer. Current research indicates there may be no increased risk for these cancers above the risks already present for any individual based on genetics. Please check with your provider regarding recommendations for routine cancer screening.

Possible elevation of cholesterol, increased blood pressure, and other changes to the body may increase risk of cardiovascular disease (heart attacks, strokes and blockages in the arteries) when on testosterone therapy long-term. However, current research indicates that individuals taking gender affirming testosterone do not have increased rates of cardiovascular events than those seen in cisgender men. Family history may reveal a specific genetic risk for heart disease, which should be discussed with your provider.

Possible changes in the body that might increase the risk of developing diabetes.

Increased appetite is common and may result in weight gain.

Increased risk of sleep apnea (breathing problems while you are sleeping) appears related to testosterone treatment.

Possible increase in the hemoglobin and hematocrit (the number of red blood cells). If this increases to higher levels, it may cause problems with circulation, and increase the risk of blood clots, strokes, and heart attacks.

Increased sweating.

Increased risk of tendon injury.

Possible worsening or triggering of headaches and migraines.

Possible increase in frustration, irritability or anger; possible increased aggression and worsened impulse control.

Possible destabilization of bipolar disorder, schizophrenia and psychotic disorders or mood disorders.

Brain structures respond differently to testosterone and estrogen. Testosterone therapy may have long-term effects on the functioning or structure of the brain that we do not yet fully understand. Some limited research suggests a decrease in verbal fluency (talkativeness or using lots of words).

Smoking cigarettes may increase some of the risks of taking testosterone therapy.
APPENDIX 1

Risks and Benefits of Testosterone

Expectations, Rights, and Responsibilities

- Take testosterone only at the dosage and in the form prescribed.
- Taking testosterone in doses that are higher than recommended may increase risks from testosterone. There is no evidence that higher doses will work better or faster. The body converts (aromatizes) testosterone into estrogen, and this may occur at increased rates if testosterone levels are higher than recommended, which may lead to undesired effects.
- Suddenly stopping testosterone after a long time on the medication may have negative physical and mental health effects. It is recommended to speak to your provider before stopping the medication.
- You may choose to stop hormone therapy at any time and for any reason. You are encouraged to discuss this decision with your medical provider prior to making any changes in your medication. It is best to make a plan for stopping the treatment with a medical provider familiar with hormone therapy.
- If you have or develop any condition you think may cause harm or worsen while taking hormone therapy, work with your medical provider to evaluate and manage that condition.
- Inform your medical provider if you are taking or start taking any other prescription drugs, dietary supplements, herbal or homeopathic drugs, street/recreational drugs, or alcohol. Being honest about what you are taking/using will help your medical provider prevent or reduce potentially harmful reactions or interactions.
- Inform your medical provider of any new physical or emotional symptoms and any medical conditions that develop before or while you are taking hormone therapy.
- Inform your provider if you think you are having bad side effects from the medication.
- Your provider may recommend decreasing the dose of or, on rare occasions, stopping testosterone because of medical reasons and/or safety concerns. You can expect the medical provider to discuss all treatment decisions with you. Some people may also need to change, decrease, and/or stop hormone therapy as they age.
- Keep appointments for follow-up monitoring and other preventative health care needs, as recommended by your medical provider.
- Blood testing may be recommended to monitor your health and hormone treatment. Your medical provider will discuss which tests are necessary and any recommendations for ongoing care and monitoring.
- Hormone therapy is not the only way to affirm your gender. Your medical provider and/or a mental health provider are able to talk with you about other options if you are interested.
The goal of this form is to provide the most up to date information about the expected effects of hormone therapy, including both the desired effects as well as possible unwanted side effects. You should have the information you need to make decisions about your care. Please do not hesitate to ask questions and talk about any concerns you have at any time.

Estrogen treatment (usually estradiol) results in certain changes to the body that some people find affirming, including softening of the skin, decreased muscle mass, changes in facial and body hair, fat redistribution, and breast growth. Some also use an androgen blocker, a medication that can reduce or block the effects of testosterone and can sometimes enhance the effects of estrogen. Each person responds to hormones differently, and it is difficult to predict some aspects of how your body might change.

Hormone therapy will not change certain body features. Bone structure and height will not change, and the Adam’s apple will not shrink. The pitch of the voice also will not change. Hormone therapy is not the only way to achieve your goals - we can always talk about other options (such as non-medical affirming products, other medications, and/or surgeries) that might be right for you.

You and your medical provider will review which formulation and dose of estrogen (oral tablets, injections, topical gels, patches) and/or androgen blocker may be best for you based on your gender affirmation goals, personal needs, and any medical or mental health conditions you might have. As part of this treatment, you agree to take the medications only as prescribed and to talk with your medical provider before making any changes in your medication. You and your medical provider can work together to best support your goals for care as safely as possible.

Fenway has worked with gender diverse people for many years. Our approach to gender affirming care is based on scientific evidence whenever possible, national and international guidelines, and the feedback and experience we get from our own gender diverse community. Continuing research on gender affirming hormone therapy provides us with more information on the safety and effectiveness of these medications in helping you to achieve your goals. Despite the available research, the long-term effects of hormone therapy across the lifespan are not yet fully understood. This document outlines what we currently know about these medications. We will pass along any new information or research we learn, especially as it affects your health and wellbeing.
APPENDIX 2
Risks and Benefits of Estrogen and Spironolactone

Expected Physical and Emotional Effects of Estrogen Therapy

The changes in your body may take several months to become noticeable and may take up to 3 to 5 years to progress fully.

Some changes are PERMANENT and will not go away, even if you decide to stop taking estrogen or take a lower amount:

- Breast growth and development. Breast size on estrogen therapy varies greatly. Taking estrogen often leads to breast growth and tenderness. Breast size tends to reach full potential after 1-2 years of continual estrogen therapy, and many people report breast size around an A or B cup. Breasts may look smaller on broader chests. If you stop taking estrogen your breasts may decrease in size, but will not go away completely.

Some changes are NOT PERMANENT and will likely return to the way your body looked or worked before treatment if you stop taking estrogen and/or an androgen blocker. This may take a few weeks to months or longer depending on the change:

- Loss of muscle mass and decreased strength, particularly in the upper body.
- Decreased metabolism and weight gain. If you gain weight, the fat will tend to localize, or redistribute, more typically in the buttocks, hips, and thighs.
- Skin may become softer, drier, and existing acne may decrease.
- Facial and body hair will get softer and lighter and grow more slowly, but will not go away.
- Hair loss at the temples and crown/top of the head (androgenic alopecia) may slow down or stop, but hair will typically not regrow.
- Changes in mood or thinking may occur; some people may feel increased emotional reactions and others may feel more balanced or less emotional.
- Sex drive may decrease. This can range from a very slight change, to a much more significant decrease.
- Decreased strength of erections or inability to get an erection. The ejaculate may become thinner and watery and there will be less of it. Over time, ejaculate may completely disappear.
- The testicles will get smaller, softer, and will produce less sperm.
APPENDIX 2
Risks and Benefits of Estrogen and Spironolactone

Possible Fertility Effects of Estrogen Therapy and Decreased Testosterone

- The ability to get someone pregnant may decrease significantly or stop (infertility). The time this takes and whether infertility becomes permanent varies greatly from person to person. Fertility may or may not return after stopping estrogen.
- Possible loss of fertility; you may not be able to get someone pregnant after being on estrogen therapy for some time. How long this may take is unknown. Even if you stop taking estrogen, fertility may not come back. Whether this becomes permanent is difficult to predict. Some people choose to bank sperm before starting estrogen.
- Estrogen therapy is not a method of birth control. There is no way to predict when or if a person will become infertile (unable to get someone pregnant) when taking estrogen. Other birth control methods will be necessary (condoms, oral contraceptives, etc.) to prevent pregnancy if you are having any type sex that could result in a pregnancy.

Possible Side Effects and Risks of Estrogen Therapy

- Brain structures respond differently to testosterone and estrogen. Estrogen therapy may have long-term effects on the functioning or structure of the brain that we do not yet fully understand.
- Possible increased risk of developing blood clots. Risks are uncertain overall, with higher risks in those with a family or personal risk of blood clots, those with certain underlying health conditions, and those using high doses of certain forms of estrogen. Risks include developing blood clots in the legs or arms, in the lungs, or in the arteries, including the arteries of the brain. Blood clots in the lungs, heart, or brain could result in death. Research suggests lower cardiovascular risk (risk of blood clots, strokes, and heart attacks) with the use of transdermal estrogen (patches or gel).
- Possible increased risk of heart attack or stroke. This risk may be higher if you use tobacco products, are over age 45, or already have high blood pressure, high cholesterol, diabetes, or a family history of cardiovascular disease, and if you have low physical activity.
- Possible increase in blood pressure requiring treatment with medication.
APPENDIX 2
Risks and Benefits of Estrogen and Spironolactone

- Possible increased risk of developing diabetes. Limited research has found an increase in insulin resistance in people taking estrogen therapy. The effect of estrogen therapy on the risk of developing or on the management of diabetes remains unclear.
- Possible nausea and vomiting, especially when first starting on estrogen therapy.
- Possible increased risk of gallbladder disease and gallstones.
- Estrogen may lead to liver inflammation and/or contribute to existing liver damage.
- May cause or worsen headaches and migraines. Migraine headaches have a clear hormonal element. Estrogen may increase the intensity or frequency of migraines.
- May cause elevated levels of prolactin (a hormone made by the pituitary gland). It remains rare, but a few people taking estrogen for hormone therapy have developed prolactinomas, a benign tumor of the pituitary gland that can cause headaches and problems with vision as well as other hormone problems.
- Some people may feel their mental health and social comfort improves, and others may feel it worsens. While affirmation of gender is associated generally with improved mental health outcomes, the effect of estrogen therapy on specific mental health conditions is unknown. There is no clear evidence that estrogen therapy is directly responsible for causing or making any mental health condition worse. If you have a history of mental health diagnoses, discuss these with the clinic staff to explore which supports and services may be best to meet your needs.
- Risks of breast cancer are unclear. The risk may be higher than that in cisgender men, but does appear significantly lower than the rates seen in cisgender women. Risk factors include family and genetic history of breast cancer, length of time on estrogen therapy, age when starting estrogen therapy, and possible exposure to progesterone.
- If you develop enough breast tissue and are over the age of 50, your provider will recommend breast cancer screenings following similar guidelines as those recommended for cisgender women.

*Smoking, inhaling second-hand smoke, and use of tobacco products may greatly increase the risks of taking estrogen therapy, especially the risk of blood clots and cardiovascular disease.*
APPENDIX 2

Risks and Benefits of Estrogen and Spironolactone

Risks and Possible Side Effects of Spironolactone (Androgen Blocker):

- Increased urine production and need to urinate (i.e., pee) more frequently, along with possible changes in kidney function.
- A drop in blood pressure and feeling lightheaded, especially when standing up from sitting or lying down.
- Increased thirst and/or dehydration.
- Increase in the potassium in the blood in your body; this can lead to muscle weakness, nerve problems and dangerous heart arrhythmias (irregular heart rhythm).
- If used without additional hormone therapy, androgen blockers may cause hot flashes and low mood or energy.
- Long-term use of androgen blockers to fully block testosterone without additional hormone therapy may result in bone loss.

Expectations, Rights, and Responsibilities

- Take androgen blockers and/or estrogens only at the dosage and in the form prescribed. Taking medications in doses that are higher than recommended will increase any risks from these medications. There is no evidence to suggest that higher doses than generally recommended will work better or faster.
- You may choose to stop taking hormone therapy at any time or for any reason. Suddenly stopping estrogen after you have been on it for a long time may have negative physical and mental health effects. You are encouraged to discuss decisions with your medical provider prior to making any changes in your medication. It is best to make a plan for stopping the treatment with a medical provider familiar with hormone therapy.
- If you have or develop any condition you think may cause harm or worsen while taking hormone therapy, work with your medical provider to evaluate and create a plan to best manage that condition.
- Inform your medical provider if you are taking or plan to start taking other prescription drugs, dietary supplements, herbal or homeopathic drugs, street/recreational drugs, or alcohol. Being honest about what you are taking/using will help your medical provider prevent or reduce potentially harmful reactions or interactions.
APPENDIX 2
Risks and Benefits of Estrogen and Spironolactone

- Inform your medical provider of any new physical symptoms and any medical conditions that may develop before or while you are taking hormone therapy.
- Inform your provider if you think you are having bad side effects from the medications.
- Your provider may recommend decreasing your dose or, on rare occasions, stopping estrogen and/or androgen blockers because of medical reasons and/or safety concerns. You can expect the medical provider to discuss all treatment decisions with you. Some people may also need to change, decrease, and/or stop hormone therapy as they age.
- If you want or need surgery in the future, surgeons may require that you stop taking estrogen for a few weeks before and after surgery. The surgeon will determine when this is necessary.
- Keep appointments for follow-up monitoring and other preventative health care needs, as recommended by your medical provider.
- Blood testing may be recommended to monitor your health and hormone treatment. Your medical provider will discuss with you what tests are necessary and any recommendations for ongoing care and monitoring.
- Hormone therapy is not the only way to affirm your gender. Your medical provider and/or a behavioral health provider are able to talk with you about other options if you are interested.
For many, androgen blockers are needed or desired to drive down one’s own production and response to testosterone, and allow the effects of estrogen to be more apparent. Estrogen alone can suppress testosterone, but for some estrogen alone may not be enough to suppress testosterone sufficiently.

### ORAL

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Aldactone (spironolactone)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth once or twice daily</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>A potassium-sparing diuretic that can directly inhibit testosterone production and its effects, as well as potentially having its own small estrogenic effect. Those who are smaller and thinner, have lower blood pressure, are on certain blood pressure medications, and/or have underlying kidney disease may be at increased risk of experiencing adverse side effects. This is currently the anti-androgen of choice in the United States.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medication names</th>
<th>Propecia, Proscar (finasteride), Avodart (dutasteride)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth once daily</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>Blocks the conversion of testosterone to its more potent form, DHT. It does not inhibit the production of testosterone and therefore will not lower blood testosterone levels. May be most effective for those with hair loss/baldness, significant facial hair, or those who are unable to tolerate higher doses of spironolactone.</td>
</tr>
</tbody>
</table>
## ORAL (continued)

<table>
<thead>
<tr>
<th>Medication name</th>
<th>bicalutamide</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth once daily</td>
</tr>
</tbody>
</table>

**Additional comments**

A nonsteroidal androgen blocker that works by blocking the androgen receptor. Bicalutamide does not suppress testosterone itself, but blocks its ability to bind to the receptor. Bicalutamide can also have indirect estrogenic effects, such as increased breast growth. This occurs when testosterone levels increase as a result of blocked receptors, and the body then converts this excess testosterone to estrogen.

Bicalutamide has a rare, but severe potential side effect of liver toxicity (fulminant hepatitis). There are only several documented cases worldwide. Though uncommon, fulminant hepatitis can result in death.

Bicalutamide can be used for GAHT, but there are very few studies examining its use and the relative risk/benefit for this purpose. Because of reported cases of fulminant hepatitis, consensus is that its use in gender affirming hormonal regimen should be carefully considered, used only after alternative options have been trialed or offered, and an in-depth discussion of these potential risks have been had.

## INJECTABLES

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Lupron (leuprolide)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frequency</strong></td>
<td>Injected monthly or every 3 months, depending on the formulation. This injection is done by a medical provider.</td>
</tr>
</tbody>
</table>

**Additional comments**

Decreases one's own production of sex hormones, and is used for the purpose of blocking gonadal (testicular or ovarian) function. In youth, this can also reversibly block pubertal development prior to starting on gender-affirming hormone therapy.

Lupron can be an option for some adults as part of a hormone therapy regimen, but it may be cost prohibitive and is not first-line use.
**APPENDIX 4**

**Hormone Options: Estrogen Therapy**

17β-estradiol, more commonly known as estradiol, is the bioidentical formulation of estrogen and the most effective form with the lowest risk profile when used for gender affirming therapy. There are several options for administration, and the choice is typically based on patient preference, accessibility, effectiveness, cost, and individual safety considerations.

**Oral Estrogen Formulations**

Oral estradiol is dosed daily and therefore provides steady levels of estrogen in the body. This formulation is relatively cheap, accessible, and easy to administer.

<table>
<thead>
<tr>
<th>ORAL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
<td>Estradiol tablets</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth daily</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>Some dissolve these tablets under the tongue, called sublingual (SL) dosing. The theory is that SL dosing may decrease the potential for estradiol affecting the liver (and the liver affecting the medication). However, this is not evidence-based and there is no data to support that SL dosing is any safer or more beneficial than swallowing the tablets. The amount absorbed under the tongue is likely to be variable and unpredictable. The benefits versus risks of this dosing method are largely unknown.</td>
</tr>
</tbody>
</table>
APPENDIX 4
Hormone Options: Estrogen Therapy

Topical Estrogen Formulations

Topical estradiol appears to be the safest formulation from a cardiovascular standpoint, showing little impact on lipids (cholesterol) and decreased risk of thromboembolic events (blood clots, strokes) when compared to other formulations. This makes topical formulations ideal for those with higher than average cardiovascular risk, such as patients who are hypertensive, diabetic, or smokers. Topical formulations are also dosed daily, thereby providing the benefit of steady levels, as well as ease of use.

<table>
<thead>
<tr>
<th>PATCHES</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication name</td>
<td>multiple brands available (Climara, Vivelle-dot)</td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>Patch(es) applied once or twice a week, depending on the brand.</td>
<td></td>
</tr>
<tr>
<td>Additional comments</td>
<td>Patches formulated for twice weekly use (change every 3-4 days) may be preferable for patients for whom adhesiveness is an issue.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>GELS</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication name</td>
<td>Divigel packets, EstroGel actuated pump</td>
<td></td>
</tr>
<tr>
<td>Frequency</td>
<td>Applied daily</td>
<td></td>
</tr>
<tr>
<td>Additional comments</td>
<td>May be more expensive than other formulations. Less likely to cause a skin reaction (no adhesive as with the patch).</td>
<td></td>
</tr>
</tbody>
</table>
**APPENDIX 4**

**Hormone Options: Estrogen Therapy**

**Injectable Estrogen Formulations**

Injectable estradiol is typically dosed intramuscularly (IM) every 2 weeks, though dosing weekly with smaller amounts is possible, with the benefit of decreasing the fluctuations between doses. The peak levels that occur just after dosing can feel affirming for some, and others have felt these may also produce changes more rapidly. However, there is no evidence to suggest that higher levels produce better or quicker results. Some avoid injectable formulations due to needlephobia, the inconvenience and time of injections (whether self-injecting or by a medical professional), and the wider fluctuations in hormone levels from dose to dose.

<table>
<thead>
<tr>
<th>INJECTABLES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
</tr>
</tbody>
</table>

| **Medication name**          | Depo-estradiol (estradiol cypionate) |
| **Frequency**                | Injected every 2 weeks IM. |
| **Additional comments**      | If switching from the valerate to the cypionate formulation, there is a dose adjustment needed. The dosing of estradiol cypionate is lower. Estradiol cypionate tends to produce a lower, later, and longer peak level when compared to estradiol valerate, but the average levels in the blood, and effects on the body, should be the same. |
The benefit of progestins for gender affirmation is not well established. Some patients and medical providers report progesterone may help improve breast development, promote improvement in mood and libido, and have other positive benefits. However, progesterone has also been known to cause weight gain, fatigue, irritability and negative mood changes in other individuals. Progesterone is part of a cisgender female’s hormonal makeup, and may be desired on this basis as part of a patient’s gender affirming hormone therapy. It is important to weigh the benefits vs potential risks of starting progesterone.

In a few studies progesterone has been shown to play a role in suppressing testosterone production, which supports its use as another, or alternative, anti-androgen when needed. Progesterone may be considered if estrogen alone or estrogen and spironolactone are not effective in adequately suppressing testosterone.

Micronized progesterone (Prometrium) is the bioidentical formulation and appears to be the safest option in terms of cardiovascular health.

<table>
<thead>
<tr>
<th>ORAL</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
<td>Prometrium (micronized progesterone), 100 mg, 200mg capsules</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth once daily, or cyclical dosing (10 days every month)</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>Some patients may prefer cyclic dosing as its effects may mimic a menstrual cycle, which can be affirming for some. However, others may find the hormonal fluctuations with cyclic dosing troubling, and may prefer to take this medication daily. Progesterone’s role in breast development has yet to be proven. Reported increases in breast size seem most likely due to general weight gain and fat deposition in the breasts as caused by progesterone and estrogen, and not the direct effect of progesterone on the breast tissue itself. So far, there is no evidence to show any specific benefit (or lack of benefit) regarding progesterone’s effect on breast development.</td>
</tr>
<tr>
<td><strong>Medication name</strong></td>
<td>Provera (medroxyprogesterone acetate)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>By mouth once daily or injected every 3 months (Depo Provera)</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>Medroxyprogesterone has been shown to have a slightly higher risk of blot clotting than micronized progesterone. In addition, this medication has been associated with bone loss in cisgender women, as well as mood changes (irritability, depression). The benefit may be the 3 month injectable dosing, but the risks may outweigh the benefits in many individuals.</td>
</tr>
</tbody>
</table>
Gonadotropin-releasing hormone agonists, or GnRH agonists, are medications that work to suspend the body’s own production of sex hormones. GnRH agonists block the gonads (testicles or ovaries) from producing sex hormones (testosterone or estrogen) and, as a result, block the effects of these hormones on the body. These medications are therefore often referred to as “blockers.” In young people, these medications can reversibly block pubertal development (menstruation, breast growth, genital enlargement, vocal changes, etc.) prior to starting on gender affirming hormone therapy.

GnRH agonists can decrease dysphoria by blocking these pubertal changes, while also allowing more time for the patient and their family to decide the best course of treatment moving forward. Many people will continue on these puberty blockers up through the time of starting on affirming hormone therapy (testosterone or estrogen) when it is developmentally appropriate to do so. However, if at any time puberty blockers or moving on to hormone therapy are no longer desired or indicated, stopping these medications will allow for the body to restart producing its own hormones and will continue on through puberty as it previously would have.

### APPENDIX 6

**Hormone Options: Puberty Suppression**

<table>
<thead>
<tr>
<th><strong>Injectables</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
<td>Lupron (leuprolide), Triptodur (triptorelin)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Injected monthly or every 3 months, depending on the formulation.</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>This injection is often done by a medical provider. However, in rare cases can be done at home by a trained and trusted support person if accessing the clinic is challenging. Lupron (and most GnRH agonists) are quite expensive and will often require your medical provider to request approval of coverage from your insurance. It is also common that these medications will have to be supplied by a specialty pharmacy and shipped to the health center for administration. This may require coordination between the patient, the insurance, the pharmacy, and the medical provider.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Implants</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
<td>Supprelin LA (histrelin acetate)</td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
<td>Implanted every 12 - 18 months.</td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
<td>Supprelin must be implanted under the skin by a medical professional who specializes in this service. In most cases this can be done as a simple office procedure, but can also be done under anesthesia if there is a significant fear of needles and procedures. Patients should talk to their provider about where and how these procedures are offered.</td>
</tr>
</tbody>
</table>
APPENDIX 7

Hormone Options: Testosterone Therapy

There are several options for administration of testosterone, including injectables, topical gels or patches, and implantable long-acting pellets. Choosing which formulation is best often depends on patient preference, ability to self-inject, risks of medication transfer to others, response to hormone therapy, insurance coverage, and cost.

**Injectable Testosterone Formulations**

The most common form of testosterone are injectables, due to their low cost and ability to increase testosterone quickly and efficiently. Testosterone can be injected subcutaneously (SC) or intramuscularly (IM).

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Testosterone cypionate (cottonseed oil) or Testosterone enanthate (sesame seed oil)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Injected weekly or every two weeks, IM or SC</td>
</tr>
<tr>
<td>Additional comments</td>
<td>SC injections use smaller needles than IM, and tend to be less painful. IM injections may be preferred or necessary for largervolumes. Biweekly dosing reduces the number of injections, but leads to wider fluctuation in testosterone levels which can be uncomfortable. Weekly dosing may be a better choice for those concerned about the impact of fluctuating hormone levels on mood or other medical conditions.</td>
</tr>
</tbody>
</table>
Topical Testosterone Formulations

Topical testosterone may provide a steadier level that is considered to be more similar to physiologic fluctuations of testosterone since it is dosed daily. Consider starting on topical formulations especially if there are concerns about the effects of significant fluctuations in hormone levels, and/or if more gradual changes are desired.

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Androgel packets, Androgel actuated pump, Testim tubes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>Applied Daily</td>
</tr>
<tr>
<td>Additional comments</td>
<td>Patients must use caution in avoiding skin to skin contact at application area(s) with partners, children, or pets until the medication is completely absorbed. Hands should be washed immediately after application. If skin to skin contact is anticipated, the area should be washed with soap and water or covered. The majority of the dose will be absorbed within 4 hours of application.</td>
</tr>
</tbody>
</table>

*Recommended application site is at upper arms.*

<table>
<thead>
<tr>
<th>Medication name</th>
<th>Androderm patch, 2mg or 4mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>New patch(es) applied daily</td>
</tr>
<tr>
<td>Additional comments</td>
<td>Patches are known to commonly cause skin irritation. Not recommended for patients known to have sensitive skin.</td>
</tr>
</tbody>
</table>
### Long-Acting Testosterone Formulations

Long-acting formulations can be good options for those who find regular injections difficult and who are not candidates for topical formulations. These injections and implantable pellets may provide more consistent levels of testosterone over longer periods of time. They tend to be higher cost and need to be administered by a medical professional in the clinic. Typically, long-acting formulations are recommended only after other methods have been tried.

<table>
<thead>
<tr>
<th><strong>IMPLANTABLE PELLETS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>LONG ACTING INJECTABLES</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
## APPENDIX 7
### Hormone Options: Testosterone Therapy

### Oral Testosterone Formulations

<table>
<thead>
<tr>
<th>ORAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medication name</strong></td>
</tr>
<tr>
<td><strong>Frequency</strong></td>
</tr>
<tr>
<td><strong>Additional comments</strong></td>
</tr>
</tbody>
</table>
## APPE NDI X 8

**Onset and Timing Effects of Hormone Therapy**

<table>
<thead>
<tr>
<th>EFFECT</th>
<th>ONSET (MONTHS)</th>
<th>MAXIMUM (YEARS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin oiliness/acne</td>
<td>1-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Fat redistribution</td>
<td>1-6</td>
<td>2-5</td>
</tr>
<tr>
<td>Cessation of Menses</td>
<td>2-6</td>
<td></td>
</tr>
<tr>
<td><strong>Clitoral Enlargement</strong></td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Vaginal atrophy</td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Emotional changes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased sex drives</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Deepening of voice</strong></td>
<td>3-12</td>
<td>1-2</td>
</tr>
<tr>
<td><strong>Facial/Body Hair Growth</strong></td>
<td>6-12</td>
<td>4-5</td>
</tr>
<tr>
<td><strong>Scalp Hair Loss</strong></td>
<td>6-12</td>
<td></td>
</tr>
<tr>
<td>Increased Muscle Mass &amp; Strength</td>
<td>6-12</td>
<td>2-5</td>
</tr>
<tr>
<td>Coarser Skin/Increased Sweating</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight Gain/Fluid Retention</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Breast Atrophy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weakening of Tendons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Text in **bold** indicates changes that tend to be permanent.
## EFFECTS OF ESTROGENS & ANTI-ANDROGENS

<table>
<thead>
<tr>
<th>EFFECT</th>
<th>ONSET (MONTHS)</th>
<th>MAXIMUM (YEARS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Decreased Libido</td>
<td>1-3</td>
<td>1-2</td>
</tr>
<tr>
<td>Decreased Spontaneous Erections</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Breast Growth</strong></td>
<td>3-6</td>
<td>2-3</td>
</tr>
<tr>
<td><strong>Decreased Testicular Volume</strong></td>
<td>3-6</td>
<td>2-3</td>
</tr>
<tr>
<td>Decreased Sperm Production</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
<tr>
<td>Redistribution of Body Fat</td>
<td>3-6</td>
<td>2-3</td>
</tr>
<tr>
<td>Decrease in Muscle Mass</td>
<td>3-6</td>
<td>1-2</td>
</tr>
<tr>
<td>Softening of Skin</td>
<td>3-6</td>
<td>Unknown</td>
</tr>
<tr>
<td>Decreased Terminal Hair</td>
<td>6-12</td>
<td>&gt; 3</td>
</tr>
</tbody>
</table>

**NOTE:** Possible slowing or cessation of scalp hair loss, but no regrowth. No change in voice.

*Text in **bold** indicates changes that tend to be permanent.*
This appendix material is taken directly from the Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People, 7th Version.²

**Criteria for Breast/Chest Surgery (One Referral)**

Criteria for mastectomy and creation of a male chest in FtM patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the SOC for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Hormone therapy is not a prerequisite.

**Criteria for Breast Augmentation (implants/lipofilling) in MtF patients**

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country (if younger, follow the SOC for children and adolescents);
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.

Although not an explicit criterion, it is recommended that MtF undergo feminizing hormone therapy (minimum 12 months) prior to breast augmentation surgery. The purpose is to maximize breast growth in order to obtain better surgical (aesthetic) results.
Criteria for Genital Surgery (Two Referrals)

The criteria for genital surgery are specific to the type of surgery being requested.

Criteria for hysterectomy and salpingo-oophorectomy in FtM patients and for orchiectomy in MtF patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.
5. 12 continuous months of hormone therapy as appropriate to the patient’s gender goals (unless hormones are not clinically indicated for the individual).

The aim of hormone therapy prior to gonadectomy is primarily to introduce a period of reversible estrogen or testosterone suppression, before the patient undergoes irreversible surgical intervention.

Criteria for metoidioplasty or phalloplasty in FtM patients and for vaginoplasty in MtF patients:

1. Persistent, well-documented gender dysphoria;
2. Capacity to make a fully informed decision and to consent for treatment;
3. Age of majority in a given country
4. If significant medical or mental health concerns are present, they must be reasonably well controlled.
5. 12 continuous months of hormone therapy as appropriate to the patient’s gender goals (unless hormones are not clinically indicated for the individual).
6. 12 continuous months of living in a gender role that is congruent with the patient’s identity.

Although not an explicit criterion, it is recommended that these patients also have regular visits with a mental health or medical professional (pp. 104-106).
Letters of Referral for Surgery

Surgical treatments for gender dysphoria can be initiated by a referral (one or two, depending on the type of surgery) from a qualified mental health professional. The mental health professional provides documentation—in the chart and/or referral letter—of the patient’s personal and treatment history, progress, and eligibility. Mental health professionals who recommend surgery share the ethical and legal responsibility for that decision with the surgeon.

1. One referral from a qualified mental health professional is needed for breast/chest surgery (e.g., mastectomy, chest reconstruction, or augmentation mammoplasty).

2. Two referrals—from qualified mental health professionals who have independently assessed the patient—are needed for genital surgery (i.e., hysterectomy/salpingo-oophorectomy, orchiectomy, genital reconstructive surgeries). If the first referral is from the patient’s psychotherapist, the second referral should be from a person who has only had an evaluative role with the patient. Two separate letters, or one letter signed by both (e.g., if practicing within the same clinic) may be sent. Each referral letter, however, is expected to cover the same topics in the areas outlined below.

3. No letter is required for hysterectomy/salpingo-oophorectomy or orchiectomy to be performed for reasons unrelated to gender dysphoria or due to other diagnoses.

The recommended content of the referral letters for surgery is as follows:

1. The client’s general identifying characteristics;
2. Results of the client’s psychosocial assessment, including any diagnoses;
3. The duration of the mental health professional’s relationship with the client, including the type of evaluation and therapy or counseling to date;
4. An explanation that the criteria for surgery have been met, and a brief description of the clinical rationale for supporting the patient’s request for surgery;
5. A statement that informed consent has been obtained from the patient;
6. A statement that the mental health professional is available for coordination of care and welcomes a phone call to establish this.

For providers working within a multidisciplinary specialty team, a letter may not be necessary, rather, the assessment and recommendation can be documented in the patient’s chart (pp. 27-28).