Endocrine Therapy for Transgender Adults in British Columbia: Suggested Guidelines

Physical Aspects of Transgender Endocrine Therapy

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Assessment of Hormone Eligibility and Readiness

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Assessment of Hormone Eligibility and Readiness
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Copies of this manual are available for download from the Transgender Health Program website: http://www.vch.ca/transhealth. Updates and revisions will be made to the online version periodically. For more information or to contribute updates, please contact:

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Introductory Comments

Endocrine therapy is a strongly desired medical intervention for many transgender* individuals. The goal of transgender endocrine therapy is to change secondary sex characteristics to reduce gender dysphoria and/or facilitate gender presentation that is consistent with the felt sense of self. While there are risks associated with taking feminizing/masculinizing medications, when appropriately prescribed they can greatly improve mental health and quality of life for transgender people.[1,2] In addition to inducing physical changes, the act of using cross-sex hormones is itself an affirmation of gender identity – a powerful incentive for this population.[3,4]

With the closure of the Vancouver Hospital Gender Dysphoria Program in 2002 and the subsequent adoption of a decentralized community-based model of care,[5] clinicians with varying degrees of transgender training and experience are now responsible for care of transgender individuals in BC. This document is intended to assist endocrinologists, family physicians, and nurse practitioners whose patients may ask for feminizing/masculinizing medication. It is written for professionals who are already familiar with basic terms and concepts in transgender care and are seeking more advanced clinical guidance in work with transgender adults. Endocrine treatment of transgender adolescents is discussed separately in *Caring for Transgender Adolescents in BC: Suggested Guidelines.*[6]

The first chapter of this document, *Physical Aspects of Transgender Endocrine Therapy*, provides protocols for the prescribing clinician relating to physical assessment, prescription planning, initiation of endocrine therapy, and ongoing maintenance. The second chapter of this document, *Assessment of Hormone Eligibility and Readiness*, is adapted from *Counselling and Mental Health Care of Transgender Adults and Loved Ones*[7] to help prescribing clinicians understand the process of psychological assessment prior to initiation of endocrine therapy. Family physicians and nurse practitioners with training and experience in behavioural health, gender identity concerns, and sexual issues may choose to have sole responsibility for all aspects of transgender endocrine care, including assessment of eligibility and readiness. Alternatively, the primary psychological assessment may be performed by a mental health clinician, with the prescribing physician providing a briefer corroborating evaluation.

As discussed in the Harry Benjamin International Gender Dysphoria Association (HBIGDA)'s *Standards of Care*,[8] transgender endocrine therapy is best undertaken in the context of a complete approach to health that includes comprehensive primary care and a coordinated approach to psychosocial issues. While the HBIGDA *Standards* do not require psychotherapy prior to initiation of endocrine therapy, ideally a trans-experienced therapist will be available as needed to assist the patient in adjusting to the profound physical and psychosocial changes involved in endocrine therapy. Advocacy may also be required to assist with changes to legal name or identification. Issues in counselling and clinical advocacy are discussed further in *Counselling and Mental Health Care of Transgender Adults and Loved Ones*[7] and *Social and Medical Advocacy with Transgender People and Loved Ones: Recommendations for BC Clinicians*.[9]

Just as the HBIGDA SOC are intended as a flexible framework to guide the treatment of transgender people, the recommendations made in this document should not be perceived as a rigid set of guidelines. In any clinical practice it is paramount that protocols be tailored to the specific needs of each patient, and clinicians are encouraged to adapt and modify our suggested protocols to address changing conditions and emerging issues. Research in transgender health is still in its infancy, and there are widely diverging clinical (and consumer) opinions about "best" practice. In this document we offer suggestions based on an in-depth review of transgender health research (available from the Transgender Health Program), a review of protocols used in 16 clinics, interviews with expert clinicians, and the authors' clinical experience. Ongoing research and collegial meetings are needed to further develop practice protocols.

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* In this document, *transgender* includes any person who (a) has a gender identity that is different from their natal sex, and/or (b) who expresses their gender in ways that cross or transcend societal expectations of the range of possibilities for men and women. This umbrella term includes crossdressers, drag kings/queens, transsexuals, androgynous individuals, Two-Spirit individuals, and individuals who are bi-gendered or multi-gendered.

Physical Aspects of Transgender Endocrine Therapy

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There is great variation in the extent to which hormonal changes are undertaken or desired. Some individuals seek maximum feminization/masculinization, while others experience relief with an androgynous presentation resulting from minimization of existing secondary sex characteristics. Endocrine therapy must be individualized based on the patient's goals, the risk/benefit ratio of medications, the presence of other medical conditions, and consideration of social and economic issues.

Most of the medications listed in this guide are considered eligible prescription drugs under the BC Fair PharmaCare program (although a Special Authority application may be needed in some instances). However, economic factors may still be a barrier for patients seeking medications. Approximate cost is included in our discussion of recommended regimens.

Responsibilities of the Prescribing Clinician

In British Columbia, feminizing/masculinizing medication is typically prescribed by a family physician, endocrinologist, or nurse practitioner.[*] With appropriate transgender health training, endocrinologic manipulation of secondary sex characteristics can usually be managed by the primary care provider. Medical visits relating to hormone maintenance provide an opportunity for broader care to a population that is often medically underserved, and many of the screening tasks involved in long-term hormone maintenance fall within the scope of primary care rather than specialist care. For this reason we suggest that if hormones are prescribed by an endocrinologist rather than the primary care provider, there be close communication between the two clinicians to ensure adequate care. A trans-experienced endocrinologist should be involved if the primary care provider has no experience with transgender health, or if the patient has a pre-existing metabolic or endocrine disorder that may be affected by endocrine therapy.

The HBIGDA SOC state that the prescribing clinician should:

- perform an initial evaluation that includes health history, physical examination, and relevant laboratory tests
- explain what feminizing/masculinizing medications do and the possible side effects/health risks
- confirm that the patient has the capacity to understand the risks and benefits of treatment and to make an informed decision about medical care
- inform the patient of the HBIGDA SOC and eligibility/readiness requirements (Appendix B)
- provide ongoing medical monitoring, including regular physical and laboratory examination to monitor hormone effects and side effects

[*] In BC nurse practitioners can prescribe anti-androgens, estrogen, and progestins, but not testosterone.[10]

Male-to-Female (MTF) Endocrine Therapy

Mechanisms of action

Endocrinologic feminization is achieved by (a) direct or indirect suppression of the effects of androgens, and (b) induction of female physical characteristics.[11, 12] Androgen suppression can be achieved by:

- agents that suppress the production of gonadotrophic releasing hormone (GNRH) or are GNRH antagonists: e.g., progestational agents
- suppressing the production of luteinizing hormone: e.g., progestational agents, cyproterone acetate
- interfering with the production of testosterone or metabolism of testosterone to dihydrotestosterone (DHT): e.g., spironolactone, finasteride, cyproterone acetate
- interfering with the binding of androgens to receptors in target tissues: e.g., spironolactone, cyproterone acetate, flutamide

Estrogen is the principal agent used to induce female characteristics, and works primarily by direct stimulation of receptors in target tissues.[13] Although estrogen also suppresses luteinizing hormone (LH), the estrogen dose required for effective LH suppression is dangerously high.[12]

Expected feminizing effects

Rapidity and degree of change from feminizing endocrine therapy depends on the agents used, dosage, and the patient's responsiveness to endocrine therapy. Typically, within the first 1-6 months there is gradual redistribution of body fat to more closely approximate a female body habitus, decreased muscle mass and decreased upper body strength, softening of skin, decreased libido and possible difficulty reaching orgasm, reduction of ejaculate, and decreased spontaneous/morning erections.[8,11,14-21] Testicular volume is reduced by up to 25% within the first year,[11,22,23] with gradual reduction up to 50% of the original volume over a long period of time.[24] The shrinkage of testes may make them feel softer on palpation.[14] Testicular atrophy impacts sperm maturation and motility, and this may be permanent.[25]

Tender breast buds may start to form within 3-6 months, with gradual breast growth (highly variable) and nipple development taking two or more years.[11,19,20,22,23,26,27] Typically breast growth is not as pronounced in MTFs as in non-transgender women, and it is rare for MTF breasts to reach Tanner Stage 5 appearance.[28,29] If after 18-24 months of feminizing endocrine therapy breast growth is not sufficient for patient comfort, surgical augmentation may be considered (see *Care of the Patient Undergoing Sex Reassignment Surgery*[30]). Weight increase may help promote breast development in thin MTF patients.

Over a period of several years body and facial hair becomes finer and growth is slowed,[11,12,14,16,17,21,22,31-33] but typically cannot be eliminated by hormones alone (electrolysis, laser treatments, or other forms of hair removal may be desired).[34-38] While feminizing endocrine therapy may gradually slow or stop the progression of male pattern baldness, scalp hair does not completely regrow in bald areas.[8,11,14,17,31,32]

Most of these changes are reversible if treatment is discontinued. Breast growth and development of the nipple-areolar complex are permanent. As discussed in *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia*[39] it is not known if changes to fertility are completely reversible, and options for sperm banking should be discussed prior to initiation of endocrine therapy.[8,40]

Recommended feminizing regimen

Table 1 below summarizes our recommendations for a basic regimen for the MTF patient who desires maximum feminization. A combination of estrogen + spironolactone (an androgen antagonist) is recommended as spironolactone has a direct effect of reducing male pattern hair growth and also minimizes the dosage of estrogen needed to suppress testosterone (thereby reducing risks associated with high dose exogenous estrogen).[41,42] Finasteride may be added to slow male pattern balding.

Androgen antagonists (aka “anti-androgens”) may be prescribed alone for patients who wish to reduce masculine characteristics for a more androgynous appearance. As spironolactone can induce irreversible gynecomastia, 5α-reductase inhibitors are preferred for those who do not want visible breast development.

With both estrogen and androgen antagonists, the starting dose for patients who are at low risk for adverse effects can be gradually increased to the recommended maximum if needed to achieve the desired changes and to bring free testosterone to the lower half of the female range (see page A-13). Following orchiectomy, the dosage should be adjusted as endogenous androgen production is significantly reduced. To preserve bone density following orchiectomy estrogen supplementation should be maintained throughout life (or consider bisphosphonates), and calcium/Vitamin D supplementation is recommended.

Table 1: Basic feminizing regimen

	Estrogen			**Androgen antagonist**		
Agent	17β-estradiol			spironolactone	***and/or***	finasteride
Administration	transdermal	***or***	oral	oral		oral
Brand name	Estradot®, Estraderm®, Oesclim®		Estrace®	Aldactone®		Proscar®
Pre-orchiectomy	*Use transdermal if > 40 yrs or at risk for DVT* start at 0.1 mg/24 hrs, applied twice per week; gradually increase up to maximum of 0.2 mg/24 hrs, applied twice per week		*Oral is an option if < 40 yrs and low risk for DVT* start with 1-2 mg qd; gradually increase up to maximum 4 mg qd	start with 50-100 mg qd; increase by 50-100 mg each month up to average 200-300 mg qd (maximum 500 mg qd) *modify if risks of adverse effects: see below*§		2.5-5.0 mg qd for systemic anti-androgen effect; 2.5 mg every other day if solely for alopecia androgenetica
Post-orchiectomy	0.375-0.1 mg/24 hrs, applied twice per week		1-2 mg qd	25-50 mg qd		2.5 mg qd
Monthly cost	0.1 mg/24 hours, applied twice per week: ~$25/month*		2 mg qd: ~$14/month*	300 mg qd: ~$22/month*		5.0 mg qd: ~$58/month*

§ If taking ACE-inhibitors or other potassium-sparing medication, spironolactone should not go above 25 mg qd, and serum potassium should be closely monitored. If the patient has low blood pressure or renal insufficiency start at 50 mg and increase by up to 50 mg per week to a maximum of 300 mg qd, with a renal function test 1-2 weeks after each increase.

* Plus the dispensing fee set by each pharmacy and billed each time a prescription is refilled. In BC this is currently an average of $9.25, although compounding pharmacies may charge significantly more.

Estrogen

There is evidence that MTFs taking estrogen are at increased risk for venous thrombosis, pulmonary embolism, and cholelithiasis.[11,43-46] These risks may be mitigated by the type of endocrine agent chosen, the route of administration (transdermal vs. oral), dosage, and by other factors (e.g., smoking cessation). Some centres taper or temporarily discontinue estrogen 2-4 weeks before any major surgery (including genital surgery) to minimize thrombosis risk, restarting after the patient has recovered sufficiently to be significantly mobile.[14,19,26,31,32]

In the absence of empirical evidence that one type of estrogen (esterified vs. conjugated vs. estradiol) is a more effective feminizing agent than another, our recommendation to use 17β-estradiol is based on concerns about thromboembolic risk. Evidence suggests the lowest thromboembolic risk with transdermal estradiol.[45,47] This is particularly important for those with vascular or thrombotic risks (including smokers and people age 40+) and people with co-morbid conditions. If an oral agent is desired, oral 17β-estradiol is recommended rather than oral ethinyl estradiol or conjugated estrogens (e.g., Premarin®) due to studies suggesting higher risks of blood clots with the latter forms.[48]

The Drug and Poison Information Centre of BC's *Drug Information Reference* lists three clinically significant interactions between estrogen and other medications: anticonvulsants (decreased estrogen effect), rifampin (decreased estrogen effect), and corticosteroids (increased corticosteroid effect). A more detailed list of interactions is available from the Transgender Health Program (Appendix A).

Spironolactone

In the mid-1980s, clinicians at the Vancouver Gender Dysphoria Program began using spironolactone as part of the feminizing regimen for MTFs, based on its anti-androgenic properties and its use for treatment of hirsutism in non-transgender women. [12,41,42] It has since been adopted for use by many other transgender centres.[18,19,26,32,33,49,50] Possible adverse effects of spironolactone include hyperkalemia (particularly in conjunction with ACE-inhibitors, Angiotensin Receptor Blockers, and Type IV renal tubular acidosis – found in some patients with diabetes), renal insufficiency, hypotension, and rash.[14,41]

Alternative regimens and agents

Progestins

The inclusion of progestins in MTF feminizing therapy is controversial.[51] Some clinicians believe progestins are necessary for full nipple development.[52] However, a clinical comparison of feminization regimens with and without progestins found that the addition of progestins neither enhanced breast growth nor lowered serum levels of free testosterone.[23] There are concerns regarding potential adverse effects of progestins (including weak androgen receptor stimulation, depression, weight gain, and lipid changes),[23,26,49] and the findings of the Women's Health Initiative study (increased risk of coronary heart disease, stroke, pulmonary embolism, and invasive breast cancer in postmenopausal women taking combined estrogen and progestin HRT) are also noteworthy.[53] Many of the clinical protocols reviewed did not include progestins, and some clinicians explicitly recommended against their use.[13,18,26,31,44,49,54] Others included medroxyprogesterone acetate as part of their basic feminizing regimen.[12,14,33]

We do not recommend progestin unless further androgen suppression effects are required after maximum estrogen doses, or the patient cannot tolerate an estrogen-based regimen.[32] Table 2 represents our recommended doses for progestin use in these circumstances.

Table 2: Progestin options in a MTF feminizing regimen

	Progestin options	Cost per month
Oral	Micronized progesterone (Prometrium®): 100-400 mg qd	300 mg qd: ~$87/month*
	Medroxyprogesterone acetate (Provera®): 5-30 mg po qd (in divided doses at higher range)	30 mg qd: ~$33/month*
Transdermal single patch	140 ug or 250 ug norethindrone acetate (progestin) with 50 ug 17β-estradiol§ twice per week (Estalis®)	140/50 patch: ~$26/month*

§ If also taking estradiol alone, adjust the dosage of estradiol accordingly.

* Plus the dispensing fee set by each pharmacy and billed each time a prescription is refilled. In BC this is currently an average of $9.25, although compounding pharmacies may charge significantly more.

Alternative forms of estrogen

There is no empirical evidence that one form of estrogen brings about greater feminization than other forms of estrogen. However, it has been observed that IM estrogen tends to give slightly faster results compared to oral/transdermal estrogen, and patients may therefore request it. IM estrogen is typically not a first choice as IM administration results in larger fluctuations in blood levels than transdermal/oral administration (with according greater risks of adverse effects and mood lability). We recommend that IM injection only be used if the clinician has high confidence in patient compliance and if the patient is low risk for DVT. If in the first two years of treatment there is minimal breast development or an early plateau in growth (no change in three months despite being on the maximum dose) some clinicians switch to IM estradiol valerate (Delestrogen®: 20-40 mg IM q 2 weeks) for 3-6 months to see if it is possible to boost breast development. Clinician-administered IM estrogen may also be the preferred agent in conditions where the patient may be pressured to share or sell oral or transdermal medication (e.g., incarceration).

Transdermal gel (Estragel®) is a possible alternative to the transdermal patch for those who experience a skin reaction from the patch. Two pumps of gel applied daily is roughly equivalent to Estradot 50®. The amount of skin needed for absorption of this amount of gel is quite large (both legs) so Estragel® is not a first choice for most patients.

Alternative androgen antagonists

Cyproterone acetate (Androcur®) is used by some transgender clinics as an alternative to spironolactone. [31,33,44,55] Cyproterone acetate inhibits the production of luteinizing hormone, is a 5α-reductase inhibitor, and interferes with the binding of testosterone at receptor sites. Possible adverse effects include liver enzyme elevation and depression,[12] and for this reason we do not recommend it unless spironolactone cannot be tolerated.

Flutamide (Euflex®) use was reported by two transgender clinics surveyed (750 mg po qd).[19,33] Hepatotoxicity has been reported in men receiving comparable doses of flutamide for treatment of prostate cancer,[56] and for this reason we do not recommend flutamide as part of MTF feminization. A clinical trial of flutamide, finasteride, and spironolactone in the treatment of hirsute non-transgender women found all agents equally effective in reducing facial hair.[57]

Assessment prior to initiating MTF endocrine therapy

1. Comprehensive primary care evaluation

A full primary care evaluation (as discussed in *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia*[39]) should be completed, with particular attention to risks/history of venous thrombosis, atherosclerotic vascular disease, cholelithiasis, glucose intolerance, dyslipidemia, estrogen-dependent cancer, migraine, and hepatic disease. If there are additional primary care concerns these should be appropriately investigated. When possible, efforts should be made to stabilize and control co-morbid conditions (with medication, lifestyle changes, or other suitable interventions) prior to initiating hormones.

Cigarette smoking is associated with increased risk for venous thrombosis. We recommend a harm reduction approach that strongly encourages patients to reduce or stop smoking along with a clear recommendation that their estrogen dosage must be kept low as long as they are smoking.

2. Baseline evaluation

To assist in monitoring of adverse effects, baseline values should be recorded for lipid profile, fasting blood glucose (and A1c if diabetes or suspected glucose intolerance), liver enzymes, prolactin, electrolytes, urea, and creatinine. If there are clinical concerns there may be indications for additional tests, including complete blood count, creatinine/eGFR, and coagulation profile.

To assess feminizing effects, laboratory investigation should include baseline free testosterone[*] and baseline measurements of the breasts and hips should be recorded. Measure breasts in a standing position (a) vertically from the midclavicular line to the inframammary fold, across the largest portion of the breast, and (b) from the anterior axillary line to the midsternum, across the largest portion of the breast.

3. Written informed consent document

The HBIGDA SOC state that a written informed consent document reflecting a detailed discussion of the anticipated effects and possible risks of hormone therapy must be included as part of the medical record. Sample informed consent forms for MTF endocrine therapy are included as Appendix C.

Monitoring recommendations following initiation of MTF endocrine therapy

At minimum patients should be seen every month after initiating treatment or while adjusting medication dosages, then every 3-4 months for the first year, then every six months thereafter. The primary focus of monitoring cross-sex hormone use is to assess the degree of feminization and the possible presence of adverse effects of medication. However, as with monitoring of any long-term medication, monitoring should take place in the context of comprehensive care of all health concerns.

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[*] There are varying clinical opinions on the accuracy and reliability of testosterone assays. The values given in this document reflect local laboratory practices as of early 2005. One local lab now offers bio-available testosterone (BAT) as an alternative to free testosterone (fT), and it is possible that BAT may become more widely used in the near future.

1. Evaluation of feminization

Feminization takes place gradually over a period of years. Observed changes to male pattern hair growth, breast/nipple development, and testicular volume should be noted; breast and hip measurements recorded; and the patient asked about changes to male pattern hair quality and growth (e.g., mechanical hair-removal frequency), mood changes, libido, and sexual function. Other changes should also be noted. Breast budding should be discussed in advance to reassure the patient that it is not a malignant process.

Free testosterone level should be checked every 3 months until stable in target range (typically < 7.2 pg/mL or 75 pmol/L; if not achieving desired feminization, try to decrease to low end of female range).

2. Monitoring of adverse effects

All exams should include careful assessment of cardiovascular and thrombosis risk, including measurement of blood pressure and weight, lung exam, and examination of the extremities for peripheral edema, localized swelling, or pain.

At minimum, laboratory tests should include (see page A-13 for summary):

- Liver enzymes: 1 month after starting estrogen or changing dose, 3 months thereafter, and every 6 months once estrogen dose is stable. Investigate rise with abdominal ultrasound and hepatitis serology; discuss alcohol use.
- Lipid profile: 1 month after starting estrogen or changing dose, 3 months thereafter, and every 12 months once estrogen dose is stable.
- Fasting glucose: 1 month after starting estrogen or changing dose, 3 months thereafter, and every 6 months once estrogen dose is stable. Monitor more frequently and include evaluation of A1c if significant weight gain, increase in fasting glucose levels, or family history of diabetes mellitus.
- Prolactin: 3 months, 6 months, then annually to three years; stop if stable at that point. Hyperprolactinemia is usual with estrogen administration, and is typically mild and reversible if estrogen is reduced or temporarily discontinued. Hyperprolactinemia may also result from antidepressants or other medication, thyroid hypofunction, supplementation with additional estrogen, or prolactin-secreting pituitary adenoma. Further investigation may be warranted if prolactin levels are unusually high or do not reverse with reduction of estrogen dosage.
- If taking spironolactone: serum potassium, urea, and creatinine 1 week after commencement or dosage change; with other bloodwork if levels and dose have been stable.

3. Ongoing comprehensive primary care

Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia[39] provides detailed protocols for primary care of MTFs undergoing endocrinologic feminization (both prior to and following orchiectomy). As noted in those guidelines, cardiovascular risk factors should be aggressively screened for and treated, osteoporosis assessment should be considered for MTFs who are at risk (e.g., thin and age 50+, particularly those who have taken hormones intermittently or have had orchiectomy), and breast cancer screening should be implemented as breast tissue develops. Primary care of the MTF patient includes screening for all other types of cancer (e.g., lung, colorectal, anal) and regular prostate evaluation as for natal males, as well as periodic screening for concerns relating to sexual health, mental health, and substance use.

Female-to-Male (FTM) Therapy

Mechanisms of action

Endocrinologic masculinization is achieved by the use of testosterone to induce male physical characteristics. Testosterone works primarily by direct stimulation of receptors in target tissues; clinical effects correlate to elevation of serum testosterone level to a male reference range, rather than a decrease in serum estradiol.[13] Testosterone also has antigonadotropic action in high doses.[11]

Expected masculinizing effects

Rapidity and degree of change from masculinizing endocrine therapy depends on the agents used, dosage, and the patient's responsiveness to endocrine therapy. Typically, within the first 1-3 months patients experience oilier skin/acne, increased muscle mass and upper body strength, and redistribution of fat to a more masculine pattern (shifting from the hips and buttocks to the abdomen).[16,18,21,22,26,31,32,58-61] There are case reports of tendon rupture in both FTM patients on testosterone and natal men taking anabolic steroids,[62,63] and FTMs who are involved in strength training should be cautioned to increase weight load gradually, with an emphasis on repetitions rather than weight.

The voice often starts to crack and deepen within the first 3-6 months, but it can take a year or more for the voice pitch to fully drop.[18] In 75% of FTMs, testosterone will cause voice pitch to drop to a level sufficient for passability as male even on the telephone.[64]

Clitoral growth begins within the first few months of testosterone initiation and typically plateaus within the first year.[22,23] The degree of enlargement is variable, with studies reporting a range of 3.5-6 cm maximal length when stretched.[15,22,23] Clitoral growth does not appear to be enhanced by topical application of testosterone to the clitoris. Long-term testosterone use causes vaginal and cervical atrophy,[16,65] with decreased vaginal secretions and difficult penetration reported by some patients.[61]

In most cases menses stop within 1-6 months.[14,15,19,21-23,26,31,32,61] If after three months menses have not stopped, the dosage of testosterone may be increased (to the maximum recommended dose) until serum free testosterone is within the upper quartile of the normal male range (page A-13) or menses stop. Despite endometrial atrophy, cessation of menses, and reduced fertility there is evidence of ovulation even after several years of testosterone administration,[65] and testosterone should not be relied upon as a failsafe contraceptive.

There is gradual increased growth, coarseness, and thickness of hairs on the torso and extremities in the first year.[15,16,18,26,31] Facial hair increases more slowly, typically taking 1-4 years to reach full growth.[11] Some patients experience male pattern baldness during this later stage of masculinization.[18,26,31,32,50,60]

Voice changes, facial hair growth, and male pattern baldness are not reversible, while other changes are reversible (to varying degrees) if hormonal treatment is stopped. Clitoral growth and sterility may or may not be reversible. Reproductive counselling may be advised, particularly for young patients.

Recommended masculinizing regimen

Table 3 on the following page summarizes our recommendations for a basic regimen for the FTM patient who desires maximum masculinization. The starting dose for patients who are at low risk for

adverse effects can be gradually increased to the recommended maximum if needed to achieve the desired changes and to bring free testosterone to the lower half of the male range (see page A-13). Once maximum masculinization has been reached (typically changes plateau after two years, although there may still be facial hair growth/male pattern baldness after that time), the dosage can be reduced to the low-normal male range (page A-13) even prior to oophorectomy. To preserve bone density following oophorectomy, testosterone supplementation should be maintained throughout life (or consider bisphosphonates), and Calcium/Vitamin D supplementation is recommended.

Table 3: Basic masculinizing regimen

	Intramuscular injection (esterified testosterone)		**Transdermal gel**	**Transdermal patch**
Agent	Testosterone cypionate	Testosterone enanthate	Testosterone crystals dissolved in gel	
Brand name	Depo-Testosterone®	Delatestryl®	AndroGel®	Androderm®
Pre-oophorectomy	25-40 mg every week (or 50-80 mg every two weeks); gradually increase each month until blood testosterone is within normal male range or there are visible changes (typically 50-100 mg every week, or 100-200 mg every 2 weeks) *ensure patient knows how much to inject – there are 100 mg/ml and 200 mg/ml preparations*		5-10 g qd; start with 2.5 g qd if there are comorbid conditions that may be exacerbated by testosterone (see discussion below)	5-10 mg/24 hours, applied daily; start with 2.5 mg patch if there are comorbid conditions that may be exacerbated by testosterone (see discussion below)
Maintenance (after 2 years)	Reduce to level needed to keep serum free testosterone within the lower-middle end of the male reference interval (page A-13). Monitor risk of osteoporosis.			
Monthly cost	150 mg every two weeks: ~$10/month*		5 g qd: ~$120/month*	5 mg qd: ~$120/month*

* Plus the dispensing fee set by each pharmacy and billed each time a prescription is refilled. In BC this is currently an average of $9.25, although compounding pharmacies may charge significantly more.

The largest transgender hormone study done to date found no increased mortality in androgen-treated FTMs, and concluded that morbidity was generally “minor and reversible with appropriate treatment or temporary discontinuation of hormone treatment”.[45] However, given the methodological limitations of this study, the long-term risks of androgen therapy in FTMs are unclear. Some reports suggest that androgen use may worsen lipid abnormalities, obstructive sleep apnea, obesity, and acne.[11,14,18,21,23,32,45,50,66-69] Increased visceral depot, particularly pronounced in FTMs who gained weight after starting testosterone,[58,70] is a concern as this is associated with increased risk for cardiovascular disease and non-insulin-dependent diabetes mellitus. The aromatization of testosterone to estrogen may increase risk of malignancy in patients with a strong family history of estrogen-dependent cancers.[13,19,71] There are case reports of polycythemia in non-trans men treated with androgens,[72,73] and erythrocytosis may be a concern for FTMs with chronic hypoxemic respiratory disease or those who are at risk of hemachromatosis.

Parenteral androgen preparations (intramuscular and transdermal) minimize hepatic exposure to androgens so have the potential to reduce adverse hepatic effects. Because intramuscular androgen preparations are administered intermittently, some people may notice cyclic variation in effects (e.g., fatigue and irritability at the end of the injection cycle, aggression or expansive mood at the beginning of the injection cycle). This may be mitigated by using a more frequent dosage schedule (weekly rather than every two weeks) or by using a transdermal or oral preparation. Transdermal

testosterone may be preferred by patients who have difficulty self-injecting, have significant adverse effects related to the injection cycle, or need a slow, even titration.[8]

Testosterone increases serum levels of anticoagulants and sulfonylureas, and may interact with corticosteroids.

Alternative regimens and agents

Alternative forms of testosterone

Testosterone undecanoate (Andriol®) does not have the hepatotoxicity associated with older 17-alkylated forms of oral testosterone (e.g., methyltestosterone) and is considered safe for FTM masculinization (160-240 mg po qd).[11] It is generally not preferred as it is less effective than IM or transdermal testosterone in suppressing menstruation, with only 50% of patients experiencing menstrual cessation after six months taking oral testosterone.[22,74] It is also much more expensive than testosterone esters (160 mg po qd: ~$120/month + pharmacy fee).

Progestins

Progestins are not typically included in FTM endocrine therapy, but can be used for a short period of time to assist with menstrual cessation. Depo-Provera® can be given by IM injection (150 mg every three months) to stop menses either before or concurrent with starting testosterone, stopping the injections after 3-6 months on testosterone.[11,18,27,44] One transgender clinic performs a progestin challenge[75,76] within 3-6 months of menstrual cessation (and every 2-3 months thereafter until there is no further bleeding) to reduce risk of endometrial hyperplasia.[77]

Gonadotropin-releasing hormone (GnRH) analogues

GnRH-analogues (e.g., leuprolide acetate, Lupron®) have a longer half-life than natural GnRH and after a period of brief overstimulation down-regulate the pituitary, with consequent reduction of follicle-stimulating hormone and luteinizing hormone. This causes a decrease in estrogen levels similar to postmenopausal levels. GnRH analogues are often used with strongly dysphoric young adolescents to delay puberty, but are not commonly used in the treatment of transgender adults. They are expensive and tend to have stronger adverse effects than testosterone. However, they may be used if testosterone or progestins are not tolerated.[11]

Assessment prior to initiating FTM endocrine therapy

1. Comprehensive primary care evaluation

A full primary care evaluation (as discussed in *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia*[39]) should be completed, with particular attention to weight and risks/history of cardiovascular disease, diabetes/glucose intolerance, dyslipidemia, estrogen-dependent cancer, gynecologic disease (including polycystic ovarian disease), and hepatic disease. If there are additional primary care concerns these should be appropriately investigated (e.g., consider stress testing for patients at high risk for cardiovascular disease or with any cardiovascular symptoms). When possible, efforts should be made to stabilize and control co-morbid conditions (with medication, lifestyle changes, or other suitable interventions) prior to initiating hormones. Pregnancy and unstable coronary artery disease are absolute contraindications to androgen use. Patients at risk of becoming pregnant require adequate birth control.

Cigarette smoking is associated with increased risk for cardiovascular disease. We recommend a harm reduction approach that strongly encourages patients to reduce or stop smoking, along with a clear recommendation that their testosterone dosage must be kept low as long as they are smoking.

2. Baseline evaluation

To assist in monitoring of adverse effects, baseline values should be recorded for lipid profile, fasting glucose (and A1c if high risk for diabetes/glucose intolerance), complete blood count, and liver enzymes. Serum free testosterone* may be evaluated if there is clinical suspicion of hyperandrogenism or if the patient wants to be informed of changes to serum testosterone levels with androgen therapy.

3. Written informed consent document

The HBIGDA SOC state that a written informed consent document reflecting a detailed discussion of the anticipated effects and possible risks of hormone therapy must be included as part of the medical record. Sample informed consent forms for FTM endocrine therapy are included as Appendix D.

Monitoring recommendations following initiation of FTM endocrine therapy

At minimum patients should be seen every month after initiating treatment or while adjusting medication dosages, then every 3-4 months for the first year, then every six months thereafter. The primary focus of monitoring cross-sex hormone use is to assess the degree of masculinization and the possible presence of adverse effects of medication. However, as with monitoring of any long-term medication, monitoring should take place in the context of comprehensive care of all health concerns.

1. Evaluation of masculinization

Masculinization takes place gradually over a period of years. Observed changes to male pattern hair growth and voice should be noted, and the patient should be asked about changes to menstrual pattern, mood, clitoral growth, libido, and sexual function. Other changes should also be noted.

To avoid a supraphysiological dose of testosterone, serum free testosterone should be checked 2-4 weeks after starting testosterone or after a dose adjustment, and every 6-12 months thereafter. The biochemical goal is to achieve levels within the male reference interval (page A-13). Some clinicians check trough levels for patients using IM testosterone preparations; others prefer midcycle levels.

2. Monitoring of adverse effects

All exams should include assessment of weight, cardiovascular risk, diabetes risk, and blood pressure. There are case reports of destabilization of bipolar disorder, schizophrenia, and schizoaffective disorder in non-transgender men with the use of testosterone, and clinicians have also found this in FTMs.[74] Mental health should be monitored carefully in FTMs with these conditions for the duration of testosterone therapy.

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* There are varying clinical opinions on the accuracy and reliability of testosterone assays. The values given in this document reflect local laboratory practices as of early 2005. One local lab now offers bio-available testosterone (BAT) as an alternative to free testosterone (fT), and it is possible that BAT may become more widely used in the near future.

At minimum, laboratory tests should include (see page A-13 for summary):

- Fasting blood glucose: 3 and 6 months after starting testosterone or after a dose adjustment, then annually. Increase frequency and monitor A1c if elevated lipids, significant weight gain, elevated fasting glucose levels, personal history of glucose intolerance, or family history of diabetes.
- Hgb: 3 and 6 months after starting testosterone or after a dose adjustment, then annually.
- Lipid profile: 3 and 6 months after starting testosterone or after a dose adjustment, then annually; increase frequency if pre-existing high lipid levels or an increase in lipid levels, significant weight gain, personal history of glucose intolerance, or family history of diabetes
- Liver enzymes: 3 and 6 months after starting testosterone or after dose increase, then annually.

3. Ongoing comprehensive primary care

Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia[39] provides detailed protocols for primary care of FTMs undergoing endocrinologic masculinization. As noted in those guidelines, cardiovascular risk factors should be aggressively screened for and treated, and osteoporosis assessment should be considered for FTMs who are at risk (age 60+ if taking testosterone for < 5-10 years; age 50+ if taking testosterone for > 5-10 years; earlier for patients who have taken testosterone intermittently, have had oophorectomy, or are otherwise at risk). Primary care of the FTM patient includes screening for all other types of cancer (e.g., lung, colorectal, anal) as for natal females, as well as periodic screening for concerns relating to sexual health, mental health, and substance use.

FTMs should receive regular monitoring by a primary care provider for breast cancer both before and after chest surgery, as chest reconstruction typically does not involve the removal of all breast tissue. If the uterus and cervix are present, regular gynecologic screening is also recommended as part of basic primary care, with total hysterectomy and oophorectomy recommended for patients who cannot tolerate regular pelvic and Pap exams (see *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia*[39]). After androgen-induced cessation of menses, vaginal bleeding should be evaluated as for post-menopausal women.

Summary of Laboratory Investigations

Tables 4 and 5 on the following page are minimum timelines. Closer monitoring should be done for patients at risk for or with co-existing cardiovascular disease, diabetes, hepatic disease, etc.

Table 4: Male-to-Female (MTF) laboratory summary

Timeline for Laboratory Tests	
Baseline (before starting feminizing endocrine therapy)	• Free testosterone, lipid profile, fasting blood glucose (and A1c if diabetes or suspected glucose intolerance), liver enzymes, prolactin, electrolytes, urea, creatinine • Additional tests as clinically indicated (e.g., CBC, coagulation profile)
1 week after starting/changing dose of spironolactone	• Serum potassium, urea, creatinine
1 month after starting/changing dose of estrogen	• Liver enzymes, lipid profile, fasting glucose • If taking spironolactone: serum potassium, urea, and creatinine
3 months after starting estrogen	• Free testosterone: repeat every 3 months until free testosterone is in target range of < 7.2 pg/mL or 75 pmol/L • Liver enzymes, lipid profile, fasting glucose, prolactin • If taking spironolactone: serum potassium, urea, and creatinine
6 months after starting estrogen and every 6 months thereafter if dose is stable	• Liver enzymes, fasting glucose • If taking spironolactone: serum potassium, urea, and creatinine • Add lipid profile every 12 months (once estrogen dose is stable) • Add prolactin at 6 months, 12 months, 24 months, and 36 months

Testosterone Reference Ranges
(goal: reduce to low end of normal female range)

	BC Bio Medical Labs	MDS Metro	Vancouver Hospital
Free testosterone	• F, 3-50 yrs: 0.6-7.5 pmol/L • F, > 50 yrs: < 6.5 pmol/L	• F, 21-60 yrs: 0.5-8.1 pmol/L • F, > 61 yrs: < 6.5 pmol/L	• F, 3-60 yrs: < 7.5 pmol/L • F, > 60 yrs: < 6.5 pmol/L
Total testosterone	• F, > 17 yrs: 0.5-2.6 nmol/L	• F: < 4.5 nmol/L	• F, > 11 yrs: < 1.4 nmol/L

Table 5: Female-to-Male (FTM) laboratory summary

Timeline for Laboratory Tests	
Baseline (before starting masculinizing endocrine therapy)	• Lipid profile, fasting glucose (and A1c if high risk for diabetes/glucose intolerance), complete blood count, and liver enzymes • Free testosterone if clinical suspicion of hyperandrogenism or if patient wants to know of changes after starting testosterone
2-4 weeks after starting/changing dose	• Free testosterone (trough or midcycle if IM)
3 months after starting testosterone	• Hgb, fasting blood glucose, lipid profile, liver enzymes
6 months after starting testosterone	• Hgb, fasting blood glucose, lipid profile, liver enzymes • Free testosterone (trough or midcycle if IM)
12 months after starting testosterone and annually thereafter	• Hgb, fasting blood glucose, lipid profile, liver enzymes • Free testosterone (trough or midcycle if IM)

Testosterone Reference Ranges
(goal: elevate to within normal male range)

	BC Bio Medical Labs	MDS Metro	Vancouver Hospital
Free testosterone	• M, 20-29 yrs: 32-92 pmol/L • M, 30-39 yrs: 30-87 pmol/L • M, 40-60 yrs: 23-83 pmol/L • M, > 60 yrs: 22-63 pmol/L	• M, 21-30 yrs: 24-95 pmol/L • M, 31-40 yrs: 25-89 pmol/L • M, 41-50 yrs: 23-82 pmol/L • M, 51-60 yrs: 23-80 pmol/L • M, > 61 yrs: 22-74 pmol/L	• M, 20-29 yrs: 32-92 pmol/L • M, 30-39 yrs: 30-87 pmol/L • M, 40-60 yrs: 23-83 pmol/L • M, > 60 yrs: 22-63 pmol/L
Total testosterone	• M, > 17 yrs: 8.4-28.7 nmol/L	• M: 10-30 nmol/L	• M, > 15 yrs: 10-38 nmol/L

Assessment of Hormone Eligibility and Readiness

Walter Bockting, Gail Knudson, & Joshua Goldberg
adapted from *Counselling and Mental Health Care of Transgender Adults and Loved Ones*[7]

Responsibilities and Qualifications of the Assessor

When any patient requests medication, the clinician is responsible to determine that the medication is an appropriate form of treatment prior to prescription. In addition to the physical evaluation described in the preceding section, the Harry Benjamin International Gender Dysphoria Association (HBIGDA) *Standards of Care* (SOC)[8] state that prior to initiation of endocrine therapy the patient should be assessed by a health professional with:

- a master's degree or its equivalent in a clinical behavioral science field, granted by an institution accredited by a recognized national or regional accrediting board
- specialized training and competence in the assessment of the DSM-IV/ICD-10 Sexual Disorders (not just gender identity disorders)
- documented supervised training and competence in psychotherapy
- continuing education in the treatment of gender dysphoria (e.g., attendance at professional meetings, participating in research related to gender identity issues).

This assessor is responsible for making a recommendation relating to hormone therapy based on the patient's eligibility and readiness for the therapy, defined in the HBIGDA SOC as summarized in Table 6.

Table 6: HBIGDA *Standards of Care* – Eligibility and readiness criteria

Eligibility	Readiness
1. Able to give informed consent 2. Informed of anticipated effects and risks 3. Either completion of 3 months "real-life experience" *or* psychotherapy for duration specified by the assessor (usually a minimum of 3 months) The HBIGDA *Standards of Care* note that: "in selected circumstances, it can be acceptable to provide hormones to patients who have not fulfilled criterion 3 – for example, to facilitate the provision of monitored therapy using hormones of known quality, as an alternative to black-market or unsupervised hormone use".	1. Consolidation of gender identity 2. Improving or continuing mental stability 3. Likely to take hormones in a responsible manner

If the prescribing clinician has the appropriate training and a practice structure that allows extended appointments (at least 30 minutes), this screening may be performed as part of their overall assessment regarding endocrine therapy. A mental health clinician may be asked to conduct assessment of hormone eligibility and readiness if:

- the prescribing clinician desires a more detailed assessment or a second opinion
- the patient prefers to be assessed by a mental health professional
- the prescribing clinician's time constraints prevent full assessment in the primary care setting

- the patient is considering or planning to have sex reassignment surgery (SRS) at a later date (the assessment to be done prior to SRS will be smoother if the mental health clinician who does that evaluation has seen the earlier client for hormone assessment)

The recommended framework for evaluation of hormone eligibility/readiness in the primary care setting is the focus of this chapter. Evaluation in the mental health setting is discussed in detail in *Counselling and Mental Health Care of Transgender Adults and Loved Ones.*[7]

Assessing the New Patient

In some cases, the request for hormone assessment will be made by a pre-existing patient whose medical history is already known to the clinician. In other cases a new patient will ask for hormones on their first appointment. As with any new patient, time is needed to build therapeutic rapport, record patient history, and evaluate capacity to make medical decisions.

Many transgender individuals and loved ones have had negative experiences with health and social service professionals, and may be wary about entering unreservedly into a relationship with the clinician. In addition to the regular techniques used to build therapeutic rapport in the primary care setting, it can be helpful to actively demonstrate trans-specific sensitivity. General recommendations for primary care clinicians are discussed in *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia*.[39]

Intake for the new transgender patient includes all the standard components of a new patient exam (personal health history, family history, psychosocial history, sexual health history) and also a history of feminizing/masculinizing interventions. Trans-specific considerations for each, including recommended questions, are discussed in *Transgender Primary Medical Care: Suggested Guidelines for Clinicians in British Columbia.*[39]

Hormone Assessment

Some transgender patients who request endocrine therapy have, prior to the request, made an informed decision (supported by self-directed research about treatment options, substantial internal reflection, and in some cases peer or professional counselling), undertaken preparations for beginning endocrine therapy (e.g., disclosing transgender identity to loved ones, developing a transition plan for school/work), and have relatively good supports and overall stability. In these cases a relatively short evaluation may be feasible. Others have made an impulsive decision, have unrealistic expectations, lack information about possible risks and complications, are unprepared for the psychosocial consequences of endocrine therapy, or have a condition that is complicating the ability to make an informed decision. In these cases a more prolonged process is required to clarify whether endocrine therapy is the best course of action, and to identify additional supports that may be needed as part of the process. Typically 2-6 thirty-minute appointments (or 1-3 fifty-minute appointments) are sufficient to determine whether the patient is (a) eligible and ready to begin endocrine therapy, or (b) in need of further assistance to move toward eligibility/readiness.

Discussing patient and clinician goals and expectations

Every patient has goals and expectations (and often fears) about approaching a clinician for assistance with endocrine therapy. Transgender patients may have a particular idea about what to expect based on previous experience with health professionals or the experiences of

peers. Clinicians also come to this work with particular goals and expectations, as well as a framework for how the initial evaluation and subsequent care planning and treatment will proceed. It is recommended that the protocols and approach used by the clinician be explained so the patient knows what to expect. In particular, it is important to ensure the patient understands the process the clinician will use to conduct the evaluation, the specific eligibility and readiness criteria to be evaluated, and the way the clinician will handle possible outcomes of the evaluation process. The patient should be informed that the assessment will not be based on judgments about the patient's gender presentation or passability, but that instead, assessment will focus on core gender identity and psychosocial adjustment.

The "gatekeeper" role and the impact on therapeutic rapport

Clinicians conducting assessment prior to initiation of hormones or surgery are in a "gatekeeper" role that involves a power dynamic which can significantly affect therapeutic rapport.[78] The transgender patient often perceives the evaluation not as a desired tool to help them therapeutically determine a plan of action, but rather as a hoop that must be jumped through to access treatment, a loss of physical and psychological autonomy, or a type of institutionalized transphobic discrimination – as psychological evaluation is not required for non-transgender individuals requesting hormone replacement therapy.[79] In our experience, patients who feel prepared for hormone evaluation (with assistance by peers or clinicians as part of this process) are more willing to share information than patients who are highly anxious or fearful about the process.

If tension arises related to the assessor's role of gatekeeper to desired medical interventions, it may be helpful to openly discuss this. Normalizing emotional reactions patients commonly have (e.g., anger, anxiety, fear) and associated behaviours (e.g., trying to tell the assessor what the patient thinks they want to hear, being belligerent/uncooperative, being manipulative) helps frame this as a systems issue rather than a personal power struggle. Discussion about what the assessment process involves (discussed in the next section) is imperative as patient anxiety or anger is often heightened by inaccurate understanding of the process. When the gatekeeper issue is posing a serious barrier to therapeutic rapport (for the clinician or the patient), it may be advisable to separate hormone eligibility/readiness assessment from the rest of primary care practice so assessment is performed by a mental health clinician.

Evaluating eligibility

1. Capacity to provide informed consent

As in the non-transgender population, most transgender patients will not present any challenge in terms of ability to consent to care, and the evaluation is usually a spontaneous and straightforward judgment based on routine interactions between a clinician and the patient.[79] If determination of the capacity to make medical decisions is more challenging because a patient has limited cognitive capacity (due to neurological illness, developmental disability, head injury, intoxication, etc.), formal capacity assessment such as the Aid to Capacity Evaluation (ACE),[80] collateral information from loved ones or caregivers, or additional evaluation by a specialist in medical competency may be appropriate.

2. Informed of anticipated effects and risks

Informed consent requires an understanding of the specific treatment options that are proposed. The general risks and benefits of transgender endocrine therapy (including the irreversibility of some changes, an appreciation that the long-term health impacts of cross-sex hormone use are not yet known, and possible psychosocial impacts) and the risks, potential adverse effects, and

complications associated with specific medications should be discussed with the patient. The HBIGDA SOC state that "the medical record must contain a written informed consent document reflecting a discussion of the risks and benefits of hormone therapy". Sample informed consent forms are included as Appendices C and D.

3. Recommended completion of "Real-Life Experience" (RLE) or psychotherapy

The HBIGDA SOC recommend (but do not require) completion of "real-life experience" or psychotherapy prior to starting endocrine therapy. Both provide a way for the patient to carefully consider options before making physical changes. For the patient who intends to undergo genital reconstruction at a later date, RLE completed as part of endocrine therapy will count towards the RLE that is required for genital surgery (a minimum of one year in the HBIGDA SOC, and two years for BC Medical Services Plan coverage).

"Real-Life Experience" (RLE)

The HBIGDA SOC define "real-life experience" (RLE) as "the act of fully adopting a new or evolving gender role or gender presentation in everyday life", with the intention of achieving an experiential understanding of the familial, interpersonal, socioeconomic, and legal consequences of gender transition.[78] RLE is a way for the transgender person who wishes to permanently change their gender role to move from an imagined experience to a lived experience. For some individuals this experience is liberating and exhilarating, and for others there is disappointment that the real experience does not live up to a fantasized ideal.

A fundamental premise of the RLE is that the person should experience life in the desired role before making irreversible physical changes. The HBIGDA SOC explicitly state that RLE is not a diagnostic test to evaluate whether gender concerns are present, but that the process tests "the person's resolve, the capacity to function in the preferred gender, and the adequacy of social, economic, and psychological supports". From a behavioural perspective, RLE is a time of adjustment, exploration, and experimentation, learning (often through trial and error) how to relate to oneself and to others as the previously hidden self emerges. Psychotherapy is not a requirement during this process, but it can be a valuable support during a time of profound internal and external change.

It is important to note that the real-life experience is not defined by adherence to stereotypical ideas of masculinity or femininity. Just as there is a range of gender expression among non-transgender women (with many choosing not to wear makeup, dresses, or otherwise displaying attributes conventionally considered feminine), transgender women also have a range of gender expression. Similarly, not all transgender men are masculine in appearance or behaviour. The real-life experience is not defined by ability to pass as a non-transgender woman or man. Rather, it is defined by actualizing and continuously expressing one's unique gender identity.

If the patient and assessor agree to a period of RLE prior to endocrine therapy, regular appointments may be scheduled throughout the RLE to try to get a sense of how the patient is progressing and to offer support to those who are having difficulty. If the clinician or patient feels that the assessor's role as gatekeeper prevents frank discussion of challenges, disappointments, and surprises in the RLE process, involvement of a peer or external professional counsellor may be useful in providing a space for the patient to discuss problems or concerns without fear that endocrine therapy will be delayed or blocked.

Psychotherapy

Psychotherapy is not an absolute requirement prior to initiation of endocrine therapy. As with any major life decision, there are varying decision-making pathways for endocrine therapy, and for some transgender individuals self-directed reflection, peer counselling, and discussion with loved ones are sufficient to make a reasoned and informed decision. Psychotherapy may be recommended if the assessor feels the patient needs professional assistance to explore gender issues or psychosocial concerns prior to making a decision about endocrine therapy, or to assist with psychosocial stabilization (to meet readiness criteria).

Assessing readiness

As defined in the HBIGDA SOC, *readiness* relates to:

- a relative stability of gender identity
- the psychological stability needed to cope with the physical, emotional, and social consequences of the decision to take hormones
- the psychological stability needed to take hormones as prescribed

1. Consolidation of gender identity

While some degree of ambivalence and uncertainty is to be expected with any life-changing process, the patient should have a clear sense of the gendered self prior to initiating hormones/surgery. Physical change is not appropriate for patients who are just beginning to explore their identity or options for gender expression. While it is not necessary for transgender feelings to be lifelong or for dysphoria to have existed since childhood, caution (i.e., longer period of assessment) is needed if dysphoria is transient, episodic, or newly discovered. A detailed history of transgender identity development and expression should be conducted, as per the topic areas indicated in Table 7 below.

Table 7: Potential Areas of Inquiry – Transgender Identity Development

Gender identity	• How would your describe your gender identity? • How did you come to recognize that your experience of gender is different than most individuals? • Were there any life events that you feel were significant in influencing your gender identity? • Have there been changes to your gender identity over time? • What do you remember feeling about your gender as a child? What was puberty/adolescence like? • How do you feel about your gender now? • How does your gender identity impact how you feel about work, relationships, family, or other aspects of your life?
Gender expression	• Are there any activities you did as a child or that you do now as an adult that you think of as being cross-gendered? If so, how have these been viewed by your family and others in your life? • Did you prefer to be around individuals of any particular gender as a child? Is this different than your preferences now? • Have you ever cross-dressed? If so, what was that experience like for you? If not, what do you imagine it would be like? • If you could change your external appearance in any way you wanted to more closely match your sense of who you are, what would this look like in terms of your gender? • Have you taken any other steps to change your outward appearance to make it more closely match your identity? If so, what was that like for you? *continued on next page*

Table 7: Potential Areas of Inquiry – Transgender Identity Development *cont.*

Perceptions of others	• How do you think others perceived your gender when you were a child? How do you think others perceive your gender now? • How do you want to be perceived in terms of your gender? • How important is it to you that there be a fit between how you feel about your gender and how others perceive you?
Sexuality	• How does gender play out in your sexual desires or fantasies? Does it impact the kinds of sexual activities you do (on your own or with others) or wish you could do? • What is a typical sexual fantasy for you? • Do your sexual fantasies involve other men, women, or trans people, or do you mainly fantasize about yourself? If you are in your fantasies, do you imagine yourself to be female, male, or transgender? • What are your feelings about the parts of your body that are often associated with sexuality (e.g., genitals, chest/breasts)?
Support resources	• Do the people in your life know that you are transgender? If so, what was it like to tell them? If not, how do you feel about them not knowing? • Have you had any contact with other transgender individuals? What was that like for you? • What is your relationship to the transgender community now? What would you like it to be in the future? • Have you used the internet to access support and information about being transgender? What have you learned? In what ways was it helpful or not helpful for you?
Hormones and transgender identity	• What leads you to want to start hormones at this time in your life? • What are your hopes and dreams relating to hormones? What do you expect hormones to change? What do you think is not likely to change? • How do you think hormones may affect your relationships with loved ones? What do you think the impact will be at work/school or in terms of your involvement in the broader community? • What will you do if the change process doesn't turn out as you had hoped? • Are there any issues in your life that you think might complicate a decision to take hormones, or that might increase stress during this time? What kinds of supports do you feel might be helpful? • Which changes are you most looking forward to? Are there any changes you are not sure about?

2. Improving or continuing mental stability

Mental health concerns, psychosocial concerns, or substance use issues are not absolute contraindications to sex reassignment. Sometimes these issues are a direct result of the gender dysphoria or suppressed transgender feelings and alleviate or remit entirely as the gender conflicts are addressed. However, the clinician should be confident that supports are adequate and that any co-existing conditions are under control to the degree that (a) the introduction of a new stressor will not seriously destabilize the patient, and (b) the patient has sufficiently clear thinking to be competent to consent to treatment.[78] If there are concerns about competency or substance use, formal evaluation by a specialist may be required.

Rarely, thought disorders, dissociative disorders, obsessive/compulsive disorders, and severe distress about sexual orientation can cause a transient wish for sex reassignment which disappears when the underlying mental health condition is treated. It is important to treat these disorders before proceeding with endocrine therapy to ensure that sex reassignment is not a temporary desire. In evaluating the patient's gender history, parameters to consider include:

- *Are there obsessive/compulsive features?* Compulsive crossdressing, obsessive pursuit of validation of transgender identity through sexual pursuits, or other obsessive/compulsive behaviours should be evaluated. Where there is sexual compulsivity, diagnoses of Sexual Disorder NOS or Transvestic Fetishism* may be appropriate.[81] Obsessive/compulsive features should first be addressed (see *Counselling and Mental Health Care of Transgender Adults and Loved Ones*[7]), with subsequent reassessment to determine whether gender concerns persist.[82]

- *Is there a history of homosexuality combined with internalized homophobia?* Patients who have difficulty accepting same-sex/same-gender desires may fantasize about or describe themselves as being of the other gender.[83,84] Assessment of gender concerns should include a thorough sexual history, and appropriate psychotherapeutic treatment offered for any concerns about sexual orientation. Gender concerns should be reassessed after treatment.

- *Are there delusions about sex or gender?* In rare cases, schizophrenia or other thought disorders manifest as gender- or sex-based delusions[78] – e.g., that one's body has spontaneously transformed from one sex to another, or that internal organs of the other sex are present even after laboratory examination confirms there is no evidence of intersexuality. In some cases the delusion may be expressed as "really being of another gender". This can be distinguished from gender dysphoria by persistence (gender concerns are usually longstanding) and presence when the patient is not actively delusional.

- *Is there evidence of dissociation?* For some individuals, growing up transgender is experienced as traumatic. Others have experienced additional trauma. Coping strategies with such trauma may include dissociation of the self, and this may involve a split of identity into a separate male and female self. By addressing this trauma in therapy, an integrated self can be achieved.[85] A diagnosis of Dissociative Identity Disorder (as defined in the *DSM-IV-TR*) is "not a contraindication to either eligibility or readiness for SRS"[19] but should be very carefully evaluated as part of the overall care plan. DID diagnosis is not appropriate for individuals who have a bi-gender or multi-gender identity (even if this is described as having different "personalities" or "selves") in the absence of dissociation. As stated by Israel et al., "The transition from one gender to another occurs across psychological and physical planes and is experienced as self-fulfilling and stress-relieving for the transgender individual, in contrast to the increased confusion and insecurity felt by the person with a dissociative condition" (pp. 29-30).[19]

3. Likely to take hormones in a responsible manner

Determination of patient readiness to embark on endocrine therapy includes the clinician's confidence that the medications will be taken as they have been prescribed. Clinician-administered injection may be preferable in conditions where the patient may be pressured to share or sell oral or transdermal medication (e.g., incarceration). When there are concerns about possible supplementation with additional medication (to increase the dose), more frequent laboratory confirmation of serum hormone levels may be useful.

* The *DSM-IV-TR* definition of Transvestic Fetishism limits the diagnosis to heterosexual males. However, compulsive crossdressing for sexual purposes can theoretically be a concern for people of any gender or sexual orientation. Erotic crossdressing is not intrinsically a mental health concern, but if it becomes so consuming that it is affecting a person's ability to function, the compulsivity and obsessive qualities are of clinical significance.

Recommendation Regarding Treatment

If the assessor judges the patient to be an appropriate candidate for hormonal or surgical treatment, the medical chart should reflect a confirmation of eligibility and readiness. As outlined in the HBIGDA SOC, the chart should include:

- explanation of the type of evaluation and/or treatment provided relating to gender issues
- initial diagnoses relating to gender identity issues or any other concerns
- the rationale for hormones or surgery (why it is appropriate treatment)
- evaluation of the patient's eligibility and readiness for hormones/surgery
- the degree to which the patient and clinician have followed the HBIGDA *Standards of Care*, and the likelihood that this will continue
- mention of any other clinicians involved in the patient's care and the degree of communication/coordination undertaken prior to endocrine therapy

If the assessor feels the treatment is generally appropriate but the patient does not meet eligibility or readiness criteria, the reasons for this should be explained to the patient and a timeline established for reassessment. Concerns about hormone eligibility typically relate to a recommendation for completion of "real-life experience" or psychotherapy when the assessor feels more time is needed for the patient to make a reasoned decision. If the patient has already started this process and just needs to have logged more time, the reassessment plan is straightforward; if the patient has not been able to fulfill the mutually agreed upon conditions, the reasons should be explored and the patient assisted to gain supports needed to be able to pursue "real-life experience" or psychotherapy. If there are psychosocial readiness concerns, resources should be identified to help the patient move toward psychological/social stability, with specific and measurable goals established. In some cases reference to a trans-positive advocate or financial planner may be needed to help explore economic resources for the costs of transition. Denial of desired treatment can be highly disappointing and it is important to emphasize that reassessment is believed to be appropriate, and to ensure that the patient is aware of peer and professional supports in the interim.

In some cases the assessor may feel that hormonal or surgical feminization/masculinization is not an appropriate treatment and that reassessment of eligibility/readiness according to the HBIGDA *Standards of Care* is not indicated. This may be the case if a patient is seeking hormones/surgery for reasons other than gender dysphoria, where another type of assessment is more appropriate (e.g., a non-dysphoric male seeking hormonal or surgical castration to reduce sexual urges). If the prescribing clinician believes that the patient's physical health is too fragile to ever proceed or a patient is judged to be incompetent to make medical decisions and the cause for diminished competency is not likely to change, the patient should be supported to come to terms with this and to explore alternative forms of transgender expression rather than false hope being held out of eventual endocrine therapy.

Concluding Remarks

Individual tailoring of endocrine regimens to fit the transgender patient's history, risk factors, desired outcomes, and administration preferences holds promise both for maximization of desired effects and minimization of adverse effects. We hope that the recommendations in this document help family physicians, endocrinologists, and nurse practitioners in BC feel more confident to determine when endocrine therapy may be appropriate, and to care for patients who are undergoing endocrinologic feminization/masculinization.

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Appendices

Appendix A: Local Resources

Appendix B: Summary of Harry Benjamin International Gender Dysphoria Association's *Standards of Care* Relating to Feminizing/Masculinizing Medication

Appendix C: Informed Consent Form for Feminizing Medications

Appendix D: Informed Consent Form for Testosterone Therapy

Note: Page numbers have been removed from Appendices C and D to facilitate copying for patients.

Appendix A: Resources

Transgender Health Program

The Transgender Health Program is an anonymous and confidential free service for anyone in BC who has a transgender health question or concern.

Services for clinicians involved in transgender endocrine therapy include:

- training in the physical aspects of endocrine therapy and assessment of eligibility/readiness
- facilitation of mentorship and case consultation with more experienced clinicians
- assistance in care planning for transgender clients and loved ones
- information about best practice guidelines and standards of care
- assistance with development of trans-inclusion policies and procedures
- information about transgender health research findings and implications for practice
- free copies of patient education materials

Services for transgender people and loved ones include:

- help finding health/social services, and assistance to navigate health/social service systems
- information about best practice guidelines, standards of care, and treatment options
- peer-based exploration of gender identity, gender expression, and life stresses in a non-judgmental setting
- support and information for family members, partners, friends, and other loved ones
- outreach to transgender people working in the survival sex trade
- free training sessions for peer support volunteers
- information about transgender community organizations and peer support groups

The Transgender Health Program is an initiative of Vancouver Coastal Health.

For more information, contact:

Transgender Health Program
Three Bridges Community Health Centre
#301-1290 Hornby Street, Vancouver, BC V6Z 1W2
Phone/TTY/TDD: 604-734-1514 or 1-866-999-1514 (toll-free in BC)
Fax: 604-633-4241
Email: transhealth@vch.ca
Web: http://www.vch.ca/transhealth

Harry Benjamin International Gender Dysphoria Association

http://www.hbigda.org

The Harry Benjamin International Gender Dysphoria Association (HBIGDA) is a professional organization devoted to the understanding and treatment of gender dysphoria, with 350 members from around the world in fields such as psychiatry, endocrinology, surgery, psychology, sexology, counseling, sociology, and law. HBIGDA provides opportunities for scientific interchange among professionals through biennial conferences and publications, and develops and publishes Standards of Care.

Appendix B: Summary of Harry Benjamin International Gender Dysphoria Association's *Standards of Care*

The Harry Benjamin International Gender Dysphoria Association (HBIGDA)'s *Standards of Care* are an evolving set of guidelines representing an international consensus on best practices relating to eligibility, readiness, and appropriateness of hormones and surgery for people seeking gender transition.

- ***Appropriateness*** is the determination that hormones and/or surgery are an appropriate treatment for a patient with gender concerns.

- ***Eligibility*** refers to the minimum criteria that anyone seeking to transition must meet.

- ***Readiness*** relates to a person being mentally ready for a particular type of treatment. [Note: The HBIGDA standards explicitly state that mental illness does not necessarily mean a patient is not ready for hormones or surgery. Readiness does not mean an absence of any mental health concerns, but rather a confidence that there is sufficient stability to both make an informed decision and also withstand the stresses of hormones/surgery.]

This handout summarizes standards relating to hormone care. The complete HBIGDA *Standards of Care* are available from HBIGDA (http://www.hbigda.org).

Summary of Minimum Requirements

Eligibility criteria	Readiness criteria
1) At least 18 years of age 2) Informed of anticipated effects and risks 3) Recommended completion of 3 months "real-life experience" or have been in psychotherapy for duration specified by a mental health professional (usually minimum of 3 months): may be waived to prevent unsupervised hormone use	1) Consolidation of gender identity 2) Improved or continuing mental stability

Psychological Assessment Prior to Prescribing Hormones

Prior to prescribing hormones, the HBIGDA standards suggest assessment by a clinician who has:

- at least a master's degree in a clinical behavioural science that has a credentialing process (e.g., psychology, psychiatry, social work, counselling, nursing)
- specialized training and competence in the assessment of sexual and gender disorders as outlined in the *DSM-IV/ICD-10*
- documented supervised training and competence in psychotherapy
- ongoing education in transgender care: workshops, seminars, research, etc.

In some cases the prescribing clinician may have the required training and expertise in transgender medicine to be an assessor. If so, they should document each of the points below. If not, referral to a mental health professional may be necessary; in these cases the HBIGDA standards state that the assessor should write a letter to the prescribing clinician that includes:

- the patient's general identifying characteristics
- diagnoses relating to gender, sexuality, or any other concerns

- duration of professional relationship, including type of evaluation/therapy
- eligibility criteria that the patient has met
- the rationale for hormones (why it is appropriate treatment)
- the degree to which the patient and service provider have followed the HBIGDA *Standards of Care*, and the likelihood that this will continue
- an explanation of the assessor's relationship to others involved in the patient's care
- a statement that the assessor welcomes contact to verify any of the information in the letter

Responsibilities of the Prescribing Clinician

The HBIGDA standards state that the clinician who prescribes the hormones should coordinate all aspects of hormone care, including:

- doing an initial evaluation (health history, physical examination, bloodwork, etc.)
- determining that a patient has the capacity to appreciate the risks and benefits of treatment and to make an informed decision about medical care
- explaining what hormones do and possible side effects/health risks
- informing the patient of the HBIGDA *Standards of Care* and eligibility/readiness requirements
- referring to any specialists who need to be involved
- providing ongoing medical monitoring (regular physical exams relating to hormone effects and side effects, measurement of vital signs before and during hormones, weight measurement, laboratory assessment, etc.)

Hormone Eligibility

The HBIGDA minimum eligibility requirements for cross-gender hormones are:

1) The patient is legally able to give informed consent (considered an adult for the purposes of medical decision making and mentally competent to make decisions regarding medical care)
2) The patient can demonstrate knowledge of what hormones medically can and cannot do and their social benefits and risks

Additionally, it is recommended that patients have undertaken a documented "real-life experience" (RLE) for at least three months, or have been in psychotherapy for a duration specified by a mental health professional after an evaluation (usually at least three months). To avoid the serious health risks of medically unassisted hormone use, it is acceptable within the HBIGDA standards to prescribe hormones without requiring the patient document their RLE or see a counsellor, "as an alternative to black-market or unsupervised hormone use". In these situations, a patient would still need to fulfill the other two eligibility criteria and the prescribing clinician would still have to do a psychological and medical assessment to determine that it is safe to prescribe hormones (as with any other type of prescription).

Hormone Readiness

In addition to the eligibility requirements, the HBIGDA standards include recommendations regarding the assessment of individual readiness for hormones:

1) There is consolidation of gender identity during the real-life experience or psychotherapy;
2) The patient has made some progress in mastering other identified problems, leading to improving or continuing stable mental health;
3) The patient is likely to take hormones in a responsible manner.

Appendix C: Informed Consent Form for Feminizing Medications

This form refers to the use of estrogen and/or androgen antagonists (sometimes called “anti-androgens” or “androgen blockers”) by persons in the male-to-female spectrum who wish to become feminized to reduce gender dysphoria and facilitate a more feminine gender presentation. While there are risks associated with taking feminizing medications, when appropriately prescribed they can greatly improve mental health and quality of life.

You are asked to initial the statements on this form to show that you understand the benefits, risks, and changes that may occur from taking feminizing medication. If you have any questions or concerns about the information below, please talk with the people involved in your care so you can make fully informed decisions about your treatment. It is your right to seek another opinion if you want additional perspective on any aspect of your care.

Please initial and date each statement.

Feminizing Effects

	Patient	Provider	Date	
1.	_____	_____	__/__/__	I understand that estrogen, androgen antagonists, or a combination of the two may be prescribed to reduce male physical features and feminize my body.
2.	_____	_____	__/__/__	I understand that the feminizing effects of estrogen and androgen antagonists can take several months or longer to become noticeable, and that the rate and degree of change can’t be predicted.
3.	_____	_____	__/__/__	I understand that if I am taking estrogen I will probably develop breasts, and:

- Breasts may take several years to develop to their full size.
- Even if estrogen is stopped, the breast tissue that has developed will remain.
- As soon as breasts start growing, it is recommended to start doing monthly breast self-exam, and to have an annual breast exam by a doctor or nurse.
- There may be milky nipple discharge (galactorrhea). This can be caused by taking estrogen or by an underlying medical condition. It is advised to check with a doctor to determine the cause.
- It is not known if taking estrogen increases the risk of breast cancer.

4.	_____	_____	__/__/__	I understand that the following changes are generally not permanent (that is, they will likely reverse if I stop taking feminizing medications):

- Skin may become softer.
- Muscle mass decreases and there may be a decrease in upper body strength.
- Body hair growth may become less noticeable and grow more slowly, but it will likely not stop completely even after years on medication.
- Male pattern baldness may slow down, but will probably not stop completely, and hair that has already been lost will likely not grow back.
- Fat may redistribute to a more feminine pattern (decreased in abdomen, increased on buttocks/hips/thighs – changing from “apple shape” to “pear shape”).

Patient Provider Date

5. _____ _____ __/__/__ I understand that taking feminizing medications will make my testicles produce less testosterone, which can affect my overall sexual function:

- Sperm may not mature, leading to reduced fertility. The ability to make sperm normally may or may not come back even after stopping taking feminizing medication. The options for sperm banking (http://www.ubcivf.com) have been explained to me. I understand that I may still be able to make someone pregnant and am aware of birth control options (if applicable).
- Testicles may shrink by 25-50%. Regular testicular examinations are still recommended.
- The amount of fluid ejaculated may be reduced.
- There is typically decrease in morning and spontaneous erections.
- Erections may not be firm enough for penetrative sex.
- Libido (sex drive) may decrease.

6. _____ _____ __/__/__ I understand that there are some aspects of my body that are not significantly changed by feminizing medications:

- Beard/moustache hair may grow more slowly and be less noticeable, but will not go away.
- Voice pitch will not rise and speech patterns will not become more feminine.
- The laryngeal prominence ("Adam's apple") will not shrink.

Although feminizing medication does not change these features, there are other treatments that may be helpful. If there are any concerns about these issues, referrals can be provided to help explore treatment options.

Risks of Feminizing Medications

Patient Provider Date

7. _____ _____ __/__/__ I understand that the medical effects and safety of feminizing medications are not fully understood, and that there may be long-term risks that are not yet known.

8. _____ _____ __/__/__ I understand that I am strongly advised not to take more medication than I am prescribed, as this increases health risks. I have been informed that taking more than I am prescribed will not make feminization happen more quickly or increase the degree of change: extra estrogen can be converted to testosterone, which may slow or stop feminization.

9. _____ _____ __/__/__ I understand that feminizing medications can damage the liver, possibly leading to liver disease. I have been advised that I should be monitored for possible liver damage as long as I am taking feminizing medications.

10. _____ _____ __/__/__ I understand that feminizing medications will result in changes that will be noticeable by other people, and that some transgender people in similar circumstances have experienced harassment, discrimination, and violence, while others have lost support of loved ones. I have been advised that referrals can be made for support/counselling if I feel this would be helpful.

Medical Risks Associated with Estrogen

Patient Provider Date

11. _____ _____ __/__/__ I understand that taking estrogen increases the risk of blood clots, which can result in:

    - pulmonary embolism (blood clot to the lungs), which may cause permanent lung damage or death
    - stroke, which may cause permanent brain damage or death
    - heart attack
    - chronic leg vein problems

    _____ _____ __/__/__ I understand that the risk of blood clots is much worse if I smoke cigarettes, especially if I am over 40. I understand that the danger is so high that I have been advised that I should stop smoking completely if I start taking estrogen. I am aware that I can ask my doctor for advice about options to stop smoking.

12. _____ _____ __/__/__ I understand that taking estrogen can increase deposits of fat around my internal organs, which is associated with increased risk for diabetes and heart disease.

13. _____ _____ __/__/__ I understand that taking estrogen can cause increased blood pressure. I have been advised that if I develop high blood pressure, my doctor will work with me to try to control it by diet, lifestyle changes, and/or medication.

14. _____ _____ __/__/__ I have been informed that taking estrogen increases the risk of gallstones. I understand that if I have abdominal pain that is severe or prolonged, it is recommended that I discuss this with my doctor.

15. _____ _____ __/__/__ I have been informed that estrogen can cause nausea and vomiting, similar to morning sickness in pregnant women. I understand that if nausea/vomiting are severe or prolonged, it is recommended that I discuss this with my doctor.

16. _____ _____ __/__/__ I have been informed that estrogen can cause headaches or migraines. I understand that if I am frequently having headaches or migraines, or the pain is unusually severe, it is recommended that I talk with my doctor.

17. _____ _____ __/__/__ I understand that it is not known if taking estrogen increases the risk of non-cancerous tumours of the pituitary gland (prolactinoma). I have been informed that although prolactinoma is typically not life-threatening, it can damage vision and cause headaches. I understand that this will be monitored for at least three years when I start taking estrogen.

18. _____ _____ __/__/__ I have been informed that I am more likely to have dangerous side effects from estrogen if I smoke, am overweight, am over 40 years old, or have a history of blood clots, high blood pressure, or a family history of breast cancer.

19. _____ _____ __/__/__ I have been informed that if I take too much estrogen, my body may convert it into testosterone, which may slow or stop feminization.

Risks Associated with Androgen Antagonists

Patient Provider Date

20. _____ _____ __/__/__ I have been informed that spironolactone affects the balance of water and salts in the kidneys, and that this may:

    - increase the amount of urine produced, making it necessary to urinate more frequently
    - reduce blood pressure
    - increase thirst
    - rarely, cause high levels of potassium in the blood, which can cause changes to heart rhythm that may be life-threatening

21. _____ _____ __/__/__ I understand that some androgen antagonists make it more difficult to evaluate the results of PSA (prostate-specific antigen) test, which can make it more difficult to monitor prostate problems. I have been informed that if I am over 50, I should have my prostate evaluated every year.

Prevention of Medical Complications

Patient Provider Date

22. _____ _____ __/__/__ I agree to take feminizing medications as prescribed and to tell my care provider if I am not happy with the treatment or am experiencing any problems.

23. _____ _____ __/__/__ I understand that the right dose or type of medication prescribed for me may not be the same as for someone else.

24. _____ _____ __/__/__ I understand that physical examinations and blood tests are needed on a regular basis to check for negative side effects of feminizing medications.

25. _____ _____ __/__/__ I understand that feminization medications can interact with other medication (including other sources of hormones), dietary supplements, herbs, alcohol, and street drugs. I understand that being honest with my care provider about what else I am taking will help prevent medical complications that could be life-threatening. I have been informed that I will continue to get medical care no matter what information I share.

26. _____ _____ __/__/__ I understand that some medical conditions make it dangerous to take estrogen or androgen antagonists. I agree that if my doctor suspects I may have one of these conditions, I will be checked for it before the decision to start or continue feminizing medication is made.

27. _____ _____ __/__/__ I understand that I can choose to stop taking feminizing medication at any time, and that it is advised that I do this with the help of my doctor to make sure there are no negative reactions to stopping. I understand that my doctor may suggest I reduce or stop taking feminizing medication, or switch to another type of feminizing medication, if there are severe side effects or health risks that can't be controlled.

My signature below confirms that:

- My doctor has talked with me about the benefits and risks of feminizing medication, the possible or likely consequences of hormone therapy, and potential alternative treatment options.
- I understand the risks that may be involved.
- I understand that this form covers known effects and risks and that there may be long-term effects or risks that are not yet known.
- I have had sufficient opportunity to discuss treatment options with my doctor. All of my questions have been answered to my satisfaction.
- I believe I have adequate knowledge on which to base informed consent to the provision of feminizing medication.

Based on this:

_____ I wish to begin taking estrogen.

_____ I wish to begin taking androgen antagonists (e.g., Spironolactone).

_____ I do not wish to begin taking feminizing medication at this time.

Whatever your current decision is, please talk with your doctor any time you have questions, concerns, or want to re-evaluate your options.

_____ _____
Patient Signature Date

_____ _____
Prescribing clinician Signature Date

Appendix D: Informed Consent Form for Testosterone Therapy

This form refers to the use of testosterone by persons in the female-to-male spectrum who wish to become more masculine to reduce gender dysphoria and facilitate a more masculine gender presentation. While there are risks associated with taking testosterone, when appropriately prescribed it can greatly improve mental health and quality of life.

You are asked to initial the statements on this form to show that you understand the benefits, risks, and changes that may occur from taking testosterone. If you have any questions or concerns about the information below, please talk with the people involved in your care so you can make fully informed decisions about your treatment. It is your right to seek another opinion if you want additional perspective on any aspect of your care.

Please initial and date each statement.

Masculinizing Effects

Patient Provider Date

1. _____ _____ __/__/__ I understand that testosterone may be prescribed to reduce female physical characteristics and masculinize my body.

2. _____ _____ __/__/__ I understand that the masculinizing effects of testosterone can take several months or longer to become noticeable, that the rate and degree of change can't be predicted, and that changes may not be complete for 2-5 years after I start testosterone.

3. _____ _____ __/__/__ I understand that the following changes will likely be permanent even if I stop taking testosterone:
    - Lower voice pitch (i.e., voice becoming deeper).
    - Increased growth of hair, with thicker/coarser hairs, on arms, legs, chest, back, and abdomen.
    - Gradual growth of moustache/beard hair.
    - Hair loss at the temples and crown of the head, with the possibility of becoming completely bald.
    - Genital changes may or may not be permanent if testosterone is stopped. These include clitoral growth (typically 1-3 cm) and vaginal dryness.

4. _____ _____ __/__/__ I understand that the following changes are usually not permanent (that is, they will likely reverse if I stop taking testosterone):
    - Acne, which may be severe and can cause permanent scarring if not treated.
    - Fat may redistribute to a more masculine pattern (decreased on buttocks/hips/thighs, increased in abdomen – changing from "pear shape" to "apple shape").
    - Increased muscle mass and upper body strength.
    - Increased libido (sex drive).
    - Menstrual periods typically stop within 1-6 months of starting testosterone.

5. _____ _____ __/__/__ I understand that it is not known what the effects of testosterone are on fertility. I have been informed that even if I stop taking testosterone I may or may not be able to get pregnant in the future. I understand that even after testosterone stops my menstrual periods it may still be possible for me to get pregnant, and am aware of birth control options (if applicable). I have been informed that I can't take testosterone if I am pregnant.

Patient Provider Date

6. _____ _____ __/__/__ I understand that there are some aspects of my body that will not be changed by testosterone:

- Breasts may appear slightly smaller due to fat loss, but will not substantially shrink.
- Although voice pitch will likely drop, other aspects of speech will not become more masculine.

Although testosterone does not change these features, there are other treatments that may be helpful. If there are any concerns about these issues, referrals can be provided to help explore treatment options.

Risks of Testosterone

Patient Provider Date

7. _____ _____ __/__/__ I understand that the medical effects and safety of testosterone are not fully understood, and that there may be long-term risks that are not yet known.

8. _____ _____ __/__/__ I understand that I am strongly advised not to take more testosterone than I am prescribed, as this increases health risks. I have been informed that taking more than I am prescribed will not make masculinization happen more quickly or increase the degree of change: extra testosterone can be converted to estrogen, which may slow or stop masculinization.

9. _____ _____ __/__/__ I understand that testosterone can cause changes that increase my risk of heart disease, including:

- decreasing good cholesterol (HDL) and increasing bad cholesterol (LDL)
- increasing blood pressure
- increasing deposits of fat around my internal organs

_____ _____ __/__/__ I have been advised that my risks of heart disease are greater if people in my family have had heart disease, if I am overweight, or if I smoke.

_____ _____ __/__/__ I have been advised that heart health checkups, including monitoring of my weight and cholesterol levels, should be done periodically as long as I am taking testosterone.

10. _____ _____ __/__/__ I understand that testosterone can damage the liver, possibly leading to liver disease. I have been advised that I should be monitored for possible liver damage as long as I am taking testosterone.

11. _____ _____ __/__/__ I understand that testosterone can increase the red blood cells and hemoglobin, and while the increase is usually only to a normal male range (which does not pose health risks), a high increase can cause potentially life-threatening problems such as stroke and heart attack. I have been advised that my blood should be monitored periodically while I am taking testosterone.

12. _____ _____ __/__/__ I understand that taking testosterone can increase my risk for diabetes by decreasing my body's response to insulin, causing weight gain, and increasing deposits of fat around my internal organs. I have been advised that my fasting blood glucose should be monitored periodically while I am taking testosterone.

Patient Provider Date

13. _____ _____ __/__/__ I understand that testosterone can be converted to estrogen by various tissues in my body, and that it is not known whether this increases the risks of ovarian cancer, breast cancer, or uterine cancer.

14. _____ _____ __/__/__ I understand that taking testosterone can lead to my cervix and the walls of my vagina becoming more fragile, and that this can lead to tears or abrasions that increase the risk of sexually transmitted infections (including HIV) if I have vaginal sex – no matter what the gender of my partner is. I have been advised that frank discussion with my doctor about my sexual practices can help determine how best to prevent and monitor for sexually transmitted infections.

15. _____ _____ __/__/__ I have been informed that testosterone can cause headaches or migraines. I understand that if I am frequently having headaches or migraines, or the pain is unusually severe, it is recommended that I talk with my health care provider.

16. _____ _____ __/__/__ I understand that testosterone can cause emotional changes, including increased irritability, frustration, and anger. I have been advised that my doctor can assist me in finding resources to explore and cope with these changes.

17. _____ _____ __/__/__ I understand that testosterone will result in changes that will be noticeable by other people, and that some transgender people in similar circumstances have experienced harassment, discrimination, and violence, while others have lost support of loved ones. I have been advised that my doctor can assist me in finding advocacy and support resources.

Prevention of Medical Complications

Patient Provider Date

18. _____ _____ __/__/__ I agree to take testosterone as prescribed and to tell my doctor if I am not happy with the treatment or am experiencing any problems.

19. _____ _____ __/__/__ I understand that the right dose or type of medication prescribed for me may not be the same as for someone else.

20. _____ _____ __/__/__ I understand that physical examinations and blood tests are needed on a regular basis to check for negative side effects of testosterone.

21. _____ _____ __/__/__ I understand that testosterone can interact with other medication (including other sources of hormones), dietary supplements, herbs, alcohol, and street drugs. I understand that being honest with my doctor about what else I am taking will help prevent medical complications that could be life-threatening. I have been informed that I will continue to get medical care no matter what information I share.

22. _____ _____ __/__/__ I understand that some medical conditions make it dangerous to take testosterone. I agree that if my doctor suspects I may have one of these conditions, I will be checked for it before the decision to start or continue testosterone is made.

Patient Provider Date

23. _____ _____ __/__/__ I understand that I can choose to stop taking testosterone at any time, and that it is advised that I do this with the help of my doctor to make sure there are no negative reactions to stopping. I understand that my doctor may suggest I reduce or stop taking testosterone if there are severe side effects or health risks that can't be controlled.

My signature below confirms that:

- My doctor has talked with me about the benefits and risks of testosterone, the possible or likely consequences of hormone therapy, and potential alternative treatment options.
- I understand the risks that may be involved.
- I understand that this form covers known effects and risks and that there may be long-term effects or risks that are not yet known.
- I have had sufficient opportunity to discuss treatment options with my doctor. All of my questions have been answered to my satisfaction.
- I believe I have adequate knowledge on which to base informed consent to the provision of testosterone therapy.

Based on this:

_____ I wish to begin taking testosterone.

_____ I do not wish to begin taking testosterone at this time.

Whatever your current decision is, please talk with your doctor any time you have questions, concerns, or want to re-evaluate your options.

_____ _____
Patient Signature Date

_____ _____
Prescribing clinician Signature Date