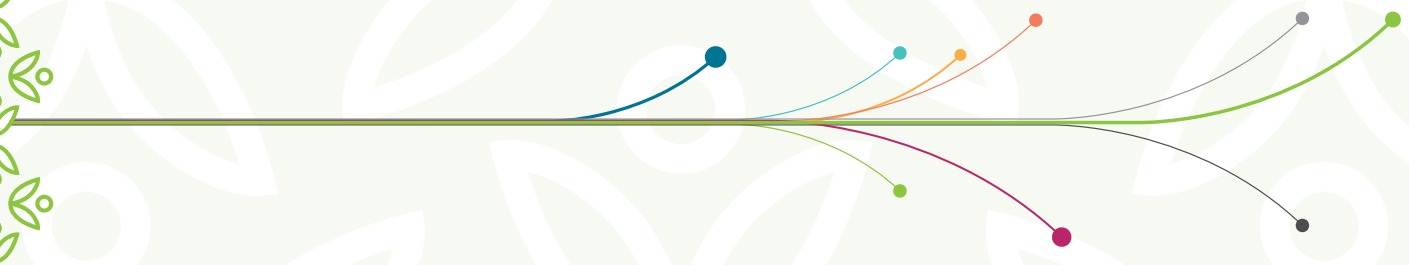
guidelines

FOR GENDER-AFFIRMING PRIMARY CARE WITH TRANS AND NON-BINARY PATIENTS



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Guidelines for gender-affirming primary care with trans and non-binary patients

Trans and non-binary is an umbrella term used to encompass all people whose gender identities and expressions do not align with norms associated with their sex assigned at birth.

Gender-affirming primary care encompasses the delivery of culturally competent care to trans patients in the context of primary care and the collaborative provision of gender-affirming medical interventions. Different medical treatment plans and psychosocial supports are offered depending on the needs and goals of the individual patient.

This publication was developed with financial support from the Province of Ontario. The publication and any views expressed herein are those of Rainbow Health Ontario and do not necessarily reflect those of the Province.

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2023 medication updates to sherbourne's guidelines

FOR GENDER-AFFIRMING PRIMARY CARE WITH TRANS AND NON-BINARY PATIENTS

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CYPROTERONE and risk of meningioma

In addition to the risks and side effects of cyproterone already covered herein, concern is emerging that prolonged use of high-dose cyproterone may be associated with the development of meningiomas.

Meningiomas are rare, most-often benign, tumours of the meninges (membranes covering the brain and spinal cord). Observations of increased incidence in cis women compared with cis men as well as the histological presence of progesterone (and to a lesser degree estrogen) receptors suggest that these tumours are hormone-sensitive.

Meningiomas may present with singular or multiple lesions which are often extremely slow-growing, and as such can remain asymptomatic for many years. Due to their location they may ultimately cause clinically significant symptoms such as headaches, focal neurologic symptoms, mental status changes and seizures. Symptomatic meningiomas may require neurosurgical resection if feasible.

Nine cases of meningioma(s) in transfeminine individuals have been reported in the literature, in whom eight of nine were using cyproterone and seven of nine were using a high dose (50-100 mg) for at least four years.[1,2]

A retrospective study of 2,555 trans women primarily using high dose (50-100 mg) cyproterone for many years following gonadectomy identified an increased standardized incidence ratio compared with the general population (4.1 compared with cis women and 11.9 compared with cis men).[3]

Based on the available data in cis populations using cyproterone, the European Medicines Agency released a statement in 2020 asserting that the risk of meningioma appears to rise with increasing cumulative doses, primarily occurring at doses >25 mg/day. They recommended that doses >10 mg be restricted to certain uses but did not make any recommendation on dose limits for gender-affirming purposes.[4]

WPATH's updated Standards of Care (SOC-8) acknowledges that there may be some concerns with prolonged use (>2 years) and higher doses (>10 mg daily) of cyproterone. They appear to recommend a maximum dose of 10 mg in Table 4, Appendix C, citing a 2021 prospective cohort study's[5] findings that the 10 mg dose provides comparable efficacy (suppression of serum testosterone into the usual range for cis women) with less adverse effects than higher doses. Importantly, however, they conclude that there is insufficient evidence to recommend the use of one androgen blocker over another.[6]

While further research is needed to demonstrate conclusive evidence of a causative relationship between cyproterone and meningioma, the following recommendations can be considered:

- The possibility of increased risk of meningioma with cyproterone should be included in the informed consent discussion with patients choosing an androgen blocker, as well as reviewed in those who have been on >10 mg for >2 years
- If resources exist to compound medications, a lower initial dose of cyproterone can be considered (eg. 2.5-5 mg), with the use of doses >10 mg limited to those with inadequate response to lower doses
- When compounding is not an option, tablets may be quartered to obtain a 12.5 mg dose [a]
- Those using cyproterone (particularly at doses >10 mg for >2 years) should be aware of and monitored for signs and symptoms of meningioma including: changes in vision, hearing loss or ringing in the ears, loss of smell, headaches, memory loss, seizures or weakness in the arms and legs
- No routine screening for meningioma is recommended for asymptomatic patients, regardless of dose/duration
- In those who present with symptoms concerning for meningioma, MRI or CT of the brain (and spinal cord if spinal meningioma is suspected) is recommended[7]
- As previously noted in these guidelines, personal history of meningioma should be considered a contraindication to cyproterone
- Cyproterone should be discontinued permanently if meningioma is identified
- Any plan for the ongoing use of higher doses of cyproterone following gonadectomy should be reconsidered given that the balance of potential risks and benefits is unlikely to favour its use in this setting

NOTE: Major adverse events remain uncommon even in those using long-term and higher-dose cyproterone.

[a] *Commercially available cyproterone in Canada is available only in a 50 mg tablet. Accounting for medication lost during the splitting process, quartering may in fact result in an average dose closer to 10 mg.*

updates,continued

TESTOSTERONE PATCHES

Testosterone patches were discontinued in 2021 and are no longer available.

ETONOGESTREL SUBDERMAL IMPLANT

The availability of the etonogestrel implant (Nexplanon) offers an additional option for contraception in transmasculine individuals. However, the common side effect of irregular spotting may limit its utility for menstrual cessation, particularly in the absence of exogenous testosterone administration.

FINASTERIDE

The benefit of 5-alpha-reductase inhibitors for the treatment of androgenic alopecia in transmasculine individuals should be balanced with the possibility of impairment of both clitoral growth and the development of facial and body hair.[6]

REFERENCES

1. Mancini, I, Rotilio, A, Coati, I, Seracchioli, R, Martelli, V, Meriggiola, MC. Presentation of a meningioma in a transwoman after nine years of cyproterone acetate and estradiol intake: Case report and literature review. Gynecological Endocrinology, 2017; 34(6), 456–459. https://doi.org/10.1080/09513590.2017.1395839

2. Ter Wengel, PV, Martin, E, Gooren, L, Den Heijer, M, Peerdeman, SM. Meningiomas in three male-to-female transgender subjects using oestrogens/progestogens and review of the literature. Andrologia, 2016; 48(10), 1130–1137. https://doi.org/10.1111/and.12550

3. Nota, NM, Wiepjes, CM, de Blok, CJM, Gooren, LJG, Peerdeman, SM, Kreukels, BPC, den Heijer, M. (2018). The occurrence of benign brain tumours in transgender individuals during cross-sex hormone treatment. Brain, 2018; 141(7), 2047–2054. https://doi.org/10.1093/brain/awy108

4. European Medicines Agency. Restrictions in use of cyproterone due to meningioma risk [internet]. [cited 2023 May 1]. Available from: https://www.ema.europa.eu/en/documents/referral/cyproterone-article-31-referral-restrictions-use-cyproterone-due-meningioma-risk_en-0.pdf

5. Kuijpers, S, Wiepjes, CM, Conemans, EB, Fisher, AD, T'Sjoen, G, & den Heijer, M. Toward a lowest effective dose of cyproterone acetate in trans women: Results from the ENIGI study. The Journal of Clinical Endocrinology & Metabolism, 2021; 106(10), e3936–e3945. https://doi.org/10.1210/clinem/dgab427

6. Coleman, E. et al. Standards of Care for the Health of Transgender and Gender Diverse People, Version 8, International Journal of Transgender Health; 2022, 23:sup1, S1-S259. https://doi.org/10.1080/26895269.2022.2100644

7. Park, JK, Epidemiology, pathology, clinical features, and diagnosis of meningioma [Internet]. UpToDate. 2023. Available from: https://www.uptodate.com/contents/epidemiology-pathology-clinical-features-and-diagnosis-of-meningioma

this update added November 2023 by Rainbow Health Ontario

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Part I: An introduction to gender-affirming care and hormone planning visits

ABOUT SHERBOURNE HEALTH AND A HISTORY OF THIS DOCUMENT

The *Guidelines for Gender-affirming Primary Care with Trans and Non-Binary Patients,* 4th edition ("the Guidelines"), outlined in this document reflect primary care practice with trans patients as approached by providers at Sherbourne Health (Sherbourne).

Sherbourne is a dynamic provider of integrated health services, community programs and capacity-building initiatives that enable people in diverse communities to achieve wellness.

As an urban health agency in downtown Toronto, Sherbourne provides holistic primary care and chronic disease management, mental health services, health promotion and education, and outreach and social supports. Sherbourne's doors are open to everyone, with a focus on the LGBT2SQ community, homeless and under-housed people, and newcomers to Canada, whose complex needs are often not met by traditional health care. Sherbourne combines high-quality clinical care with responsive, culturally appropriate community development programs that bring low-barrier services to people in the surrounding communities who need it most.

Sherbourne's focus on LGBT2SQ people has resulted in the clinic attracting a large number of trans and non-binary patients who receive a range of clinical, health promotion and support services. Rainbow Health Ontario, a program of Sherbourne Health, has a mandate to improve LGBT2SQ health outcomes in Ontario by creating opportunities for the health care system to better serve LGBT2SQ communities. This includes supporting clinicians and health care organizations to improve their knowledge, skills and abilities to serve LGBT2SQ populations across the province. Since 2011, Rainbow Health Ontario has been delivering clinical trainings based on the Guidelines.

The first iteration (2003) of the Guidelines was created by Dr. Leslie Shanks for internal use at Sherbourne. They were developed in consultation with trans community members and were informed by the limited available guidelines and practices in other parts of the world. At that time, meeting transition-related needs in the context of primary care was a relatively new approach, and Sherbourne was one of the few options in the province for trans patients.

As Sherbourne's waitlist for trans patients grew, the Guidelines were made available to other clinicians open to providing gender-affirming care to trans patients.

The Guidelines have been revised on a regular basis in order to remain up to date with current literature, and to evolve with cultural changes in the trans communities that we serve. With subsequent editions, the Guidelines have been increasingly used across Ontario and beyond as a practice resource.

Since 2003, when the Guidelines were first created, there has been a growing recognition in the medical community that trans-specific health care needs (i.e., hormone therapy and surgical planning) can be addressed in a timely and effective manner in the context of primary care.[1,2] With an increasing number of people presenting for gender-affirming care, there has also been a greater recognition of the size and diversity of trans populations.

Similarly, over time the Guidelines have expanded beyond just being a set of hormone protocols to a more comprehensive guide to gender-affirming primary care.

The 2009 edition, revised by Dr. Kate Greenaway, became the first edition that was widely distributed in paper and available publicly online. The 2015 edition, which presented an expanded discussion of long-term preventive care and introduced new tools for practice, subsequently formed the basis of the Trans Primary Care Guide,[3] an online, interactive educational tool for providers. Since this online tool was released, it has been accessed by over 85,000 users around the world, with its monthly access numbers steadily climbing.

DISCLAIMER AND LIMITATIONS

As noted above, the Guidelines are best described as a detailed summary of Sherbourne Health's approach to clinical practice with trans and non-binary patients.

The medical team at Sherbourne is made up of family physicians, nurse practitioners and nurses. While we are not gender specialists by training, we have developed expertise by virtue of the volume of patients we see and whose care we manage, and whose experiences we listen to and learn from. We have also gained expertise and knowledge through our collaboration with specialist colleagues in cases with more complex patients. Additionally, we have had the opportunity to learn from colleagues who are both providers and members of trans communities.

To our knowledge, with 573 trans patients on our active roster, we have the largest panel of trans patients of any single primary care team in Canada. The Lancet[2] identified Toronto, along with Vancouver, Boston and Sydney, as cities where effective, comprehensive care is provided to trans patients in the context of primary care. We recognize that our experience gives us the ability to provide guidance to other primary care providers (PCPs), as well as other clinicians providing care to trans patients.

The Guidelines have been prepared with this purpose in mind: they are meant to reflect our approach to gender-affirming primary care with trans patients and to help other providers by describing our practice.

Like any good practice, ours is fundamentally iterative and changing as new research becomes available. We have implemented changes as our understanding of gender diversity has evolved and our frameworks for diagnosis and treatment have become more personalized and collaborative. With each iteration, the number of providers who have peer reviewed the guidelines has increased, as has the amount of feedback we have received from providers who are using the guidelines in their practice.

We are always seeking to improve, and we welcome feedback and critique of the Guidelines both from providers and members of trans communities, across Ontario and beyond.

Available literature and the Guidelines

While every attempt is made to review the current literature, there are some limitations to consider. The Guidelines do not attempt to present an exhaustive review of the literature or a meta-analysis of trans health research. While we attempt to integrate new research into our practice (and so the Guidelines), and consider our approach to be evidence-based, we do not make formal, evidence-graded recommendations. Any guidelines in this area of practice—these guidelines notwithstanding—are also limited by the quality of available research on trans health.

Where relevant, studies of non-trans (i.e., cisgender, or "cis") populations are also considered, so as to provide the safest, most evidence-informed practice possible.

While the number of studies relating to the health of trans communities has increased markedly in the 15 years since Sherbourne began providing trans care, the vast majority of studies have had significant limitations. Most are hindered by small sample sizes obtained through convenience sampling.

Larger studies have been undertaken, such as the 2015 U.S. Trans Survey from the National Center for Transgender Equality (see the survey website for study details and findings).[4] However, while helpful in providing snapshots of issues potentially experienced by trans people in general, the convenience sampling and lack of prospective data collection limits their generalizability. Experimental research examining specific interventions with trans populations is even more scarce.

The absence of "gold-standard" research, however, does not rule out the possibility for evidence-informed practice. Our approach to primary care is informed by the wide array of studies highlighting the positive outcomes of medical interventions with trans patients,[5] and is, in turn, supported by our clinical experience.

Trans and non-binary children and youth

This document focuses on gender-affirming primary care with individuals who have completed puberty, and does not address considerations for trans and non-binary children or youth who have not completed puberty.

While some PCPs have developed expertise in this area, an in-depth discussion of this treatment is beyond the scope of this document.

At this time, providing care under the guidance of an expert or referral to a specialized clinic or another provider with expertise in supporting trans children and youth is recommended.

Of note, training sessions for primary care and other providers wishing to extend care to trans and non-binary children and youth (including pubertal suppression), are in development at RHO and are expected to launch in spring 2020.

Transition-related surgeries (TRS)

In addition, while the referral process and the role of PCPs in supporting patients seeking transition-related surgeries (TRS) is discussed, detailed guidance for conducting surgical planning visits is beyond the scope of this document. Providers interested in conducting surgical planning visits are encouraged to participate in Rainbow Health Ontario's TRS planning training session,[6] or to acquire the required competencies by comparable means (see the *"Supporting patients with transition-related surgeries (TRS)" on page 30* for more information).

Conclusion

We do not present the Guidelines as a "standard of care," but instead as an evidence-informed guide to help clinicians in their day-to-day practice. They are meant to be applied with flexibility to meet the breadth of health care needs of trans

and non-binary people. Clinicians can consider adaptations based on each patient's unique anatomic, social or psychological situation, according to patient or systemic resource limitations, or the need for harm reduction strategies.

We have presented a number of precautions, contraindications and risks associated with hormone administration, stressing the importance of considering the individual benefits and risks for each patient. Clinicians must use their own expertise and decision-making skills within each clinical encounter instead of relying on this document to provide definitive answers. We encourage providers to consult other sources of information and to seek peer support when needed (see *Appendix I* in this document for additional information and resources).

These revisions will also be reflected in a corresponding update of Rainbow Health Ontario's online Trans Primary Care Guide.[3] Originally developed in 2016 with the help of a community-based, iterative design research strategy, the *Trans Primary Care Guide* offers clinicians an interactive online platform to guide their learning.

Changes in this edition

In addition to the incorporation of recently available evidence in both general primary care and trans health, this 2019 edition includes revisions and expansions in several areas, including:

- expanded discussion of considerations for non-binary patients;
- unique considerations for older trans patients;
- incorporation of changes to the International Statistical Classification of Diseases and Related Health Problems (ICD) diagnosis;
- subtle language changes that reflect the rapid pace of cultural change;
- an expanded discussion of fertility considerations for trans people;
- discussion of alternate routes of hormone administration;
- expanded discussion of HIV prevention and treatment in transfeminine and transmasculine populations;
- an updated monitoring schedule with a reduced number of routine bloodwork parameters required;
- an overview of the role of PCPs in supporting patients with transition-related surgeries; and
- a review of the updated process for referrals and public funding for transition-related surgeries in Ontario.

An introduction to trans and non-binary communities and their health care

AN OVERVIEW OF TRANS COMMUNITIES: SIZE, DIVERSITY AND LANGUAGE

A recent compilation of population-based surveys in the United States suggests that the number of self-identified trans people is growing and currently represents approximately 0.6% of the population (as a conservative estimate), with a higher prevalence among youth.[7] The Trans PULSE Project, which studied trans people in Ontario, showed that although urban centres are often sought out by trans people wishing to access health care, approximately 70% of trans Ontarians live outside the Greater Toronto Area.[8]

Trans PULSE also painted a portrait of a very diverse patient population with respect to age, ethnicity, sexuality, income and education. However, while many trans patients may be highly educated, income security is a common concern. The study also included many findings related to experiences of transphobia and violence, as well as challenges with finding family physicians willing to provide gender-affirming care.[9,10] Taken as a whole, mental health and suicidality were marked concerns. Most significant, however, is that these problems have been shown to become much less prominent for trans patients who have undergone medical (i.e., hormonal and/or surgical) interventions to affirm their gender identity, when medical transition is part of how someone wants to transition.[11]

The use of language regarding gender identity and gender expression is constantly evolving. Over the past several years, many new terms have emerged whose meanings vary over time, and within and between disciplines.[13] In particular, terminology has expanded to reflect a spectrum of identities outside the traditional binary understanding of gender.

Trans PULSE

Trans PULSE was a multi-year community-based research initiative that used mixed methods to better understand the health of trans communities in Ontario. Its most significant component was a large 2009–2010 survey (n=433) of trans persons; through the use of respondent-driven sampling, it produced data that could be generalized to all Ontario trans people. An overview of sex and gender diversity within trans communities by Scheim and Bauer can be downloaded for free. See the Trans PULSE website for more information.[12]

The core researchers involved in Trans PULSE—together with trans and cis researchers, healthcare providers and other community partners—have recently acquired Canadian Institutes of Health Research (CIHR) funding to conduct a national study to better understand and quantify the health of trans people and their access to services. With nine priority populations across the country, Trans PULSE Canada is seeking to duplicate the success of the initial study on a national scale. In so doing, it will provide the best opportunity to date to gather large-scale, robust data about trans people across Canada.

In line with the World Professional Association for Transgender Health (WPATH) Standards of Care (SOC),[14,i] we aim to recognize and support the full spectrum of gender identity and expression. Fundamental to this work is using respectful and affirming language that aligns with a patient's self-identification whenever possible.

i WPATH, formerly the Harry Benjamin International Gender Dysphoria Association (HBIGDA), is an interdisciplinary organization that promotes evidence-based care and research in transgender health. Their Standards of Care (SOC), first published in 1979 and now in its 7th edition, provide professional consensus around medical and mental health support for trans individuals.

While providing concrete definitions for terms that are fluid and evolving is bound to be imperfect, we have made some generalizations for the sake of practicality, and to improve communication with and understanding of trans and non-binary patients. In this document, we use the term "transmasculine" to refer to patients who were assigned female at birth (or "AFAB") but whose sense of self is of being a man or on the masculine spectrum.

Similarly, we use the term "transfeminine" to refer to patients who were assigned male at birth (or "AMAB") but whose sense of self is of being a woman or on the feminine spectrum. However, the terms "trans men" or "transgender men" and "trans women" or "transgender women" are used when citing original research that uses these terms to describe their study populations.

In general, we use the term "non-binary" to refer to patients who do not identify with traditional binary concepts of gender. These patients may feel that their gender falls somewhere between (or outside of) the binary notions of "man" or "woman." Some non-binary patients may also use the terms genderqueer, genderfluid, pangender or agender, among others, to describe themselves. People who are non-binary may also choose gender-neutral pronouns, such as "they/them/their," or other gender-neutral pronouns.

With all trans and non-binary people, using the correct pronouns as well as the name they use in daily life is fundamental to culturally competent care.

We encourage the use of "cis," a short form for "cisgender," to refer to non-transgender people over terms such as "natal," "biological" or "genetic," because these suggest that trans people have a less valid claim to their gender than cis people. Additionally, using "cis" to describe our non-trans patients (as opposed to just identifying them as "men" and "women") challenges the expectation that all our patients are and will be cis. Dealing with cissexism—the privileging of cis bodies and identities over trans ones—and transphobia are unique challenges that are faced by our trans patients.[15]

More about prefixes: cis and trans

cis pr. "sis," Latin origin

- A prefix meaning "on the same side of"
- Refers to a state of alignment of one's gender identity with the gender assigned at birth

trans pr. "trans" Latin origin

- A prefix meaning "across," "beyond"
- Refers to a state of incongruence of one's gender identity with the gender assigned at birth

A glossary summarizing the meaning of several terms as we perceive them to be most commonly understood in our current cultural context can be found in *Appendix H*.

COLONIALISM, GENDER AND INDIGENOUS CULTURES

This discussion would be incomplete without acknowledging that academic and social concepts of gender and sexuality, including trans identities, are largely rooted in and informed by Western cultural belief systems. Different cultures throughout history have conceptualized diversity in gender identity and expression in a myriad of ways. Not all people align or identify with Western concepts.

Particularly relevant to the Canadian context, Indigenous peoples may not identify with Western concepts or language around gender diversity. The term Two-Spirit (also referred to as 2-Spirit or Two-Spirited) was coined in 1990 to distinguish the wide variety of Indigenous concepts of gender and sexual diversity as separate from the European concepts imposed on Indigenous communities through colonization.[16] One of the most commonly cited understandings of the term Two-Spirit is a

person who possesses both masculine and feminine spirits, but Two-Spirit can mean different things to different people and different communities, and often holds space for the flux and flow of gender and sexuality. Some may alternatively identify with a nation-specific term, as many Indigenous languages have words for the gender and sexual diversity traditionally found in their communities.[ii] Others do not identify with Indigenous terms and may identify as trans, non-binary or LGBQ.

In many traditional Indigenous cultures, sexual and gender diversity are viewed holistically, with people of many genders and sexualities holding important roles in families and communities.[17,18] It should not be assumed, however, that all Indigenous individuals who hold diverse sexual and gender identities will be embraced by their communities.

As with people who identify as trans or non-binary, those who identify as Two-Spirit may or may not seek to modify their appearance through hormones and/or surgeries. When working with any Indigenous community members, providers should make efforts to respect Indigenous understandings of health and wellness, which may be different than those of healthcare providers.[19] For more information on LGBTQ Indigenous and Two-Spirit health, see Rainbow Health Ontario's Evidence Brief: Two-Spirit and LGBTQ Indigenous Health.[20]

ii An historical exploration of the attitudes and expression around gender and sexuality in Native America can be found in Gender and Sexuality in Indigenous North America, 1400-1850, Slater and Yarbrough, University of South Carolina Press, 2015.

Introduction to gender-affirming primary care

THE ROLE OF THE PRIMARY CARE PROVIDER (PCP)

Health care professionals are increasingly in consensus that trans and non-binary communities are an underserved population—one whose health care needs can be effectively addressed in the context of primary care.[2] Accordingly, primary care providers (PCPs) have taken an increasingly important role in providing gender-affirming care to trans patients.

Since PCPs usually have familiarity and a longitudinal relationship with patients, they are ideally situated to facilitate and support a patient's transition process. In most cases, providing hormone therapy is within the scope of primary care. A 2013 study showed that 67% of trans people in Ontario who were on hormone therapy received treatment from a PCP[21] (a number that is almost certainly greater now). However, finding a PCP who will assist with medical transition and provide sensitive, knowledgeable primary care remains a frequent challenge.[9,10]

One of the historical barriers to providing gender-affirming care has been the absence of education about trans health in medical, nursing and other health professional education.[22] Individual efforts are being made to incorporate gender diversity and trans-related health topics into the curriculum at a number of Canadian medical and nursing schools, but there remains no standardized curriculum or learning objectives for these programs. While future providers are likely to have greater familiarity, providers currently in practice lack formal training, and so may find the care of trans patients unfamiliar and intimidating.

The historical lack of education and available resources—as well as lingering perceptions that transition-related care falls exclusively under the domain of specialists—has limited the number of PCPs working with trans patients. As a result, only PCPs who are invested in enhancing their knowledge, skills and cultural competency have integrated gender-affirming care into their practice. The number of providers engaged in this work has grown over the past decade as more PCPs recognize the value, reward and importance of providing gender-affirming primary care to trans patients.

While the situation is improving, the historical shortage of clinicians available to provide gender-affirming primary care has often led to trans patients experiencing protracted searches, long waitlists or distant travel to find providers able to assist with their transition goals. After undergoing an internal search to make sense of their gender (a process which can vary greatly from person to person), many patients often have to embark on a protracted external search to find a supportive PCP.

This critical time, between when a trans person feels they need to start making physiologic changes to their appearance and when they are actually able to find a provider to help with those changes, is when trans patients are most at risk for depression and suicide. Providing timely transition-related care can have a substantial positive effect on mental health, while also decreasing suicidality and suicide attempts.[23]

Research to this effect resonates with our clinical experience and underscores the importance of timely access to gender-affirming care.

ENDOCRINOLOGIST INVOLVEMENT

Referral to an endocrinologist may be appropriate and helpful, particularly in the case of a medically complex patient, but it is not required as a matter-of-course for most trans and non-binary patients.

Furthermore, outside major urban areas, an endocrinologist with experience treating trans patients may not be available, and requiring a consultation may result in an unduly long and stressful wait. If consultation is sought, it may be helpful to consider starting an androgen blocker with or without the addition of low-dose estrogen for patients desiring feminizing effects or low-dose testosterone for patients desiring masculinizing effects until the consultation can be obtained.

While most trans patients do not require referral to a specialist to begin cross-gender hormones, this does not obviate the important role that endocrinologists can have for some patients.

A common instance where there is usually active involvement of an endocrinologist is in the case of youth who have not completed puberty. If an adolescent patient has not completed puberty, in the current context we suggest providing care under the guidance of an expert or referral to a specialized clinic or another provider with expertise in supporting trans children and youth. Specialized clinics in Ontario include the Transgender Youth Clinic at The Hospital for Sick Children[24] and the Diversity Clinic at the Children's Hospital of Eastern Ontario.[25]

As previously mentioned, RHO is currently developing training sessions for PCPs and other providers interested in gaining expertise in caring for this population.

TAKING THE NEXT STEP: PROVIDING GENDER-AFFIRMING CARE TO TRANS AND NON-BINARY PATIENTS

Assisting patients with the actualization of their gender identity can be an incredibly rewarding part of our work as primary care providers (PCPs). While not without its complexities and challenges, transition can be a celebratory and revelatory journey. Being able to assist patients with actualizing their internal sense of self is an honour and privilege. We wish to share this experience with other providers and hope this document enables more PCPs to be actively involved in the care of their trans patients.

We hope that this resource can be your touchstone as you embark on this clinical journey with your patients. It is a document that you can read through once to familiarize yourself with some key fundamentals regarding the population, language and considerations that trans patients may present for your practice (for example, do trans women need mammograms?), while bookmarking key tables, dosage suggestions, monitoring parameters and so on, so that you can easily refer back to these at point of care. The previously referenced online Trans Primary Care Guide[3] is also a useful resource based on the Guidelines and includes Quick Reference Guides.

For those new to providing gender-affirming hormone therapy, it may be easier for your first patient to already be receiving hormones begun by another provider while you are gaining comfort and experience. If possible, shadowing another provider's practice may also enhance your comfort level. These are not requirements, but suggestions in case you are seeking additional support.

As increasing numbers of PCPs have incorporated aspects of trans health care into their practice, our collective capacity to provide care to trans patients, support one another's practices and develop resources has also increased. Ontario Telemedicine Network's e-consult service and Rainbow Health Ontario's trans care mentorship call[26] can also be valuable sources of timely advice and support. Appendix I lists other valuable resources, both local and international, that you can draw on when you are faced with more complex cases. You are not alone, and your efforts in enhancing your skills will be greatly valued by your current and future patients.

We hope you find this work as rewarding as we do and welcome you to this exciting facet of contemporary primary care practice.

> "I will never forget the feeling that I had after handing my first trans patient their hormone prescription after a year of them being bounced between endocrinologists and psychiatrists. It is by far one of the highlights of my career thus far."
>
> —Corey Doughty, NP, Elliot Lake Family Health Team

A FRAMEWORK FOR PROVIDING GENDER-AFFIRMING PRIMARY CARE TO TRANS AND NON-BINARY PATIENTS

Gender-affirming primary care falls into two distinct branches: delivering transition-related interventions and care, and addressing all the other primary care needs of trans patients in a way that is sensitive to the unique needs of these individuals. This section provides a high-level overview of what trans primary care includes, and in doing so introduces the various aspects of care detailed in the Guidelines.

Internationally, there are a number of protocols and guidelines regarding transition-related medical interventions that will be referenced in this document. The best-known example is the Standards of Care document from the World Professional Association for Transgender Health (WPATH).[14] While generally considered the gold standard, it does not provide specifics for hormone provision or direction around certain aspects of primary care. Similar to the Guidelines, several community and academic centres in North America[iii] have also developed publicly available protocols that provide more specific details on their practices of gender-affirming care:

- Trans Care BC's Gender-Affirming Care for Trans, Two-Spirit and Gender-Diverse Patients in BC: A Primary Care Toolkit[19]
- Fenway Health's The Medical Care of Transgender Persons[27]
- Callen-Lorde's Protocols for the Provision of Hormone Therapy[28]
- University of California, San Francisco (UCSF)'s Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People[29]

The second broad area for delivering primary care to trans patients is consideration of how a patient's trans identity requires a different approach to providing care that is not directly related to medical transition.

Trans patients can present with any of the same issues and conditions as cis patients, and in most cases there is nothing that needs to be done differently. While this may seem obvious, trans patients often describe encounters for health issues unrelated to gender during which the provider seems focused on irrelevant details such as whether or not they have had genital surgery.

However, it *is* important to consider how trans patients may need a slightly different approach in some areas of primary care practice: tasks like disease prevention and screening (e.g., when and how to approach Pap testing with transmasculine patients), or discussions about fertility or safer sex and STI testing, which may also require us to think differently.

Unfortunately, preventive health is often divided into discrete gender categories, with the assumption that these align with a particular type of body. For example, cisnormative assumptions lead us to think that cervical cancer screening is part of "women's health." This thinking is pervasive, and often reflected in prevention and education materials (e.g., province-wide reminder mail-outs to OHIP cardholders with a gender-marker of "F," most major clinical guidelines, and in electronic medical record systems).[30]

Trans-inclusive practices include consideration of how posters on the office wall, patient handout materials, and processes for data collection and management can erase trans patients, leading to suboptimal patient encounters and negative impacts on health. It is also important to reflect on approaches to clinical encounters with trans patients (e.g., consider offering to use a side-lying rather than lithotomy position when doing a Pap test with trans men) to provide a more comfortable and gender-affirming experience.

It is beyond the scope of the Guidelines, and likely an impossible task, to identify *every* instance where trans patients may require us to think differently about how we approach our work. However, beginning to reflect on these issues is an important step. When interacting with trans patients, asking what's most comfortable for them is fundamental—what one patient prefers is not always transferable to the next.

iii Acknowledgments to Tom Waddell Health Center for demonstrating early leadership in the informed consent model.

AN INDIVIDUALIZED APPROACH

Given the spectrum of gender identity and the variation in each person's expression, there is no single pathway for a trans person to follow in order to actualize the presentation of their authentic self. While hormones and/or surgeries are medically necessary for many trans people in order to create alignment with their experienced gender, for others it may be sufficient to modify their presentation through changes in legal identification and modifications to their gait, dress, voice, and/or through hair removal.

When hormones are required as part of transition, some patients may seek maximum feminization/masculinization, while others may seek a more androgynous appearance. Hormone therapy may also be helpful for patients who do not wish to make a social transition or who are unable to do so.[31] Both the dose and route of hormone treatments may be individualized to meet a patient's specific treatment goals. The duration of therapy may also be personalized: patients who have not undergone gonadectomy, for example, may opt to discontinue hormone therapy if the irreversible changes are adequate to maintain the needed presentation.

While hormone therapy is generally required prior to genital surgery or gonadectomy (unless contraindicated), it is not considered a requirement prior to breast,[iv] chest or other gender-affirming procedures.[13] The decision to undergo surgical interventions is also highly individual.

Considerations for non-binary patients

Research suggests that at least 20% of trans people do not have a binary gender identity.[33] Like other trans patients, non-binary patients may seek medical assistance with modification of primary and secondary sex characteristics. Unfortunately, lack of familiarity with non-binary identities and normative assumptions on the part of healthcare providers may lead to additional barriers to accessing gender-affirming treatments.[34,35]

People who identify as non-binary have an equally valid claim to their identities, and the same range of needs for and entitlement to gender-affirming hormone therapy and surgeries as binary-identified cis and trans people.

It is important to discuss the desired configuration of primary and secondary sex characteristics and expectations regarding outcomes with non-binary patients. While dose, duration, route and type of hormone therapy can be individualized, it may not be possible to achieve certain combinations of effects (for example, a deeper voice without facial hair growth). Some non-binary people may express the need for contrasting masculine and feminine characteristics, such as breasts and facial hair, to align with their experienced gender.[29]

Hormone therapy considerations that may be unique to non-binary patients will be referred to throughout *Part II: Feminizing hormone therapy*, and *Part III: Masculinizing hormone therapy*, later on in this document.

iv Though not required by WPATH, MOHLTC funding criteria for breast augmentation includes the absence of breast growth despite 12 months of continuous hormone therapy unless contraindicated.[32]

Hormone initiation

At Sherbourne Health we follow a common approach to the initiation of hormone therapy with patients. This approach is designed to maximize the satisfaction and well-being of the patient, fulfil the legal and ethical requirements of the PCP, and reduce the possibility of inappropriate treatment. The trans population has suffered a great deal of prejudice, misunderstanding and harm from the medical community, and systemic oppression experienced by trans patients has often resulted in denial of service.[1,36]

In traditional models of hormone provision, the healthcare provider's role in assessing a patient's eligibility and readiness for hormone therapy has contributed to an unfortunate dynamic, with the provider positioned as the "gatekeeper" to treatment. In response to this, a number of health centres in the US implemented what has become known as the "informed consent model" for hormone provision (e.g., Tom Waddell Health Center in San Francisco, Callen Lorde Community Health Center in New York City and Fenway Health in Boston).

This model focuses on obtaining informed consent as the threshold for the initiation of hormone therapy, without requiring an in-depth mental health assessment or referral, unless significant mental health concerns are identified. The WPATH SOC7 recognizes the validity of both the traditional and informed consent models to the initiation of gender-affirming hormone therapy. The informed consent model should be differentiated from "hormones on demand," which implies that anyone who asks for hormones will receive a prescription in all cases, giving no scope to the expertise or judgment of the prescribing clinician.[37,38]

At Sherbourne, we approach the decision to initiate hormone therapy as a collaborative, patient-centred process that focuses on both psychosocial preparation and informed consent. We believe that the PCP (with or without the support of a multidisciplinary team) can facilitate a decision-making process that informs, educates and supports patients. The provider or care team takes an active role in assisting a patient in meeting their transition-related goals and addressing any existing barriers to the safe administration of hormone therapy.

Many providers are concerned about the possibility of regret: treating a patient with hormone therapy who later realizes a preference for the gender role associated with the sex assigned at birth. We aim to develop realistic goals and expectations with patients to prevent post hoc disappointment or regret. Regardless, this is a very rare occurrence. A survey of 12 clinics in the United States (representing 1,944 patients treated) operating under the informed consent model revealed a prevalence of cases of regret of 0.8%, with just 0.1% leading to a reversal of gender transition. No cases of malpractice claims, settlements or judgements relating to regret were reported or found following a thorough literature review conducted as part of the same study.[39]

Providers may additionally have concerns regarding the impact of hormone therapy on a patient's physical health. As discussed above, there is a lack of long-term prospective studies for most trans-specific health issues, but a number of long-term studies on cross-sex hormone therapy from the Netherlands present some reassuring long-term safety data.[40–46] Emerging evidence indicates that modern hormone regimens do not have a significant negative impact on morbidity and mortality. Following a systematic review, Weinand and Safer concluded that "current literature suggests that hormone therapy is safe when followed carefully for certain risks," though they acknowledge the limitations associated with the lack of high-quality studies.[47]

Known risks, which we will fully explore in the Guidelines, should be considered and mitigated when possible. For each patient seeking hormone therapy, it is important to not only consider the possible risks of treatment, but also the often substantial risks of withholding treatment.

For example, data obtained as part of Trans PULSE[v] demonstrates that the highest risk for suicide among trans people occurs in those who are planning to medically transition but have not yet begun.[23]

Those who are not able to access hormone therapy through a healthcare provider may opt to take hormones without a prescription (in the case of feminizing hormones, this may include less safe forms of estrogen) without monitoring for adverse effects, potentially putting themselves at risk.[21] Two studies pointedly illustrate that the bulk of morbidity and mortality suffered by transgender patients is related to the challenges of being trans in our society, which have nothing to do with hormone therapy.[40,48]

THE HORMONE PLANNING PERIOD

At Sherbourne Health, new patients are usually seen for a number of visits prior to the initiation of hormone therapy. This period allows the provider to become acquainted with the patient, provide education regarding the anticipated effects as well as the potential risks of hormone therapy, determine the need for services such as fertility preservation, and offer additional support if needed. The number of visits needed to complete these tasks can vary depending on the length of time available for each visit, the experience of the provider and clinical factors.

The planning period tasks are listed and expanded upon below. *Appendix A* provides a checklist designed for use at the point of care, while *Appendix K–Appendix M* provide summaries that PCPs can review with patients to assist in providing patient education and ensuring informed consent.

v Trans PULSE found that past-year suicide attempts were 27% in those who wanted to undergo a medical transition but were not yet able to start or find a provider to help them. Past-year suicide attempts decreased to 1% in trans people who, by their own definition, had "completed" a medical transition.

Tasks for the planning period include:

- reviewing general medical intake and medical history;
- orienting to process and explaining rationale for the planning period and recommendations for follow up/hormone monitoring;
- obtaining/reviewing previous medical records (if patient is new to one's practice);
- exploration of gender identity and expression;
- confirming existence of gender dysphoria/gender incongruence and excluding rare differential diagnoses;
- discussion of gender-affirming goals;
- reviewing expected benefits (reversible vs. irreversible), potential side effects, risks and contraindications to hormone therapy;
- exploring social supports and plans for work/school, and discussing available ancillary supports if indicated (counselling, peer support, etc.);
- reviewing lifestyle and mental health considerations;
- performing focused physical exam and baseline investigations, reviewing routing health promotion/disease prevention/screening commensurate with age;
- discussing fertility, contraception and sexual health (NB fertility preservation, if a priority for the patient, should ideally be completed prior to hormone initiation—see *Fertility and birth control* below);
- ensuring capacity to consent;
- discussing funding of medications and other possible transition-related costs; submitting request for public funding of medication if available;

- discussing/initiating risk mitigation if conditions exist that increase risks associated with hormone therapy;
- reviewing patient information checklist;
- discussing options and choosing initial hormone regimen; and
- providing prescription and reviewing follow-up plan.

Provision of hormone therapy in some cases may be undertaken without completing the usual tasks of the planning period. This is primarily under the rubric of harm reduction; there are situations when the delay of treatment will cause significant harm to the patient. Examples of this include a patient who is already using hormones without a prescription, or someone who is experiencing extreme distress regarding their gender presentation. Other situations may warrant a degree of fast-tracking through the planning period, such as when a patient and their medical and/or gender history are well-known to the provider prior to the patient seeking hormone therapy.

Similarly, if another knowledgeable provider has recently performed part or all of the planning period tasks and the associated records are available for review, or a conversation with the prior provider can be arranged, then the planning period tasks do not all need to be repeated.

EXPLORATION OF GENDER IDENTITY AND EXPRESSION

Healthcare providers are not typically taught how to speak with patients about their history and experience with gender. However, it is an important part of understanding a patient's needs and informing the discussion around the development of an individualized care plan.

We've included suggested questions below that can be used to guide the conversation about a patient's experience of gender. Additionally, it may be helpful to explain the rationale for obtaining this history, and to reassure the patient that there are no "wrong answers" or any specific narrative that the provider is looking to hear. Not all trans people experience gender incongruence or dysphoria or display gender non-conformity during childhood. Trans identities may emerge at any stage in the life cycle.

Possible questions to explore gender identity and expression

- How would you describe your gender identity? *If prompting is needed:* For example, some people identify as a man, a transmasculine individual, genderqueer, etc.
- Do you remember the time when you realized that your gender was different from the one you were assigned at birth? *Or:* Do you remember when you first started to see your gender as _____?
- Can you tell me a bit about what's happened since realizing this? *If prompting is needed:* Some people find this to be a difficult realization and may not feel comfortable discussing it, while other people are fortunate to have people in their life they feel safe talking with—what was it like for you?
- Have you taken any steps to express your gender differently/to feel more comfortable in your gender? *If prompting is needed:* Some people ask others to use a different name and pronoun, or make changes to their hair or clothing styles.
- *If they have taken steps to express their gender differently*: What was that like for you? How did that feel?

Adapted from: Trans Care BC: Primary Care Toolkit, October 2018.[19]

DIAGNOSIS

The provision of hormone therapy has generally been preceded by a diagnosis of Gender Dysphoria as outlined in the *Diagnostic and Statistical Manual*, *Volume 5* (DSM-5).[49]

There has been a great deal of debate in both the medical and trans communities around the appropriateness of using a psychiatric diagnosis (or a diagnosis at all) for trans individuals. The aim to destigmatize gender diversity while securing access to care has been a central dilemma in this debate.[50]

Since "transvestism" first appeared in the World Health Organization's (WHO)'s 8th Edition of the *International Statistical Classification of Diseases and Related Health Problems* (ICD-8) in 1965, (and 'transexualism' in the DSM-III in 1980), the evolution of the name, criteria and categorical placement for diagnoses about trans experiences has been continuous.[51]

The revision of the diagnosis and its criteria in 2013's DSM-5 represented a step towards depathologizing gender difference and validating the spectrum of gender identities. In addition, a distinction was established between gender non-conformity and the diagnosis of gender dysphoria:

"Gender nonconformity refers to the extent to which person's gender identity, role, or expression differs from the cultural norms prescribed for people of a particular sex. Gender dysphoria refers to discomfort or distress that is caused by a discrepancy between a person's gender identity and that person's sex assigned at birth (and the associated gender role and/or primary and secondary sex characteristics). Only some gender nonconforming people experience gender dysphoria at some point in their lives."[13]

The WHO has taken a step further in depathologizing trans identities in their ICD-11, which was released in May 2019. They have renamed the diagnosis Gender Incongruence and removed the diagnosis from the category of mental health disorders, placing it instead in a category of "Conditions Related to Sexual Health." Additionally, in contrast to the DSM diagnosis, there is no criteria for significant distress or impairment.[52]

This represents a concerted effort to abandon the psychopathological model of transgender people, and supports the provision of gender-affirming treatments to a wider population of trans and non-binary people. As societal acceptance and access to supportive communities and care increases, the distress experienced by some trans people is likely to decrease. The absence of the criteria for significant distress or impairment as a prerequisite for treatment for those seeking gender-affirming therapies allows for the timely provision of care as a preventive measure, rather than waiting for distress and impairment to manifest through the withholding of these treatments.

Sherbourne Health advocates for the provision of gender-affirming care to those who meet the diagnostic criteria for gender dysphoria and/or the description of gender incongruence. In line with the updated Endocrine Society Guidelines,[53] we will thus use "gender dysphoria/gender incongruence" in this document when referring to diagnoses for which hormone therapy is indicated. We will continue to use the term "gender dysphoria" on its own when specifically referring to the discomfort/distress experienced by some trans people due to incongruence of gender.

In addition to establishing a diagnosis of gender dysphoria/incongruence, it is recommended that the provider works to rule out other diagnoses that may explain the presentation. Possible differential diagnoses include schizophrenia and other psychotic disorders, dissociative disorder and body dysmorphic disorder. These diagnoses are rarely found to be underlying the desire for gender-affirming treatment, but can occur and so should be ruled out.

If the presentation is unclear, obtaining the opinion of a psychiatrist is appropriate. The provider should take care to refer to a psychiatrist

who has experience working with trans people whenever possible. If the presentation is clear, then consultation with psychiatry is not necessary. The Gender Identity Clinic (GIC) at the Centre for Addiction and Mental Health (CAMH) discourages providers from referring uncomplicated patients seeking hormone therapy.

The criteria for the DSM-5 diagnosis of gender dysphoria[49]

A. A marked incongruence between one's experienced/expressed gender and assigned gender, of at least six months duration, as manifested by at least two of the following:

   1. A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics).

   2. A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics).

   3. A strong desire for the primary and/or secondary sex characteristics of the other gender.

   4. A strong desire to be of the other gender (or some alternative gender different from one's assigned gender).

   5. A strong desire to be treated as the other gender (or some alternative gender different from one's assigned gender).

   6. A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's assigned gender).

B. The condition is associated with clinically significant distress or impairment in social, occupational or other important areas of functioning.

Description of gender incongruence in the ICD-11[52]

Gender incongruence of adolescence and adulthood is characterized by a marked and persistent incongruence between an individual's experienced gender and the assigned sex, which often leads to a desire to "transition" in order to live and be accepted as a person of the experienced gender, through hormonal treatment, surgery or other health care services to make the individual´s body align, as much as desired and to the extent possible, with the experienced gender. The diagnosis cannot be assigned prior to the onset of puberty. Gender variant behaviour and preferences alone are not a basis for assigning the diagnosis.

PATIENT EXPECTATIONS

One of the prescribing clinician's roles is to help the patient develop reasonable expectations about the treatment before it is initiated. To begin with, changes associated with hormones can be slow. It may take years to exhibit secondary sex characteristics. Second, the underlying body structure will not change with hormones. Transfeminine patients will maintain narrow shoulder and hip bone width and existing facial bone structure. Transmasculine patients will also maintain pre-transition facial and body structure. Hormonal treatment of adults cannot impact a person's height. Additionally, feminizing hormone therapy does not affect voice pitch in trans women (see the Part II, Limitations to feminizing hormone therapy, section later in this document). Despite a desire to, people may not easily "pass" as the gender to which they are transitioning. This can be stressful and disheartening for some people, and should be tactfully discussed by the provider.

It may be helpful to provide the patient with a copy of the estimated timelines for hormonal effects, while emphasizing that physiologic responses to hormone therapy are highly individual (see *tables 4* and 8).

While some resources available on the internet espouse a "more is better" approach to hormone administration, there is no evidence to support this approach. It is the clinician's role to explain the risks with overuse of hormones, as well as to provide rationale for their approach.

PSYCHOSOCIAL PREPARATION AND SUPPORT

Gender transition can be a phase of significant adjustment in a patient's life. Like any major life stressor, the aim is to enable the patient with supports that facilitate healthy adjustment. Mental health counselling is not required prior to gender-affirming hormone therapy, but some patients may benefit from extra support. Support in a peer group setting (such as "Gender Journeys"[vi]) can be immensely beneficial for some patients.

Some patients may benefit from individual therapy with a trans-positive therapist with whom they can discuss concerns about the transition process and receive additional psychological support. Removing any requirement for the therapist to provide an "approval letter" prior to hormone initiation can enhance effectiveness of this support by allowing the therapeutic relationship to evolve in a more trusting and open manner.[37] A list of providers, including mental health professionals, with knowledge and experience working with LGBT2SQ individuals is available through Rainbow Health Ontario's online service directory.[54]

Though not a requirement for the initiation of gender-affirming hormones, we encourage patients to discuss their transition with family members (including chosen family) and friends, as they too will have their own reactions and be affected by the patient's transition. Asking about how transitioning will influence the vocational or educational situation of the patient is important. Providers can help the patient develop positive strategies for dealing with gender change in school or the workplace.[55] Unfortunately, it is

vi Gender Journeys is an 11-week program in which individuals can explore their gender identity, learn about different aspects of social and medical transitioning, and build communities. Gender Journeys was developed at Sherbourne Health and has been running since 2005. Gender Journeys groups are now offered in several cities throughout the province. Copies of the manual for this program can be downloaded free of charge from: www.rainbowhealthontario.ca/resources/.

not uncommon for transition to result in the loss of a job or struggle in the academic setting.[vii]

In the past, WPATH advocated for a three-month period of life experience in the congruent gender role prior to cross-sex hormone therapy. The rationale for this step was to enable the establishment of coping mechanisms for the above-mentioned social stressors. This requirement for a "real life experience" has been shown to be both stressful and potentially dangerous, since it requires the adoption of a gender role prior to acquiring any physical changes commensurate with that gender. Accordingly, there is no longer a requirement for a gender role experience of any duration prior to the provision of hormone therapy or surgical interventions, with the exception of external genital surgery[13] (see the *Supporting patients with transition-related surgeries* section later in this document).

Asking about psychosocial preparation and supports

Questions such as these can be used to open the conversation about psychosocial preparation and supports

- Have you thought about how you will manage the changes in your appearance and gender expression at work or school?
- Who has supported you along the way? *If they have not spoken with anyone else yet:* Who do you think might be supportive if you bring this up with them?
- Have you done anything to prepare yourself for this step? *If prompting is needed:* Have you talked with any peers or asked friends or family for support? Have you done any reading or research?
- Do you anticipate any challenges?
- Some people find it helpful to have the support of a counsellor for either decision-making or ongoing support after beginning hormone therapy—would you be interested in a referral to a trans-competent counsellor?

Adapted from Trans Care BC: Primary Care Toolkit[19]

vii See Trans PULSE E-Bulletin "*We've Got Work to Do: Workplace Discrimination and Employment Challenges for Trans People in Ontario*," available at http://transpulseproject.ca/wp-content/uploads/2011/05/E3English.pdf[56]

MENTAL HEALTH AND LIFESTYLE CONSIDERATIONS

Trans patients invariably experience some degree of minority stress. Adapting Meyer's definition in relation to lesbian, gay and bisexual populations,[57] minority stress in the trans population may be thought of as: the chronic psychological strain resulting from stigma and expectations of rejection and discrimination; decisions about disclosure of gender identity; and the internalization of transphobia that trans people face in a cis-sexist society.

In addition to minority stress, many trans people are exposed to gender-based interpersonal violence, including during the formative years of childhood and adolescence.[58] Negative experiences in health care settings can further exacerbate the effects of this trauma. As a result, in addition to ensuring that they take a gender-affirming approach, it is to the benefit of trans and non-binary patients for providers to be familiar with and practice trauma-informed care. A 2018 review in *Canadian Family Physician* describes the principles of trauma-informed care and their application in primary care.[59]

Minority stress and trauma are often associated with the adoption of behaviours such as smoking and excessive substance and alcohol use.[viii] In addition, gender dysphoria may impact a person's relationship with their body and contribute to the risk for these behaviours. Such behaviours, particularly tobacco use, may increase the risks associated with hormone therapy. It is worthwhile for the provider and patient to work to decrease modifiable risks as much as possible, with the understanding that this is not always feasible before starting treatment, and a harm-reduction approach may be necessary.

The initiation of hormone therapy and the expectation of aligning one's body with an internal sense of gender may create an opportunity for a patient to begin to develop a new relationship with their body and initiate lifestyle changes that positively impact health. We have often witnessed this time of transition provide the impetus and inspiration for lasting positive lifestyle changes.

In the past, the presence of active suicidal thoughts or plans has been considered an absolute contraindication to hormone administration, particularly testosterone. The observations of Trans PULSE demonstrate higher rates of suicidality prior to hormone administration with decreasing rates following access to transitional treatments. Additionally, a prospective study of trans men initiating testosterone demonstrated a significant improvement in psychological functioning in multiple domains, including depressive symptoms, following three months of treatment.[62]

These findings suggest the need for a reconsideration of best practice. If a patient is in acute crisis and the provider thinks they are unable to provide informed consent, then this would certainly constitute an absolute contraindication. If an acute safety issue exists, hospitalization may be necessary, and this would become the immediate priority for the PCP.

However, a patient who is at risk of suicide but able to provide informed consent may benefit greatly from the initiation of hormone therapy. This can be particularly true when gender dysphoria/gender incongruence is the main source of the patient's psychological distress. We suggest that these types of situations are best approached on a case-by-case basis, with an assessment of the risks and benefits of hormone provision in relation to the individual patient's mental health. The best course of action may be to start the patient on low-dose therapy while strategizing around suicide risk reduction (for example, by establishing a crisis

viii Like lesbian, gay and bisexual populations, trans populations have higher than average rates of problematic substance use. Screening for drug use should always be part of the initial evaluation. Unfortunately, there are few treatment programs targeted to trans people specifically, and it may be difficult or even dangerous for a trans person to enter a mainstream treatment program. Larger cities may have Alcoholics Anonymous and Narcotics Anonymous groups with an LGBT2SQ focus. In the Toronto area, Rainbow Services at CAMH [60] and Pieces to Pathways for youth[61] provide counselling and treatment services that are tailored to the needs of LGBT2SQ patients.

plan and connecting the patient with additional mental health support and/or treatment).

CAPACITY TO CONSENT

As with any other medical intervention, patients must demonstrate an understanding of the risks and benefits of hormone treatment. Obtaining informed consent is a process that PCPs engage in daily, and when prescribing hormones to trans patients the same basic principles apply.

Questions may arise around capacity to consent in individuals with cognitive or developmental disabilities, and significant mental health challenges, or in younger patients. Since there is no specific age determining when an individual is eligible to provide consent for medical interventions in Canada, it is determined on a case-by-case basis and at the discretion of the provider.[63] If there are persistent concerns regarding a patient's capacity to consent, a referral to a psychiatrist with experience working with trans people may be helpful.

In addition to considerations around consent, when working with vulnerable individuals particular care should be taken to ensure that adequate social supports are in place.

PHYSICAL EXAM AND BASELINE INVESTIGATIONS

A focused physical exam is recommended prior to the initiation of hormone therapy. The exam should include screening for conditions such as hypertension, obesity and active liver disease, which may increase the risks of hormone therapy.

Physical examination, particularly of the breasts and genitalia, may be uncomfortable for trans patients. In addition to practising trauma-informed care, it is advisable to use gender-affirming terms (e.g., "chest" for transmasculine patients, "breasts" for transfeminine patients) or general language (e.g., "genitals," "gonads"), or ask patients if they prefer a particular term. Fortunately, with the exception of STI and Pap testing (when indicated per provincial guidelines), examination of these areas is no longer recommended for routine screening. Further discussion regarding the performance of testing in transmasculine patients can be found in *Part III: Cervical cancer and Pap tests* later in this document.

Previously, genital examination was recommended prior to hormone initiation in order to rule out the possibility of an intersex condition; however, we suggest that inquiry into any history suggestive of an intersex condition (i.e., genitalia differing from phenotypically male or female norms, unexpected pubertal changes for sex assigned at birth) along with baseline hormone levels within expected ranges are sufficient. Findings suggestive of an intersex condition merit consultation with an endocrinologist prior to treatment.

For adolescent patients who may not have completed puberty, examination of the breast/chest and genitals is useful in order to establish the pubertal Tanner stage. Initial treatment options for youth who have not reached Tanner stage 5 include pubertal suppression by a GnRH analogue. Unless a provider has developed specific expertise in this area we suggest providing care to pubertal children and youth under the guidance of an expert or referral to a specialized clinic or another provider with expertise in supporting trans children and youth. Specialized clinics in Ontario include the Transgender Youth Clinic at The Hospital for Sick Children[24] and the Diversity Clinic at the Children's Hospital of Eastern Ontario.[25]

Of note, training sessions for primary care and other providers wishing to care for trans and non-binary children and youth (including pubertal suppression), are in development at RHO and are expected to launch in spring 2020.

In the case of patients seeking feminizing hormone therapy, there may be utility in obtaining a baseline inspection of the breasts, with particular attention to Tanner stage, pre-existing gynecomastia or subcutaneous fat. This can be helpful in the

future determination of a patient's eligibility for publicly funded breast augmentation, since public funding in Ontario currently requires a patient to have experienced no breast growth following twelve consecutive months of feminizing hormone therapy (unless hormones are contraindicated). Some providers may also find the comparison of objective measurements (e.g., chest circumference at the fullest part of the breast and areolar diameter) helpful in making this determination. Aside from interest in surgery, some patients may simply like to track changes to these measurements, while others may find such measurements uncomfortable or intrusive.

Laboratory tests should reveal any existing health problems such as liver dysfunction, high cholesterol or diabetes. If present, these conditions should ideally be managed prior to or concurrently with the initiation of hormones. The values will also provide a useful baseline to help with future monitoring for endocrine changes. Measurement of hormone levels may reveal whether any exogenous hormones are being taken. Any major irregularities could also indicate an intersex condition.

HORMONE COVERAGE THROUGH THE ONTARIO DRUG BENEFIT (ODB) AND EXCEPTIONAL ACCESS PROGRAM (EAP) FORMS

Patients covered by the Ontario Drug Benefit (ODB) program include those on Ontario Works (OW), the Ontario Disability Support Program (ODSP), seniors ≥65 years of age, youth ≤24 years of age (via OHIP+) and those on the Trillium Drug Program. For those on OHIP+, ODB formulary medications are covered barring existing coverage through a private drug plan. For patients covered by ODB, injectable testosterone is covered with the submission of an Exceptional Access form (EAP) (see Appendices N & O), while anti-androgens and oral estradiol are covered without the need for EAP approval.

When indicated, we suggest submitting the EAP application early in the planning process, since processing time by the MOHLTC can vary. Approval does not commit the provider to prescribing hormone therapy and prevents undue delays once the planning period is complete. Blank EAP forms[64] can be downloaded from the Ontario Ministry of Health and Long-term Care website.

FERTILITY AND BIRTH CONTROL

Masculinizing and feminizing hormone therapy regimens have variable temporary and long-term impacts on fertility. Accordingly, there is a need for discussion regarding both birth control and fertility preservation prior to the initiation of hormone therapy.

Trans people have the same range of reproductive interests as cis people, and many are at childbearing age at the time of transition.

Though there are numerous ways that people may create families without the use of their own gametes, many people have a wish for genetically related children. Patients who are planning to conceive in the near future may even wish to delay medical transition in order to minimize the need for harvesting, storage and/or advanced reproductive technologies (ARTs), which can be costly and involve procedures that can intensify feelings of gender dysphoria.

Options for fertility preservation in trans and non-binary people are similar to those undergoing gonado-toxic therapies for malignancy or elective preservation for social reasons. Some costs associated with fertility preservation for those planning to medically transition may be covered by the Ontario Ministry of Health and Long-term Care (MOHLTC) at certain clinics.

Care should be taken to refer patients for fertility services at centres that have experience working with trans people whenever possible. If indicated, referral for fertility preservation should be initiated as soon as possible. This process may take several months. While the cryopreservation of

sperm is much less costly than the harvesting and cryopreservation of ova, in both scenarios budgeting in the short and the long term for up-front and ongoing storage costs may be required.

It is important to note that many trans people have conceived successfully following the discontinuation of hormone therapy. Whether long-term hormone therapy confers unique risks to those undergoing ART or has an impact on gametes or future offspring is unknown.[29] Several healthy live births have been reported, but patients should be counselled regarding the lack of knowledge in this area.

Considerations specific to those with ova and those with sperm are discussed below. For more information, see Rainbow Health Ontario's fact sheet *Reproductive Options for Trans People*,[65] and the LGBTQ Parenting Network's resources *Fertility Preservation for Trans People Who Produce Eggs*[66] and *Fertility Preservation for Trans People Who Produce Sperm*.[67]

TRANS PATIENTS WITH OVA

In most cases, testosterone therapy leads to reversible amenorrhea without depletion of ovarian follicles. However, there may be an adverse effect on the growth of follicles, particularly in the more mature stages of follicular development.[68] Debate is ongoing regarding whether masculinizing therapy induces a polycystic ovarian syndrome (PCOS)-like picture.[69,70] The theory that androgens induce high anti-mullerian hormone (AMH) levels—a particular feature of PCOS—is debatable. In fact, a 2015 study found a decrease in AMH levels following 16 weeks of masculinizing hormone therapy in 22 trans men.[71]

Despite reduced fertility during testosterone administration, it should not be considered an adequate method of contraception. Given the teratogenic potential of testosterone, transmasculine patients on testosterone should be counselled on the risk of pregnancy, and those who are sexually active with people with sperm should be offered contraceptive options, such as progesterone-only contraception or an intrauterine system/device (IUS/IUD). Anecdotally, it may be easier to insert an IUS/IUD prior to initiating testosterone due to the subsequent atrophic changes of the vaginal and cervical tissues.[72]

Once testosterone is initiated, the provider should check with the patient periodically regarding their sexual behaviour and reiterate the necessary precautions if the patient becomes sexually active with people who produce sperm. If accidental pregnancy does occur, counselling regarding all options, including pregnancy termination, should be provided. If termination is chosen, it may be helpful for the provider to directly contact a local abortion clinic to ensure that the patient will be received appropriately.

While many transmasculine people have intentionally become pregnant after discontinuing testosterone to pursue pregnancy,[73] patients may wish to consider postponing testosterone initiation if they would like to become pregnant in the future, since fertility may be permanently affected.

Patients should also be counselled regarding options for fertility preservation prior to starting hormones. While ideally completed prior to starting hormones, fertility preservation can also be performed following (temporary or permanent) discontinuation of testosterone. In a 2014 study by Light et al. involving 41 trans men, 80% resumed menstruation after six months of hormone cessation, with the majority resuming within three months.[73] Some fertility specialists advise waiting until menstruation returns before undergoing preservation (or trying to conceive otherwise), while others may be comfortable starting the process without waiting for menstruation.

Fertility preservation for those with ovaries involves the cryopreservation of either oocytes or of embryos created via fertilization with sperm from a partner or donor. While embryo banking has historically resulted in greater pregnancy rates than oocyte banking, new freezing techniques have drastically improved pregnancy

rates from frozen oocytes.[74] Some patients may choose to preserve both embryos and oocytes. Both options require the harvesting of oocytes following controlled ovarian stimulation through the administration of female hormones, as well as multiple transvaginal ultrasounds and a transvaginal procedure to aspirate the oocytes. This often represents a substantial physical and psychological burden on transmasculine patients.

The cryopreservation of ovarian cortical tissue is a promising but currently experimental technology that could overcome the need for ovarian stimulation and oocyte aspiration; it could also be done concurrently with gender-affirming gonadectomy. For more information on fertility preservation for trans people with ova, see the LGBTQ Parenting Network's resource *Fertility Preservation for Trans People who Produce Eggs*.[67]

TRANS PATIENTS WITH SPERM

The administration of feminizing hormone therapy results in a reduction of testicular volume and has a suppressive effect on sperm motility and density in a cumulative, dose-dependent manner.[75] Hamada et al. (2015) noted poor sperm quality in trans women even prior to the initiation of hormone therapy, an effect which may be related to factors such as the practice of "tucking,"[ix] psychological stress, undisclosed hormone use or unidentified genetic polymorphisms.[76]

Nonetheless, it is important to counsel transfeminine patients regarding the need for birth control if they are sexually active with partners who may become pregnant.

Patients should also be counselled regarding options for sperm banking prior to starting hormones. Sperm cryopreservation following ejaculation is the simplest and most reliable form of preservation.

ix Tucking refers to the process of concealing the penis and scrotum so that they are not conspicuous through clothing. One common method involves 'tucking' the genitalia back between the legs and binding along the perineum and/or between the buttocks.

STI screening (i.e., chlamydia, gonorrhea, HIV, syphilis and hepatitis serologies) is required prior to banking, and PCPs can expedite the process for patients by completing these tests prior to referral.

Testicular sperm extraction (TESE) involves percutaneous removal of sperm from the testes or epididymis under local anesthetic.[74] This procedure may be considered when ejaculation is overly burdensome or difficult. Resulting sperm counts are often low and thus multiple samples and/or the use of in vitro fertilization (IVF) or intra-cytoplasmic sperm injection (ICSI) may be required.[68] The cryopreservation of testicular tissue is a promising technology that could overcome the need for ejaculation and be performed concurrently with gender-affirming gonadectomy, but is currently considered experimental.[77]

Patients with sperm may also attempt conception or undergo fertility preservation following the suspension of hormone therapy for three to six months, since testicular function may recover to a variable degree.[77] TESE and ART can be useful in overcoming reduced fertility secondary to hormone therapy.

In a variety of scenarios, semen analysis can be helpful in assessing current fertility and informing options. Community-based PCPs can order MOHLTC-covered semen analysis of ejaculate.

For more information on fertility preservation for trans people with sperm, see the LGBTQ Parenting Network's resource *Fertility Preservation for People Who Produce Sperm*.[67]

SEXUALITY

Exogenous hormones may not only affect libido, but have also been noted to impact sexual attraction. Patients may notice an expansion of their sexual interests or a shift in their sexual orientation, which can be transient or permanent. This is often unforeseen and can create challenges for existing relationships. This effect has been most

commonly noted with masculinizing therapies,[78] but can be discussed as a possibility in all patients considering hormone therapy. Integrating a respectful ongoing sexual health history is helpful in assessing for changes in risks for sexually transmitted infections and unplanned pregnancy.

DISCONTINUATION OF HORMONE THERAPY

The discontinuation of hormone therapy may be required for procedures such as fertility preservation, pregnancy or surgery. Discontinuation may also be chosen for a myriad of other reasons, such as older age, health issues, financial issues or a need to make a change in gender presentation, including to a more non-binary presentation, or in order to "retransition."[x]

The desire to retransition is very rare, and is more often chosen due to the hardships associated with being visibly trans than a realization that one is "not" or "no longer" trans. Anecdotally, those who ultimately choose to retransition may feel that their medical transitions were a necessary part of their journey and thus do not express regret for the decision to initiate hormone therapy. Conversations with patients expressing a wish to retransition should be approached with sensitivity and openness. An exploration of the factors contributing to a patient's desire to retransition can be helpful in identifying situations in which additional supports may be needed. Ultimately, patients should be supported in their decisions.

In agonadal patients, the decision to stop hormone therapy should be made with consideration to maintenance of bone density. If consistent with a patient's goals, exogenous hormones consistent with sex assigned at birth may be appropriate.

x There is lack of consensus on the preferred terminology to describe the choice to move toward a gender presentation and/or sex characteristics consistent with sex assigned at birth. Alternative terms that have been used include "detransition" and "transition further."[79]

Depending on the indication, it may be preferable to slowly taper the dose of hormone therapy over a period of weeks in order to minimize the side effects that can be associated with a more sudden change in serum hormone levels.

REFERRALS AND ADVOCACY IN SUPPORT OF TRANS PATIENTS

As with cis patients, trans patients often seek assistance from their PCP in order to access services and supports they may need. When supporting trans patients, it may be helpful to be familiar with some of the most common requests. This section provides an overview of the referrals and support letters about which PCPs are frequently asked.

Changing sex designation on government ID: support letters

Note: While we recognize that indicators of gender rather than sex are being discussed, Ontario's documentation consistently uses the term "sex designation," so, for simplicity, we will use this term here.

Medical providers have historically played a significant role as gatekeepers to the changing of one's sex designation associated with various forms of government-issued identification. While having had TRS is no longer a requirement for changing one's sex designation in Ontario, a letter of support from a provider is required attesting to the fact that they agree that a change in sex designation is appropriate.

Appendices Appendix P and *Appendix Q* provide sample letters that can be used as a basis to draft letters of support for patients seeking to change their sex designation on their Ontario birth certificate and driver's licence, respectively. If the sex designation on an individual's birth certificate has been changed, their driver's licence alternatively may be changed simply by presenting the new birth certificate.

Ontario birth certificate and driver's licence holders are now also able to choose the sex designation "X." This change was made in order to accommodate non-binary and Two-Spirit people, as well as binary people who do not wish to disclose their gender identity. A change of designation to "X" on a birth certificate requires the same supporting documentation as changing to an M or F, while no supporting documentation is required in order to make the change to an "X" on a driver's licence.

As of June 2016, new Ontario health cards will no longer display a sex designation on the face of the card, although a sex designation remains part of the information associated with the card. If an individual has already changed the sex designation on their Canadian Citizenship document (such as a birth certificate issued by a Canadian province or territory) or other OHIP-eligible immigration status document, they can use that document to change their OHIP sex designation. The applicant can alternatively write a declaration along with a letter from their PCP to support the change of OHIP sex designation. Currently, there is no option for a sex designation of "X" to be associated with a person's OHIP card.

Along with the support letter, patients will also have to provide other documentation and forms of identification. Patients seeking information about the precise requirements may be directed to the Canadian Centre for Gender and Sexual Diversity's guide to Ontario ID changes,[80] or the Ontario Government ID information that is available online.[81]

Advocacy with income supports

Being trans does not, in and of itself, constitute a permanent disability.

However, the combination of gender dysphoria with profound experiences of cis-sexism and transphobia in the workplace can make working through parts of someone's transition not only difficult, but potentially unsafe. While beyond the scope of this document to explore fully, a number of factors shape why some patients face particularly difficult challenges when transitioning in the workplace, such as:

- the type of work that they may be doing (e.g., if it is a very gendered workplace);
- their role and relationship to other staff and management (e.g., transition can exacerbate pre-existing tensions);
- the extent to which they need to work with the general public (i.e., encountering more people every day leads to more opportunities to experience transphobia or cis-sexism); and
- the extent to which an individual is able to be "assumed cis" (or pass as cis) in their day-to-day lives.

Variations in resiliency and social support are unique to each patient. Gender dysphoria can be time limited for some, alleviated by their social and/or medical transition, and it can be persistent for others. For many trans patients, their everyday challenges improve with time over their transition. For others, however, these challenges can persist.

In some cases, providers may need to write a letter of support to assist patients in applying for employment insurance if they have left work with "just cause."[82] Alternatively, some patients may be able to access workplace disability benefits or Ontario's Disability Support Program. *Appendix S* provides an example of a support letter that the provider can use as a starting point in developing letters for patients seeking these supports.

Patients may ask for support letters in other instances, such as carrying injectable medication and supplies internationally, confirming that a patient has a particular diagnosis, or the completion of a guarantor form. In general, since these are not significantly different concerns from those for cis patients, sample templates have not been included here.

Supporting patients with transition-related surgeries (TRS)

Disclaimer: This section provides a brief overview of the Ontario system for TRS assessment and referral. It is neither exhaustive nor intended as training for conducting TRS planning visits. For more information about TRS planning visits, referral and care, see the resources listed in Appendix I.

PCPs play an important role in supporting patients who wish to undergo transition-related surgery (TRS)[6,xi]. TRSs are procedures that change a patient's primary and/or secondary sex characteristics to better align their physical body with their gender identity.[xii]

Current MOHLTC-funded transition-related surgeries[29]

	For patients assigned male at birth	For patients assigned female at birth
Upper body	Augmentation Mammoplasty[a]	Mastectomy[b]
Gonadal	Orchiectomy	Hysterectomy Salpingo-oophorectomy
External genital	Vaginoplasty	Clitoral release with vaginectomy Metoidioplasty Phalloplasty Testicular implants with scrotoplasty Penile implant

a MOHLTC funding criteria includes having "completed twelve (12) continuous months of hormone therapy with no breast enlargement (unless hormones are contraindicated)."[32]
b Masculinizing chest contouring is not currently MOHLTC-funded. Patients may choose to pay for this privately. Surgeons' fees for masculinizing chest contouring may vary.

xi TRS is also known as gender-affirming surgery (GAS), gender-confirming surgery (GCS), gender-reassignment surgery (GRS) and sex reassignment surgery (SRS).
xii MOHLTC-funded surgeries include "additional surgery that is required because of complications causing significant physical symptoms or functional impairment," when prior authorization has been obtained from the ministry.

Previously, patients could only access MOHLTC-funded TRS referrals through the Centre for Addiction and Mental Health (CAMH)'s Adult Gender Identity Clinic (GIC). Patients were referred to the CAMH GIC for surgical assessments and then subsequently referred to TRS surgeons.

On March 1, 2016, Ontario legislation changed, allowing qualified providers outside of CAMH to conduct surgical assessments and TRS referrals. Historically, the term "surgical assessment" was used to describe visits between the patient and provider where TRS was discussed. At our clinic, we use "transition-related surgery planning visit" to describe the collaborative approach of these visits.

An initial step in supporting a patient who wishes to undergo TRS is deciding which qualified provider(s) will conduct the TRS planning visit(s) and be the one to complete and sign the Ontario MOHLTC "Request for Prior Approval for Funding of Sex-Reassignment Surgery" (also known as the "Prior Approval") form. Patients and PCPs may choose what works best for the individual given their needs and local resources: patients may choose to have TRS planning visits in primary care, with a specialist, a community mental health provider, at the CAMH Adult GIC, or a combination thereof. The CAMH Adult GIC serves all of Ontario and is able to conduct visits via telemedicine. Their involvement can be particularly helpful for patients with serious or complex mental health histories.

A TRS planning visit is a collaborative visit between client and a qualified provider to discuss TRS and how to optimize the patient's experience and outcome. Topics discussed include WPATH and MOHLTC criteria, confirming the diagnosis of gender dysphoria, reviewing the stability of medical and mental health conditions, a surgery-specific informed consent discussion and aftercare planning. Also known as "surgical assessment" at other clinics.

In contrast to the referral and funding process for other types of publicly funded surgeries in Ontario, the referring provider shares responsibility with the surgeon for ensuring that surgery is appropriate for the patient, and that the patient is fully informed and prepared for the procedure. So, just as when initiating hormone therapy, the PCP is responsible for making the diagnosis of gender dysphoria,[xiii] for educating patients about the proposed treatment, and for ensuring capacity to consent.

Given this, the surgery-specific planning component of the TRS visits include a discussion of intended results, surgical techniques and options, alternatives, complications, and pre- and post-operative considerations. Rainbow Health Ontario's surgical summary sheets[84] are valuable resources for facilitating this discussion between provider and patient. The surgical summary sheets are also a valuable reference for aftercare considerations that are unique to TRS and are important to discuss with patients.

Within the Ontario system of TRS planning visits and referral:

A) The MOHLTC requires the Prior Approval form be completed by "a provider trained in the assessment, diagnosis and treatment of gender dysphoria in accordance with the World Professional Association for Transgender Health (WPATH) Standards of Care…"[xiv]

B) It is expected that a qualified provider who signs the Prior Approval form has conducted a complete TRS planning visit.

xiii At the time of publication of this document, the MOHLTC's criteria for funded surgery aligns with WPATH's SOC7, including the requirement for a diagnosis of gender dysphoria.[32]

xiv Providers who can be involved in referrals and supporting referrals are Physicians, Nurse Practitioners, Registered Nurses, Psychologists and Registered Social Workers. See the OHIP TRS Funding Application Process section below for more specificity about which providers can do what.

QUALIFIED PROVIDERS: SELF-DETERMINED, BASED ON EXPERIENCE AND KNOWLEDGE

Many PCPs wish to provide TRS planning visits but are unsure if they are considered a "qualified provider" by the MOHLTC. The MOHLTC has maintained that providers should determine for themselves if TRS planning visits and referrals fall within their scope of practice, since providers would generally self-determine in other areas of care.[85]

There is no single training course that "qualifies" a provider. A provider who is new to this area of practice may want to combine a number of the following activities to gain the necessary expertise:

- having significant experience in trans health care;
- having attended continuing medical education on trans surgical care through Rainbow Health Ontario, or the World Professional Association for Transgender Health (WPATH), or the Canadian Professional Association for Transgender Health (CPATH) Conference, or CAMH's Trans Health ECHO;
- having completed independent learning on trans surgical care through review of WPATH guidelines or other research or clinical resources;
- having had mentorship from an experienced colleague; or
- participation in the Rainbow Health Ontario Trans Health Mentorship Call.

Providers themselves determine whether they can provide safe, informed surgery planning visits given their experience with trans patients and gender dysphoria; their understanding of the WPATH SOC; their knowledge of the surgeries themselves; and their appreciation of the shared responsibilities between referring provider and surgeon. Further resources for education and training on trans surgical care can be found in *Appendix I*.

Note that a provider may be asked to provide documentation of their training upon request by the MOHLTC. In particular, when applying on behalf of a patient younger than 18 years of age, PCPs will be asked to provide their qualifications specific to gender dysphoria in children and adolescents, in accordance with the competencies outlined in WPATH's SOC.[14] If a provider cannot provide information or documentation on their qualifications when requested, the patient will not be approved for insured surgery. If funding approval has been granted and subsequently the provider indicates to the MOHLTC that they do not have the qualifications to complete the assessment, then the approval will be revoked.

FORMS AND LETTERS USED FOR TRS PLANNING IN ONTARIO

MOHLTC TRS Prior Approval form:

The official MOHLTC form is named *Request for Prior Approval for Funding of Sex-Reassignment Surgery*. After the completion of TRS planning visits, this form is completed and signed by one or two qualified providers and faxed to the MOHLTC.[85]

Approved Funding Letter:

A letter from the MOHLTC confirming that prior funding for a patient who has applied for a specific TRS is confirmed and approved.

TRS Referral Letters:

A referral letter sent to the TRS surgeon, which includes a large amount of information regarding the topics covered in the TRS planning visits, including WPATH criteria. Attachments may include documentation of TRS planning visits, discussed topics and the Approved Funding Letter.

OHIP TRS FUNDING APPLICATION AND REFERRAL PROCESS

The number of qualified providers who must complete independent TRS surgery planning visits and sign a Prior Approval form is based on the type of surgery requested. Upper body surgery requires a TRS planning visit(s) by one qualified provider (either a physician or NP). Gonadal or external genital surgery requires independent TRS planning visits with two qualified providers, one of whom must be a physician or NP. The second can be a physician, NP, registered nurse, psychologist or a registered social worker with a Masters of Social Work.

Once TRS planning visits have been completed, the Prior Approval form[86] is signed and sent to the MOHLTC. Only the prior approval form should be sent to the MOHLTC; TRS clinical notes and referral letters should not be sent. The MOHLTC will then send a response letter with the outcome of the funding application. If the MOHLTC approves the application, then an Approved Funding Letter is sent to the providers, the surgeon and the patient. If the application is declined, a letter will also be sent.

If an application is rejected, the Ministry can be contacted with missing information they might have identified, and the application resubmitted, or the Ministry can be contacted in writing to request an internal review for the application or a Health Services Appeal and Review Board (HSARB) hearing.

Once an approved funding letter is received, the qualified provider(s) can then send TRS referral letters to the TRS surgeon. TRS referral letters are different from typical referral letters—they include a large amount of information regarding the topics covered in the TRS planning visits. Providers should be familiar with the WPATH recommendations for TRS referral letters.[13] Most surgeons will require complete documentation of thorough TRS planning visit(s). Additional documentation may be requested by some surgeons prior to the patient receiving an appointment. When the surgeon accepts the referral, a pre-operative consultation will ideally be booked; however, due to financial/travel constraints, an in-person preoperative consultation may not be possible in advance of the date of surgery.[xv]

Whether a patient has surgery planning visits in primary care or with CAMH or another provider, there are many ways that a PCP can support a patient throughout the TRS process. PCPs can help prepare patients for surgery by assisting in the optimization of medical and mental health conditions, supporting smoking cessation, discussing the aftercare plan, planning for travel, finances and supplies, and providing emotional support. Some patients may benefit from peer support and information such as that provided by Sherbourne Health's Surgical Support Groups for Community Members.[87]

If a patient lacks suitable housing or supports for the immediate post-operative recovery period, referral to Sherbourne Health's Acute Respite Care (ARC) program[88] for a one- to three-week post-operative TRS stay can be considered. The ARC online referral form is on the Sherbourne Health website.[89] In order to facilitate a safe discharge from ARC back to the community, it is recommended that PCPs work with patients to create plans for safe housing and initiate community supports that may be required post-operatively (e.g., home and community care services), well in advance of the surgical date.

If patients are travelling long distances for TRS and are at higher risk for complications, preparing a plan to manage possible post-operative complications is beneficial. This may involve connecting patients pre-operatively with a local surgical specialist who is agreeable to consult in the event of post-operative complications.

An overview of the TRS planning visits and referral process described above can be found in the flowchart in *Appendix T*. Additionally, a resource published by Ontario's Trans Health Expansion[6] that addresses patients' frequently asked questions is available on the Rainbow Health Ontario website.

xv Travel expenses are the responsibility of the patient. Patients may be eligible for MOHLTC transportation funding, travel grants or HOPE Air (https://hopeair.ca).

For a variety of reasons, patients may choose to pay directly for TRS, provided they have the resources. In these instances, providers may also be asked to provide TRS referral letters. While most surgeons' expectations align with WPATH's criteria for TRS referral letters, it may be worthwhile to check specific requirements with the individual surgeon, particularly those outside of North America whose routine requirements may differ.

REFERENCES

1. Hammond R. The social organization of health care for trans youth in Ontario [Internet] [MSc thesis]. [Halifax, Nova Scotia]: Dalhousie University; 2010 [cited 2019 Feb 4]. Available from: https://DalSpace.library.dal.ca//handle/10222/13105
2. Wylie, K, Knudson, G, Khan, SI, Bonierbale, M, Watanyusakul, S, Baral, S. Serving transgender people: clinical care considerations and service delivery models in transgender health. Lancet, The 2016;388(10042):401-411.
3. Speck K. Trans Health Guide [Internet]. Trans Primary Care. 2016. Available from: https://www.rainbowhealthontario.ca/TransHealthGuide/
4. James S, Anafi M, Herman J, Keisling M, Mottet L. 2015 U.S. Transgender Survey [Internet]. 2015 U.S. Transgender Survey. 2015. Available from: http://www.ustranssurvey.org/
5. Lee M, Leung R, Kumar R. Psychiatric outcomes in transgender persons after hormone therapy or gender-affirming surgery: A systematic review. Poster presentation presented at: Canadian Psychiatric Association Conference; 2017 Sep; Ottawa, ON.
6. Rainbow Health Ontario. Transition-related surgeries: planning, referral and care. [Internet]. 2019 [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/training/#eight
7. Flores A, Herman J, Gates G, Brown T. How many adults identify as transgender in the United States? [Internet]. California: The Williams Institute; 2016 Jun p. 13. Available from: https://williamsinstitute.law.ucla.edu/wp-content/uploads/How-Many-Adults-Identify-as-Transgender-in-the-United-States.pdf
8. Bauer J, Hammond R, Pyne J, Redman N, Scanlon K, Travers A. Trans PULSE [Internet]. Trans PULSE. 2012. Available from: http://transpulseproject.ca/
9. Giblon R, Bauer G. Health care availability, quality, and unmet need: a comparison of transgender and cisgender residents of Ontario, Canada. BMC Health Serv Res. 2017;17(1):283.
10. Bauer G, Zong X, Scheim A, Hammond R, Thind A. Factors impacting transgender patients' discomfort with their family physicians: A respondent-driven sampling survey. PLoS ONE. 2015;10(12):1–16.
11. Bauer G, Scheim A, Pyne J, Travers R, Hammond R. Intervenable factors associated with suicide risk in transgender persons: a respondent driven sampling study in Ontario, Canada. BMC Public Health. 2015;15:525.
12. Trans PULSE Project - Research on health of transgender Ontarians [Internet]. Trans PULSE. n.d. Available from: http://transpulseproject.ca/
13. Coleman E, Bockting W, Botzer M, Cohen-Kettenis P, DeCuypere G, Feldman J. Standards of care for the health of transsexual, transgender, and gender-nonconforming people, Version 7. Int J Transgenderism. 2012;13(4):165–232.
14. The World Professional Association for Transgender Health. Standards of care for the health of transsexual, transgender, and gender nonconforming people [Internet]. 2012 [cited 2019 Feb 4]. Available from: https://www.wpath.org/publications/soc
15. Bauer G, Hammond R. Toward a broader conceptualization of trans women's sexual health. Can J Hum Sex. 2015;24(1):1–11.
16. Two-Spirited People of Manitoba - A cultural imperative [Internet]. Two-Spirited People of Manitoba. 2018. Available from: https://twospiritmanitoba.ca/we-belong
17. Roscoe W. Changing ones: Third and fourth genders in Native North America. New York: St. Martin's Press; 1998. 320 p.
18. Pullin Z. Two Spirit: The story of a movement unfolds. Native People's Magazine [Internet]. 2014 Jun; Available from: https://www.kosmosjournal.org/news/two-spirit-the-story-of-a-movement-unfolds/
19. Davey, C. Indigenous LGBTQ and Two-Spirit Health. In: Caring for LGBTQ2S People: A Clinical Guide. University of Toronto Press: in press.
20. Rainbow Health Ontario. Two-Spirit and LGBTQ Indigenous Health [Internet]. Rainbow Health Ontario; 2016 [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/two-spirit-and-lgbt2sq-indigenous-health/
21. Rotondi N, Bauer G, Scanlon K, Kaay M, Travers R, Travers A. Nonprescribed hormone use and self-performed surgeries: "do-it-yourself" transitions in transgender communities in Ontario, Canada. Am J Public Health. 2013;103(10):1830–6.
22. MacKinnon K. Predisposing, reinforcing, and enabling factors of trans-positive clinical behaviour change: A summary of the literature. Int J Transgenderism. 2016;17(2):83–92.
23. Bauer G, Pyne J, Francino M, Hammond R. La Suicidabilite parmi les personnes trans en Ontario : Implications en travail social et en justice sociale. Serv Soc. 2013;59(1):35–62.
24. The Hospital for Sick Children. Transgender Youth Clinic [Internet]. SickKids. n.d. Available from: http://www.sickkids.ca/AdolescentMedicine/transgender-youth-clinic.html
25. CHEO – Diversity clinic for children and youth, Children's Hospital of Eastern Ontario [Internet]. Gender Creative Kids. 2013. Available from: https://gendercreativekids.ca/providers/diversity-clinic-for-children-and-youth-childrens-hospital-of-eastern-ontario/
26. Rainbow Health Ontario. Trans health mentorship call [Internet]. Rainbow Health Ontario. 2018. Available from: https://www.rainbowhealthontario.ca/trans-health/#mentorship
27. Cavanaugh T, Hopwood R, Gonzalez A, Thompson J. The medical care of transgender persons [Internet]. Boston, MA: Fenway Health; 2015 Oct. Available from: https://www.lgbthealtheducation.org/publication/transgender-sod/
28. Callen-Lorde Community Health Center. Protocols for the provision of hormone therapy [Internet]. New

York, NY: Callen-lorde; 2018. Available from: http://callen-lorde.org/graphics/2018/05/Callen-Lorde-TGNC-Hormone-Therapy-Protocols-2018.pdf

29. Deutsch M. Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people [Internet]. Centre of Excellence for Transgender Health. 2016. Available from: http://transhealth.ucsf.edu/protocols
30. Bauer G, Hammond R, Travers R, Kaay M, Hohenadel K, Boyce M. "I Don't Think This Is Theoretical; This Is Our Lives:" How Erasure Impacts Health Care For Transgender People. J Assoc Nurses AIDS Care. 2009;20(5):348–61.
31. Meyer W. World Professional Association for Transgender Health's Standards of Care requirements of hormone therapy for adults with gender identity disorder. Int J Transgenderism. 2009;11(2):127–32.
32. Ministry of Health and Long-Term Care. Sex Reassignment Surgery [Internet]. n.d. [cited 2019 June 24]. Available from: http://www.health.gov.on.ca/en/pro/programs/srs/
33. Grant J, Mottet L, Tanis J. Injustice at every turn: A report of the National Transgender Discrimination Survey. Washington, D.C.: National Centre for Transgender Equality; 2011 p. 228.
34. Koehler A, Eyssel J, Nieder T. Genders and individual treatment progress in (non-)binary trans individuals. J Sex Med. 2018;15(1):102–13.
35. Puckett J, Cleary P, Rossman K, Mustanski B. Barriers to gender-affirming care for transgender and gender nonconforming individuals. Sex Res Soc Policy. 2018;15(1):48–59.
36. Bauer G, Scheim A, Deutsch M, Massarella C. Reported emergency department avoidance, use, and experiences of transgender persons in Ontario, Canada: Results from a respondent-driven sampling survey. Ann Emerg Med. 2014;63(6):713–20.
37. Cavanaugh T, Hopwood R, Lambert C. Informed consent in the medical care of transgender and gender non-conforming patients. J Ethics. 2016 Nov;18(11):1147–55.
38. Informed consent FAQs [Internet]. Catherine White Holman Wellness Centre. n.d. Available from: http://www.cwhwc.com/about-us/informed-consent-faqs/
39. Deutsch M. Use of the Informed Consent Model in the provision of cross-sex hormone therapy: A survey of the practices of selected clinics. Int J Transgenderism. 2012;13(3):140–6.
40. van Kesteren P, Asscheman H, Megens J, Gooren L. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clin Endocrinol (Oxf). 1997;47(3):337–43.
41. Gooren LJ, Giltay EJ, Bunck MC. Long-term treatment of transsexuals with cross-sex hormones: extensive personal experience. J Clin Endocrinol Metab. 2008 Jan;93(1):19–25.
42. Wierckx K, Van Caenegem E, Schreiner T, Haraldsen I, Fisher A, Toye K. Cross- sex hormone therapy in trans persons Is safe and effective at short- time follow- up: Results from the European Network for the Investigation of Gender Incongruence. J Sex Med. 2014;11(8):1999–2011.
43. Martin dH, Bakker A, Gooren L. Long term hormonal treatment for transgender people. BMJ Br Med J Online. 2017;359.
44. van Kesteren P, Lips P, Gooren L, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. Clin Endocrinol (Oxf). 1998;48(3):347–54.
45. Elbers JMH J, Giltay E, Teerlink T, Scheffer P, Asscheman H, Seidell J. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. Clin Endocrinol (Oxf). 2003;58(5):562–71.
46. Mueller A, Gooren L. Hormone-related tumors in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol. 2008;159(3):197–202.
47. Weinand J, Safer J. Hormone therapy in transgender adults is safe with provider supervision; A review of hormone therapy sequelae for transgender individuals. J Clin Transl Endocrinol. 2015;2(2):55–60.
48. Asscheman H, Giltay E, Megens J, de Ronde W, van Trontsenburg M, Gooren L. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol. 2011;164(4):635–42.
49. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) [Internet]. New York: American Psychiatric Association Publishing; 2013. Available from: https://dsm.psychiatryonline.org/doi/book/10.1176/appi.books.9780890425596
50. Beek T, Cohen-Kettenis P, Bouman W, de Vries A, Steensma T, Witcomb G. Gender incongruence of adolescence and adulthood: Acceptability and clinical utility of the World Health Organization's proposed ICD-11 criteria. PLOS One. 2016;11(10):e0160066.
51. Kreukels B, Steensma T, de Vries A. Gender dysphoria and disorders of sex development: Progress in care and knowledge. New York: Springer; 2014.
52. World Health Organization. International Classification of Diseases 11th Revision [Internet]. Cited July 16, 2019. Available from: https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/90875286%0D.
53. Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869–903.
54. Rainbow Health Ontario. Service Provider Directory [Internet]. [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/service-directory/
55. Mizok L, Woodrum T, Riley J, Sotilleo E, Yuen N, Ormerod A. Coping with transphobia in employment: Strategies used by transgender and gender-diverse people in the United States. Int J Transgenderism. 18(3):282–94.
56. Bauer G, Nussbaum N, Travers R, Munro L, Pyne J, Redman N. We've got work to do: Workplace discrimination and employment challenges for trans people in Ontario [Internet]. 2011 May [cited 2019 Feb 4]. (Trans PULSE E-Bulletin). Report No.: Volume 2, Issue 1. Available from: www.transpulseproject.ca
57. Testa R, Habarth J, Peta J, Balsalm K, Bockting W. Development of the Gender Minority Stress and Resilience Measure. Psychol Sex Orientat Gend Divers. 2014;2(1):65–77.
58. Richmond K, Burnes T, Carroll K. Lost in Trans-Lation: Interpreting Systems of Trauma for Transgender patients. Traumatology. 2012;18(1):45–57.
59. Purkey E, Patel R, Phillips S. Trauma-informed care: Better care for everyone. Can Fam Physician. 2018;64(3):170–2.
60. Centre for Addictions and Mental Health. Rainbow Services LGBTQ [Internet]. [cited 2019 Feb 4]. Available from: https://www.camh.ca/en/your-care/programs-and-services/rainbow-services-lgbtq
61. Pieces to Pathways [Internet]. Breakaway Addiction Services. [cited 2019 Feb 4]. Available from: https://www.breakawayaddictions.ca/p2p/
62. Keo-Meier C, Herman L, Reisner S, Pardo S, Sharp C, Babcock J. Testosterone treatment and MMPI-2 improvement in transgender men: A prospective controlled study. J Consult Clin Psychol. 2015;83(1):143–56.
63. Policy Statement #3-15, Consent to Treatment [Internet]. College of Physicians and Surgeons of Ontario; 2015. Available from: https://www.cpso.on.ca/CPSO/media/documents/Policies/Policy-Items/Consent-To-Treatment.pdf?ext=.pdf
64. Government of Ontario. Central Forms Repository - Request for an Unlisted Drug Product - Exceptional Access Program

[Internet]. n.d. [cited 2019 Feb 4]. Available from: http://www.forms.ssb.gov.on.ca/mbs/ssb/forms/ssbforms.nsfssminnow

65. Rainbow Health Ontario. Reproductive options for trans people [Internet]. Toronto, Ontario: Rainbow Health Ontario; 2012 [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/rho-fact-sheet-reproductive-options-for-trans-people/
66. LGBTQ Parenting Network. Fertility preservation for trans people who produce eggs [Internet]. Toronto, Ontario: Sherbourne Health; 2017 Jun. Available from: http://lgbtqpn.ca/wp-content/uploads/2018/07/Fertility-Preservation-for-Trans-People-who-Produce-Eggs-Version-2.0-Sept-2017.pdf
67. LGBTQ Parenting Network. Fertility preservation for trans people who produce sperm [Internet]. Toronto, Ontario: Sherbourne Health; 2017 Jun. Available from: http://lgbtqpn.ca/wp-content/uploads/2018/07/Fertility-Preservation-for-Trans-People-who-Produce-Sperm-Version-2.0-Sept-2017.pdf
68. De Roo C, Tilleman K, T'Sjoen G, De Sutter P. Fertility options in transgender people. Int Rev Psychiatry. 2016;28(1):112–9.
69. Grynberg M, Fanchin R, Dubost G, Colau J, Brémont-Weil C, Frydman R, et al. Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. Reprod Biomed Online. 2009;20(4):553–8.
70. Ikeda K, Baba T, Noguchi H, Nagasawa K, Endo T, Kiya T. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. Hum Reprod. 2013;28(2):453–61.
71. Caanen MR, Soleman RS, Kuijper EAM, Kreukels BPC, De Roo C, Tilleman K, et al. Antimullerian hormone levels decrease in female-to-male transsexuals using testosterone as cross-sex therapy. Fertil Steril. 2015;103(5):1340–5.
72. Bachmann G, Nevadunsky N. Diagnosis and treatment of atrophic vaginitis. Am Fam Physician. 2000;61(10):3090–6.
73. Light A, Obedin-Maliver J, Sevelius J, Kerns J. Transgender men who experienced pregnancy after female-to-male gender transitioning. Obstet Gynecol. 2014;124(6):1120–7.
74. Wallace S, Blough K, Kondapalli L. Fertility preservation in the transgender patient: expanding oncofertility care beyond cancer. Gynecol Endocrinol. 2014;30(12):868–71.
75. Payer A, Meyer III W, Walker P. The ultrastructural response of human Leydig cells to exogenous estrogens. Andrologia. 1979;11(6):423–36.
76. Hamada A, Kingsberg S, Wierckx K, T'Sjoen G, De Sutter P, Knudson G. Semen characteristics of transwomen referred for sperm banking before sex transition: A case series. Andrologia. 2015;47(7):832–8.
77. De Sutter P. Reproductive options for transpeople: Recommendations for revision of the WPATH's Standards of Care. Int J Transgenderism. 2009;11(3):183.
78. Meier SC, Pardo ST, Labuski C, Babcock J. Measures of clinical health among female-to-male transgender persons as a function of sexual orientation. Arch Sex Behav. 2013 Apr;42(3):463–74.
79. Eckstein AJ. Documenting transition, transforming gender: The worldmaking work of trans men on Youtube [Communication Graduate Theses & Dissertations]. [Boulder, Colorado]: University of Colorado at Boulder; 2016.
80. The Canadian Centre for Gender and Sexual Diversity. Ontario guide to help you on changing gender markers on your identification documents [Internet]. Ottawa, ON: The Canadian Centre for Gender and Sexual Diversity; 2018. Available from: http://ccgsd-ccdgs.org/wp-content/uploads/2018/06/Ontario-Guide-to-help-you-on-Changing-Gender-Markers-On-Your-Identification-Documents_June-10-2018.pdf
81. Government of Ontario. Change the sex designation on your government IDs [Internet]. 2017 [cited 2019 Feb 4]. Available from: https://www.ontario.ca/page/change-sex-designation-your-government-ids
82. Employment and Social Development Canada. Employment Insurance (EI) and voluntarily leaving [Internet]. 2004 [cited 2019 Feb 4]. Available from: https://www.canada.ca/en/employment-social-development/programs/ei/ei-list/quit-job.html
83. Centre for Addiction and Mental Health. Personal communication - E-mail to Amy Bourns, Oct 10, 2018.
84. TRS Surgical Summary Sheets [Internet]. [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/transition-related-surgery-surgical-summary-sheets/
85. Ministry of Health and Long-Term Care. What constitutes a "qualified provider" for TRS planning - E-mail to Amy Bourns. 2018.
86. Government of Ontario. Central Forms Repository - Request for Prior Approval for funding of sex-reassignment surgery [Internet]. n.d. [cited 2019 Feb 4]. Available from: http://www.forms.ssb.gov.on.ca/mbs/ssb/forms/ssbforms.nsf/FormDetail?OpenForm&ACT=RDR&TAB=PROFILE&SRCH=&ENV=WWE&TIT=5041&NO=5041-77E
87. Sherbourne Health. Community groups & drop-ins [Internet]. Sherbourne Health. n.d. [cited 2019 Feb 4]. Available from: http://sherbourne.on.ca/get-involved/community-groups/
88. Sherbourne Health. Acute Respite Care [Internet]. 2018. Available from: http://sherbourne.on.ca/wp-content/uploads/2017/06/SHC-171_Brochure_.pdf
89. Sherbourne Health. ARC Program Referral Form [Internet]. 2017. Available from: https://sherbourne.on.ca/wp-content/uploads/2017/06/Final-MAY-2017-referral-form-ARC-1.pdf

Part II: Feminizing hormone therapy

The goal of hormone therapy in transfeminine patients is to reduce the endogenous effects of testosterone and to induce feminine secondary sex characteristics in keeping with the patient's individual goals, as determined by their experience of gender incongruence and associated dysphoria, if present.

Physiologically, this requires the suppression of endogenous androgens and the addition of estrogen. This treatment results in both reversible and irreversible feminization. General effects such as reduction in muscle mass, reduction of body and (to a lesser extent) facial hair, and changes in skin as well as sweat and odour patterns are reversible.

Changes in facial and body subcutaneous fat distribution are generally considered reversible effects but to some degree may not be. Sexual and gonadal effects, including changes in libido and reduction in erectile function, are generally considered reversible, while reduced testicular and prostatic size, sperm count reduction and the resulting impact on fertility may be irreversible.[1]

Breast development is considered irreversible and would require surgical intervention to reverse. In adolescent patients, the initiation of estrogen therapy prior to the completion of skeletal growth[i] may lead to an earlier cessation of long bone growth, and therefore shorter adult height—an effect that would be irreversible.

i Complete epiphyseal fusion can occur as early as age 14 and as late as age 19 in AMAB individuals[2]

ANTI-ANDROGENS

Treatment with physiologic doses of estrogen alone is not usually sufficient to suppress testosterone levels into the physiologic female range in transfeminine patients who have not undergone gonadectomy.[3] Due to the potential for adverse effects with higher doses of estrogen (discussed below), androgen-suppressing agents are used as part of a feminizing regimen in transfeminine patients with gonads.

The anti-androgens most commonly used at our clinic are spironolactone and cyproterone. Spironolactone is a potassium-sparing diuretic, which acts as an anti-androgen at higher doses through direct blockade of peripheral androgen receptors. It also exerts secondary suppressive effects on androgen synthesis and has weak estrogenic and progestational activity. Given that its primary mechanism of action is at the receptor level, it will not always cause a significant change in blood testosterone levels. As a result, effectiveness should be evaluated by a patient's reported response (i.e., absence of spontaneous arousal, slowing of facial and body hair growth, skin changes) rather than serum levels.

Cyproterone is a synthetic steroid with progestin-like activity. Like spironolactone, it exerts anti-androgenic effects by binding to androgen receptors. In addition, its progestational activity exerts negative feedback on testosterone production through a reduction in gonadotropins. Anecdotally, cyproterone has been shown to be a more potent anti-androgen than spironolactone, with more rapid effects and a more marked suppression of libido and erectile function.

Historically at our clinic, spironolactone was chosen preferentially as it was believed to have a superior safety profile. This practice has changed somewhat over time, as adequate anti-androgenic effects and testosterone suppression into the female range have been shown to be attainable at lower doses of cyproterone (i.e., 12.5–25 mg daily), at which adverse effects are much less likely.[4]

In the absence of sufficient data to guide a preferential choice of one anti-androgen over another, the decision can be made individually for each patient based on medical history and preference regarding risk and side effect profiles (see Table 1). Both spironolactone and cyproterone are covered by Ontario Drug Benefit (ODB) without the need for an Exceptional Access Program (EAP) form.

Table 1
Effects, side effects and contraindications of anti-androgens

	SPIRONOLACTONE	CYPROTERONE
Drug Effects	Breast growth* Reduced erectile function** Decreased fertility** Reduced prostatic and testicular volume** Slowed growth of facial/body hair Decreased androgenic alopecia	Breast growth* Reduced Erectile function** Decreased fertility** Reduced prostatic and testicular volume** Slowed growth of facial/body hair Decreased androgenic alopecia
Side Effects	Hyperkalemia Renal impairment Polyuria, polydipsia, risk of dehydration Hypotension, orthostasis, dizziness Somnolence Gastrointestinal side effects Rash	Liver enzyme elevation Hepatotoxicity (acute liver failure, rare) Depression, especially in first 6-8 weeks Possible increased risk of VTE CBC changes: Anemia, thrombocytosis, myelosuppression (rare) Prolactinemia, possible increased risk of prolactinoma (esp. with estrogen)
Contraindications	Renal insufficiency Addison's disease or other conditions associated with hyperkalemia (type IV tubular acidosis) Hyperkalemia Avoid concomitant use of: ACE Inhibitors, ARBs, other potassium-sparing diuretics (if concomitant use is not avoidable, use with caution; consider low dose, slow titration and frequent monitoring due to the high risk of hyperkalemia) trimethoprim-sulfamethoxazole potassium supplements eplerenone, heparin, low molecular weight heparin	Active liver disease and hepatic dysfunction Severe renal insufficiency Severe chronic depression (caution in all patients with a history of depression) Previous or existing liver tumours Presence or history of meningioma Existing thromboembolic process Avoid concomitant use of hepatotoxic medications

VTE - venous thromboembolism, CBC - complete blood count, ACE - angiotensin converting enzyme, ARB - angiotensin II receptor blocker

* Irreversible
** May be irreversible

Table 2 shows the starting/low, customary and maximum doses for spironolactone and cyproterone. Generally, spironolactone can be started at 50 mg once daily, and increased every 2–4 weeks or more barring negative effects. Doses can be divided twice daily, or given once daily in the morning (for those who experience problematic nocturia) or at night (for those who have concerns around daytime bathroom safety). Total daily doses up to 300 mg/day have been used but are rarely required.

Cyproterone can be initiated at 12.5 mg and increased by 12.5 mg every 2–4 or more weeks (to a rare maximum of 50 mg) if required. Lower doses and/or less frequent dosing (e.g., one-quarter of a 25 mg tablet twice weekly, one-eighth of a 25 mg tablet every other day, etc.) have been used with success for patients who wish to maintain sexual function or minimize other side effects.

Time intervals for dose titration should take into consideration existing medical conditions, bloodwork results and individual transition-related goals.

If an adequate response is not achieved with maximum doses of the initially chosen agent, or side effects prohibit titration to adequate effect, we suggest initiating a trial of the alternative agent (in the absence of contraindications). When discontinuing spironolactone, consider a taper in patients with hypertension or renal dysfunction, with monitoring of blood pressure and volume status.

Table 2
Options and recommended doses of anti-androgens in feminizing therapy

	Starting/low dose	Usual dose	Maximum dose	Cost (4 weeks)*
Spironolactone (oral)	50 mg daily-bid	100 mg bid	150 mg bid[a]	$15–$41
Cyproterone (oral)	12.5 mg (¼ 50 mg tab) q2d-daily	12.5 mg (¼ 50 mg tab) –25 mg (½ 50 mg tab) daily	50 mg daily[a]	$16–$56

[a] Rarely required or used. Maximal effect does not necessarily require maximal dosing. Use clinical judgement in selecting optimal individual dosing.

* Price quotes are provided by www.pharmacy.ca. The abovementioned prices are accurate as of May 2018 and represent the price for a 4-week supply of a generic brand of medication (ranging from low dose to maximum dose). Prices include a usual and customary dispensing fee of $9.99 that may vary from pharmacy to pharmacy.

Note: For patients on ODB, spironolactone and cyproterone are covered without the submission of an EAP form.

Table 3 displays the monitoring parameters for both spironolactone and cyproterone. Note that additional parameters are required once estrogen is initiated (see Table 6).

If contraindications exist or if intolerance is a concern for both spironolactone and cyproterone, GnRH analogues (leuprolide/"Lupron" or busrelin/"Suprefact") may be considered. GnRH analogues flood the pituitary gland's GnRH receptors, leading to a downregulation of the response to endogenous GnRH and sustained suppression of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) release.

In the absence of stimulation by these gonadotropins, endogenous sex hormone production by the gonads ceases. GnRH analogues are commonly used for pubertal suppression in trans youth and have also been used in adults (in some European regimens) undergoing gender-affirming hormone therapy.[5,6]

Drawbacks include high cost, repeat (often painful) injections or frequent nasal spray dosing, and possible side-effects, including headache, mood changes and weight gain. It should be noted that the administration of a GnRH analogue in the absence of exogenous hormone use, for a significant amount of time (i.e., > 2 years), can decrease bone mineral density. If providers lack experience with the use of GnRH analogues, we recommend consultation or communication with an endocrinologist or another experienced provider prior to initiation.

Non-steroidal anti-androgens such as finasteride, dutasteride and flutamide have been used as anti-androgens in feminizing hormone regimens. Flutamide has been reported to have hepatotoxic effects and thus is not used at our clinic. Finasteride is a less effective anti-androgen and is generally not recommended for this purpose,[7] although it may be considered for those who desire very mild anti-androgenic effects (dose range 1–5mg daily). Finasteride is commonly added to a feminizing regimen for those who continue to exhibit scalp hair loss on a standard feminizing hormone regimen (usually 1 mg daily or one-quarter of a 5 mg tab daily), though its benefit in this setting of already suppressed androgenic activity has not been firmly established. It should be noted that there have been reports of permanent sexual dysfunction with the use of finasteride for scalp hair loss in cis men.

If the administration of anti-androgens is problematic, another option is the removal of the major source of endogenous testosterone, i.e., orchiectomy. For transfeminine patients who are unable to access or are not seeking vaginoplasty (as a part of which orchiectomy is routinely performed), orchiectomy alone is a choice that may be considered and is covered under OHIP by the Ministry of Health and Long-Term Care (MOHLTC) in Ontario following surgery planning visits and referral by qualified providers (see the *Supporting patients with transition-related surgeries* section earlier in this document).

For the vast majority of transfeminine patients who have undergone gonadectomy, androgen suppression will no longer be required. The androgen-blocker can be stopped immediately after surgery or tapered over the course of 4–6 weeks or more post-operatively.

In some cases, the effects of anti-androgens may be sought without the additional feminizing effects of estrogen, or when estrogen is contraindicated. In addition to potential hot flashes, low mood and fatigue, there may be a loss of bone mineral density, akin to that demonstrated in cis men who have undergone long-term androgen blockade without hormone replacement for the treatment of prostate cancer.[8] This treatment may, however, be considered in some circumstances, following detailed discussion with the patient, and with preventive measures and monitoring for bone loss in place. Periodic bone mineral density testing for those on prolonged monotherapy with an anti-androgen can be used to identify any concerning loss of bone density.

Table 3
Recommended parameters for monitoring anti-androgen therapy

		Baseline[a]	3–6 months	12 months
SPIRONOLACTONE	History	screen for contraindications/ potential drug interactions	side effects (polyuria, orthostasis)	
	PE	| ——— BP ——— | +/- breast inspection[b] (baseline)		
	Key labs	Cr, lytes, total testosterone		
CYPROTERONE	History	screen for contraindications/ potential drug interactions	side effects (depression, low energy), desired effects	
	PE	Wt, BP +/- breast inspection[b]	Wt, BP, abdominal exam	
	Key labs	CBC, AST/ALT, Cr, lytes, total testosterone	CBC[c], AST/ALT, total testosterone, Cr, lytes	CBC[c], AST/ALT, total testosterone, fasting glucose or Hba1c, lipid profile, +/-Cr, lytes[d]

a If not done in the preceding 3 months
b Breast inspection at baseline with attention to Tanner stage (+/- measurement), for patients who may have interest in OHIP-covered breast augmentation, see Part 1 - Physical exam and baseline investigations
c Red blood cell parameters can be expected to decrease with androgen blockade, female reference ranges for lower limits of normal should be used
d Necessary only if risks/concerns identified

Note: Additional parameters required as per guidelines with estrogen; pre-existing conditions or risk factors may require earlier/more frequent monitoring of specific parameters.

ESTROGEN

Estrogens act directly on estrogen receptors to initiate feminization. The effects and expected time course of a standard regimen consisting of an anti-androgen and estrogen are shown in Table 4. The degree and rate of physical effects are largely dependent on patient-specific factors such as age, genetics and body habitus, and to some extent the dose and route used, selected according to a patient's specific goals and risk profile.[9]

There is a lack of consensus among clinicians on the preferred timing of the initiation of estrogens in relation to an anti-androgen. Common approaches have included both the initiation of an anti-androgen prior (usually 1–3 months) to the addition of estrogen, or alternatively, the simultaneous introduction and subsequent titration of both components.

When deciding on the relative timing of anti-androgen and estrogen introduction, take into consideration that:

- the effects of anti-androgens are generally considered reversible, so the initiation of an anti-androgen first may be a preferred first step for patients seeking to explore the impact of subtle bodily changes before proceeding

with estrogen, or for those wishing to take a gradual approach to medical transition;

- staggering the initiation of an anti-androgen and estrogen allows for more readily identifying the problematic agent in the case of unusual side effects or drug allergy;

- in the absence of estrogen replacement, some patients may experience hot flashes, low mood, and/or fatigue; and

- there is weak evidence (one small study) suggesting that spironolactone used alone may prematurely inhibit breast development.[10] Whether other anti-androgens may have a similar impact is unknown.

Several forms and routes of estrogen have been used for feminization. At our clinic, the most common form used is oral 17-β estradiol (Estrace).[i] Oral 17-β estradiol is covered by the Ontario Drug Benefit (ODB) program without an EAP request.[11]

Table 4
Effects and expected time course of feminizing hormones

Effect	Expected onset[a]	Expected maximum effect[a]
Body fat redistribution	3–6 months	2–3 years
Decreased muscle mass/strength	3–6 months	1–2 years[b]
Softening of skin/decreased oiliness	3–6 months	Unknown
Decreased libido	1–3 months	3–6 months
Decreased spontaneous erections	1–3 months	3–6 months
Erectile dysfunction	Variable	Variable
Breast growth	3–6 months	1–2 years
Decreased testicular volume	3–6 months	2–3 years
Decreased sperm production	Unknown	> 3 years
Thinned/slowed growth of body/facial hair	6–12 months	> 3 years[c]
Scalp hair loss stops, no regrowth	1–3 months	Variable

a Estimates represent unpublished clinical and published observations[13 14 15]
b Significantly dependent on amount of exercise
c Complete removal of male facial and body hair requires electrolysis, laser treatment, or both

Adapted from: Hembree et al. 2017, *The Endocrine Treatment of Gender Dysphoric/ Gender Incongruent Persons: An Endocrine Society Guideline*[7]

i 17-β estradiol, whether in tablet or topical form, is a bio-identical hormone, structurally identical to estrogen made by the ovary in humans. Premarin, an estrogen derived from pregnant mare urine, is not bio-identical.

Oral formulations are subject to first pass gastrointestinal (GI) and liver metabolism which, according to the "first-pass hypothesis," contribute to negative hepatic and prothrombotic effects.[16] Sublingual, transdermal and injectable routes all bypass this stage during which much estradiol is oxidized to the less potent estrone.

The administration of estrogen via the sublingual route has gained interest in recent years given its accessibility (oral formulations of micronized estradiol can be dissolved under the tongue), affordability (compared to the transdermal route) and the proposed benefits of bypassing first pass metabolism.

A study comparing oral versus sublingual single-dose pharmacokinetics of micronized 17-β estradiol in postmenopausal cis women demonstrated rapid absorption with sublingual dosing, followed by a rapid fall in serum levels over the first six hours.[17] It has been noted that this may more closely mimic natural ovarian estrogen secretion.[12] Sublingual dosing also demonstrated lower circulating ratios of estrone to estradiol, higher peak estradiol levels (up to 13-fold over corresponding oral at a 1 mg dose), and higher 24-hour area under the curve for estradiol, which the authors postulate may translate into greater physiologic action.[17] The rapid peaks and increased periodicity may make monitoring serum levels more difficult.

While it is theoretically plausible that higher peak levels and increased periodicity may lead to increased risks (and unwanted side effects), there are no data yet that demonstrate any harm[7] or establish how potential harms and benefits may be offset. So while further studies are needed, sublingual dosing may have benefits over oral dosing, and could be considered as an alternative to switching to injections or the addition of a progestin when patients are dissatisfied with their degree of feminization and are seeking to explore alternative strategies.

Similar to the sublingual route, injectable estrogens bypass first pass metabolism and result in higher peaks and increased periodicity over oral forms. Injectable estrogen (in the form of compounded estradiol valerate) is available in Ontario through some compounding pharmacies, but is not covered by ODB. A single-dose pharmacokinetic study of IM estradiol valerate demonstrated peak levels at 3–5 days with an average half-life of 4–5 days.[18] Similar pharmacokinetics were demonstrated in a single study of subcutaneously injected estradiol.[19] Physiologic levels are attained through weekly or bi-weekly administration, which some patients prefer over daily oral dosing. There

Injection tips

- The viscosity of injectable estradiol varies depending on the liquid in which it is compounded—if viscosity is high, warming the vial in the palm of the hand for a few moments will help reduce it.
- Generally, injectable estradiol is drawn up with larger-gauge needles (18–20 g) and then injected intramuscularly with medium-gauge needles (22–23 g) or subcutaneously with smaller-gauge needles (25–26 g). This can be adjusted to manage client discomfort as needed—smaller gauge needles may mean longer injections, but less pain.
- Needle lengths are determined by body habitus and route of administration.
- The use of a 1 mL syringe can improve accuracy when drawing up smaller volumes of injectable estradiol and will decrease the force required to press the plunger of the syringe upon injection, compared to a 3 mL syringe.
- Opened multi-use vials of compounded estradiol valerate should be discarded after 28 days.

have been anecdotal reports of an acceleration in breast development following a switch to injectable from oral estradiol, but no outcome studies have been done. Challenging this observation, a recent study found no association between serum estradiol levels and breast development (though only oral and transdermal forms were used).[20]

If patients wish to self-inject, it is important to instruct them on the technique for safe injection and sharps disposal. Directly observing a patient self-inject makes it possible to correct any issues with technique. A written step-by-step guide on self-injection for patients is available from Fenway Health.[21]

Transdermal estradiol bypasses first pass metabolism, results in relatively steady serum levels and seems to have the best overall safety profile. Notably, studies of transdermal estradiol in menopausal cis women suggest no increased risk of venous thromboembolism (VTE),[22] and the improved safety profile is also reflected in studies in transfeminine patients.[13,23] Because of this, transdermal estradiol is recommended preferentially for transgender feminine patients who are over 40 or who have risk factors for cardiovascular (CV) or thromboembolic disease. It is most commonly administered in the form of the estradiol patch ("Estradot"), which is available from most pharmacies in Ontario but is unfortunately more expensive than oral forms. While it is often covered by private drug insurance, it is only covered by ODB in rare circumstances, such as a patient having the inability to swallow.

Other transdermal options include creams and gels. Estradiol creams are only available via compounding. Gel is available in a product formulated for the treatment of menopausal cis women ("Estragel"), however the area of skin needed for absorption of the gel is quite large, even for low/starting doses, so it is not a first choice for most trans patients. Cream and gel formulations may be effective for some transfeminine patients, but physiologic estrogen levels may be difficult to achieve in others. Again, these transdermal forms are expensive and not covered by ODB, but may be fully or partially covered by private drug plans. Note that specific details and dosing of compounded formulations should be discussed with the compounding pharmacist.

Following gonadectomy, most transgender women will not need androgen suppression; however, ongoing estrogen supplementation is generally needed to preserve bone mineral density. Reducing estrogen dosing is not required post-operatively,[12] but some patients may find that a lower dose suffices to maintain desired feminization in the absence of any endogenous testosterone. Consideration should be given to bone mineral density in agonadal patients on low dose estrogen (see the Osteoporosis and BMD screening sections in this document).

Table 5
Formulations and recommended doses of estrogen for feminizing hormone therapy

	Starting dose	Usual dose	Maximum dose	Cost (4 weeks)
Estradiol (oral)*	1–2mg daily	4 mg daily or 2 mg bid	6 mg daily or 3 mg bid	$18–$54 (covered by ODB)
Estradiol (transdermal, patch)*[a]	50 mcg daily/ apply patch 2x/week	Variable[d]	200 mcg daily/apply patches 2x/week	$39–$76[b]
Estradiol (transdermal, gel)*[c]	2.5 g daily (2 pumps, contains 150 mcg estradiol)	Variable[d]	6.25 g daily (5 pumps, contains 375 mcg estradiol), may be limited by surface area requirements for gel application	$58–$154
Estradiol valerate** injectable	3–4 mg q weekly or 6–8 mg q2 weeks	Variable[d]	10mg q weekly	$36–$46

a Estradot® brand
b 200 mcg daily given as 2 x 100 mcg patches applied twice weekly (4 patches/week)
c Estragel® brand
d Usual doses vary significantly between individuals. Use starting doses and titrate based on patient response. Maximum doses are not often needed. Use clinical judgement in selecting optimal individual dosing.
* *Price quotes provided by* www.pharmacy.ca
** *Estradiol valerate IM must be prepared by a compounding pharmacy, commonly at the minimum concentration of 10 mg/mL. Per updated Ontario guidelines, opened multi-use vials must be discarded after 28 days. Price quote provided by Pace Pharmacy.*

The above mentioned prices are accurate as of May 2018, and represent the price for a four-week supply of a generic brand of medication unless indicated otherwise (ranging from low dose to maximum dose). Prices include a usual and customary dispensing fee of $9.99 ($10.99 for Pace), which may vary from pharmacy to pharmacy.

PROGESTINS

With the exception of cyproterone, the use of progestins in transfeminine patients continues to be controversial.[7] Progestins have a suppressive effect on LH and therefore on testosterone production, and have at times been used as part of feminizing regimens for transfeminine patients. There have also been anecdotal reports of improved breast and/or areolar development, mood, sleep and libido with the use of progestins.[24,25] However, a clear impact has yet to be demonstrated.

Progestins have a role in histologic differentiation during breast development and lactation in cis women, however it is uncertain whether progestins add to breast volume in this population. A 2014 review of the literature regarding the effects of cross-sex hormone therapy on breast development in transfeminine patients identified a small number of low-quality studies that addressed the topic. The authors concluded that there was no evidence to suggest that progestins enhanced breast development. However, the absence of such an effect was not able to be definitively confirmed.[24]

In addition to weight gain and edema, depression is an often-cited side effect of progestins. Anecdotally, some patients may experience a favourable impact on mood, while others

may experience negative effects.[12,16] Some protocols have suggested the adjunctive use of progestins when traditional treatments don't achieve adequate androgen suppression, while others suggest a trial of a progestin as an option for transfeminine patients with low libido.[26]

The use of progestins in feminizing hormone therapy has traditionally been avoided by many centres based on harms demonstrated in the Women's Health Initiative (WHI) study. The WHI examined serious long-term outcomes with combined estrogen and progestin in post-menopausal cis women, finding an increased incidence of breast cancer, heart disease, stroke and venous thromboembolism. These same outcomes were not found to the same extent with estrogen alone.[27] However, the University of California, San Francisco (UCSF) Center for Excellence in Transgender Health cautions against the direct application of this data to transfeminine patients, stating:

"Considering (the) differences in demographics and goals of therapy, extremely modest increase in overall risk, and lack of difference in mortality, as well as more recent reassuring data with other forms of estrogen, the risks of using progestogens in transgender feminine patients are likely minimal or even absent."[12]

Nonetheless, given the lack of clear benefit, and the potential risks of progestin therapy (though perhaps of less magnitude than originally thought), we do not currently recommend the routine use of progestins as part of a feminizing hormone regimen. Some patients may request progestin treatment, either in hopes of attaining anecdotal benefits, or due to a desire to more closely reflect the hormonal milieu of cis women. In such cases, a trial may be considered following a frank discussion of expectations and risks. *Appendix L* includes a summary that can help with counselling patients around these risks.

The common doses of progestins are micronized bio-identical progesterone "Prometrium" 100–200 mg daily; or medroxyprogesterone acetate/"Provera" 5–20 mg daily. Risks are likely lower with micronized progesterone than with medroxyprogesterone, so the former is chosen preferentially by most clinicians. In addition, the former may be better tolerated and have a more favourable impact on the lipid profile than medroxyprogesterone.[9] Injected depo-medroxyprogesterone acetate "Depo-Provera" is seldom used in transfeminine patients. If a progestin is prescribed, some clinicians advise limiting the treatment duration to a maximum of two to three years, or the use of cyclical dosing (i.e., administered 10 days per month).[28]

SPECIAL CONSIDERATIONS FOR OLDER TRANSFEMININE PATIENTS

There is little information in the literature to guide recommendations for the initiation or maintenance of feminizing hormone regimens in older transfeminine patients. Unique considerations in older populations include changes in endogenous hormone levels, physiologic changes that may affect response to medications, a higher burden of existing medical conditions, and multiple pre-existing medications leading to the increased potential for drug interactions.

It is not uncommon for transfeminine patients to seek to initiate hormone therapy at older ages.[29] Feminizing effects may be slower and more subtle for those initiating therapy at an advanced age. Despite this, a large number of transfeminine patients have initiated hormone therapy at advanced ages with an acceptable degree of safety and satisfaction. There is no reason to withhold hormone therapy from elderly patients simply due to age.[30] For some older transfeminine patients who have had to delay transition until later in life, maximizing feminization may take precedence over concerns about risk. For such patients, an "active period" of treatment with doses used for younger patients may be considered following a thorough discussion of risks and benefits.

For transfeminine patients over 50, it is reasonable to mimic physiologic hormone levels in menopausal cis women, which can usually be attained with

estrogen doses typically administered to post-menopausal cis women, e.g., starting/low-dose topical formulations. For those with gonads, required anti-androgen doses may also be lower due to age-related decreases in serum testosterone. The preferential use of spironolactone in older transfeminine patients (with healthy renal function) has been suggested given the possible increased thromboembolic risk associated with cyproterone.[30]

For those over age 50 who have been on feminizing hormone therapy for some time, some guidelines suggest considering complete discontinuation of hormone therapy. However, those without gonads will likely experience symptoms akin to menopause along with potential loss of bone mineral density, and those with gonads may experience a return of virilization.[12]

As with all trans patients, decisions about hormone therapy at an advanced age should be individualized following a thorough discussion of risks and benefits.

MONITORING AND DOSE ADJUSTMENTS

Standard monitoring of a feminizing regimen should be employed at baseline, three months, six months and one year (additionally, creatinine and electrolytes should be checked between four and six weeks following initiation of spironolactone). Some providers prefer to see patients monthly until an effective dose is established. Follow-up visits should include a functional inquiry, targeted physical exam, bloodwork and health promotion/disease prevention counselling as indicated. The suggested tasks for these visits are summarized in Appendix B.

Functional inquiry should include subjective positive or negative impacts on mental health as well as any noted physiologic changes. It may be helpful to remind patients that changes related to androgen blockade and estrogen administration may take months to years for full effect.

The first changes will likely be loss of spontaneous and morning arousal. Breast development, skin and hair changes, and fat redistribution take longer. Some patients may experience a small amount of physiologic galactorrhea early in the course of treatment. If galactorrhea is from more than one duct or bilateral, and non-bloody, no further workup is warranted.

Generally, physical changes are considered to be complete after 2–3 years on hormone therapy (see Table 4). Periodically, the clinician should counsel around monitoring for signs and symptoms of VTE, particularly in those at increased risk. Patients should be periodically reminded about the importance of adequate calcium and vitamin D intake. Examination should be focused and minimally include blood pressure and weight. Bloodwork should be completed according to Table 6 below, with more frequent monitoring as deemed necessary if concerns are identified.

Table 6
Recommended bloodwork for monitoring feminizing hormone therapy

In this table, smaller and lighter grey "x"s indicate parameters that are measured under particular circumstances

Test	Baseline	4–6 weeks	3 months	6 months	12 months[e]	Yearly	According to guidelines for cis patients, or provider discretion
CBC[a]	X		x	x	X	x	
ALT/AST[b]	X		x	x	X	x	X
Creatinine/lytes[c]	X	x	x	x	x	x	
Hba1c or fasting glucose	X				X		X
Lipid profile	X				X		X
Total testosterone	X		X	X	X	X	
Estradiol	X		X	X	X	X	
Prolactin[d]	X				x	x	x
Other	Hep B, C						
	Consider: HIV, syphilis and other STI screening as indicated, frequency depending on risk						

a At baseline for all, and regularly with cyproterone, for Hb/Hct use female reference for lower limit of normal and male reference for upper limit of normal

b Baseline for all and regularly with cyproterone, otherwise repeat once at 6–12 months then as needed

c Cr, lytes, should be monitored at each visit with spironolactone, but is only required at baseline and then once between 6–12 months with cyproterone unless risk factors or concerns re: renal disease are present, use male reference range for upper limit of normal for Cr

d Prolactin should be monitored at least yearly with the use of cyproterone, and more frequently if elevation is noted

e During first year of treatment only

Note: Individual parameters should be considered more frequently if concerns are identified or existing risk factors are present.

Dose titration of anti-androgen and estrogen may be performed over the course of 3–6 months or more, and will depend on patient goals, physical response, measured serum hormone levels and other lab results.

A common titration might look like:

1. initiate therapy with 1 mg oral estradiol and 50 mg of spironolactone daily;
2. check creatinine and electrolytes at one month and, barring any concerns, increase estradiol to 2 mg and spironolactone to 50 mg twice daily;
3. following three-month bloodwork and check-in, increase estradiol to 3 mg daily and spironolactone to 75 mg twice daily; and
4. continue titration as needed until maintenance dose is achieved.

Titration schedules vary between clinicians and can be tailored to individual patient needs and variables. Some patients may be eager to begin maximal therapy, but there is some evidence to suggest that excessive estrogenic action may limit breast development, and that the estrogen-receptor agonist activity of spironolactone may contribute to this effect.[10,24] The evidence is considered weak, however it suggests potential benefits to a slow upward titration. These factors can be discussed with patients in order to facilitate collaborative and informed decision making.

Hormone levels for those seeking a more androgynous appearance may intentionally be mid-range between male and female norms. For many transfeminine patients, the goal will be to achieve the suppression of testosterone into the female range (see *Appendix J*). Be mindful that patients may experience clinically relevant results without total suppression of testosterone due to peripheral androgen blockade, which is not measured.

In the vast majority of cases, the measurement of total testosterone (rather than both total and free) is adequate to assess the degree of androgen suppression. Measurements and calculated estimates of free testosterone are imprecise and generally don't add value. In rare cases, the calculation of free or bioavailable testosterone may be helpful for fine-tuning hormone regimens, for example where there is persistent virilization despite a total testosterone in the female range.[12,ii]

Serum estradiol levels should also be monitored. The *Endocrine Society Guidelines* recommend serum estradiol levels be maintained "at the level for premenopausal females (100 to 200 pg/mL),"[7] which corresponds approximately to 370–735 pmol/L. Again, it is important to keep in mind that clinical effects are the goal of therapy, not specific lab values. Anecdotally, we have found that most patients reach considerable feminization at estradiol levels between 200–500 pmol/L.

We have occasionally seen very high estradiol levels reported. In this situation, reviewing the dose (including use of estrogens without a prescription) and route (i.e., oral versus sublingual) with the patient may be helpful in elucidating the cause. For those on injectable estrogen, levels taken at peak in the cycle may be expected to exceed recommended targets. When monitoring injectable estrogen, most guidelines recommend checking serum levels at mid-cycle, while some clinicians prefer to measure at trough (i.e., just before the next injection is due). The latter adds convenience for patients who prefer to come into clinic for their injections. There may also be utility in varying the timing of bloodwork to gather information regarding serum levels throughout the cycle (peak, mid-cycle and trough), especially if a patient is reporting cyclic symptoms (e.g., hot flashes, headaches, fatigue). In such cases, wide fluctuations should prompt consideration of increased frequency of injections or a route with less periodicity.[12]

If the sex marker associated with the patient's health card has not been changed, the reported reference ranges will refer to the sex assigned at birth. As reference ranges vary between laboratories, it is important to be able to refer to reference ranges for the affirmed gender from the specific laboratory. These can often be found on laboratory websites or can be obtained by request from the lab. For those using LifeLabs in Ontario, male and female reference ranges for hormone levels are listed in *Appendix J*.

Ideally, labs would be able to report reference ranges in a patient's affirmed gender, regardless of their OHIP sex marker, or to report both male and female reference ranges with a patient's results. There are currently logistical and systems barriers to this practice in Ontario labs, though efforts are underway to make improvements in laboratories' direct service to trans patients as well as amendments to reference range reporting.

ii Total testosterone may not accurately reflect bioavailable (i.e., biologically active) testosterone, which consists of free testosterone (not bound to serum proteins) plus testosterone weakly bound to albumin. A calculated estimate of free testosterone is reported by Lifelabs when requested on the requisition, while bioavailable testosterone can be calculated with the measurement of total testosterone, serum albumin and sex hormone binding globulin, via an online calculator.[31]

Limitations to feminizing hormone therapy

In the vast majority of cases, hormone levels in the female range can be achieved fairly readily if that is the goal. Yet the physiologic results in transfeminine patients may not meet a patient's hopes and expectations for feminization, and some may experience ongoing dysphoria or dissatisfaction. These limitations to feminizing hormone therapy should be reviewed with patients before initiation to minimize disappointment from unachievable expectations.

Feminizing therapy does not affect the pitch of the voice in transfeminine patients. Some patients may benefit from voice therapy with a qualified and supportive speech and language therapist who can work with the patient to modify their vocal characteristics. Obtaining MOHLTC-covered services can be challenging, though many private extended health plans will cover voice therapy with a note from a primary care or other provider. A variety of surgical techniques have also been used to feminize the voice by altering the vocal cords. These procedures are also not covered by MOHLTC and carry risks for vocal and other complications, though some patients may benefit from these procedures if vocal therapy has not produced satisfactory changes.

Although feminizing therapy slows the rate of growth of hair on the face and neck, it does not eliminate it. Plucking, waxing or depilatory chemicals are temporary measures, therefore many patients will seek permanent hair reduction by laser hair removal or electrolysis. Both of these techniques can be painful, require multiple sessions and may require lifelong treatment for sustained effect. Unfortunately, these procedures are not covered by MOHLTC. Additionally, feminizing hormone therapy does not affect the underlying bone structure of the face. Some softening of the facial features (possibly through fat redistribution) is anecdotally reported by patients. Some transfeminine patients may desire facial feminization surgery (FFS), however this procedure is not covered by MOHLTC.

Breast growth is an aspect of feminization that is very important to many transfeminine patients. Unfortunately, many women will be dissatisfied with their degree of breast development. Though likely dependant on many factors such as genetics, body habitus and age, a 2014 review of the literature by Wierckx et al. found that most transfeminine patients experienced modest breast development (average cup size < A, at a developmental Tanner stage of 2 to 3).[24] A recent multicentre prospective cohort study of transfeminine patients on various hormone regimens found that the majority of breast development occurred during the first six months of treatment, and by the end of the one-year study period most women had AAA cup size or smaller, while only 3.6% obtained a cup size greater than A.[20]

Both Wierckx's review[24] and the cohort study[20] found that neither type nor dosage of estrogen had an effect on final breast size, with the latter study further establishing no relationship between serum estradiol levels and breast development after one year. As discussed above, there is no evidence to support that progestins confer any benefit.[24]

The extent to which the degree of testosterone suppression may affect breast development is unknown. Seal et al. found that those using spironolactone were more likely to seek augmentation mammoplasty compared with those using other anti-androgens, an effect they hypothesize may be due to estrogen-agonist effects of spironolactone contributing to premature breast bud fusion.[10] Research to date examining factors impacting breast development in transfeminine patients is scarce and of low quality. More research is needed to guide recommendations in regards to this aspect of feminizing therapy.

Currently MOHLTC will fund augmentation mammoplasty if there has been no breast development following 12 months of continuous estrogen therapy, or if estrogen is contraindicated (see Supporting patients seeking transition-related surgery).

PRECAUTIONS AND RISK MITIGATION WITH ESTROGEN THERAPY

Many providers new to trans care have concerns about the safety of estrogen, particularly with respect to cardiovascular/venous thromboembolic events and malignancies. As more evidence emerges on modern feminizing regimens, fears of a significant negative impact on morbidity and mortality are being waylaid. Following a recent comprehensive review of the literature, Weinand and Safer conclude that the compiled evidence suggests feminizing therapy for transgender individuals is "safe without a large risk of adverse events when followed carefully for a few well-documented medical concerns,"[32] which will be reviewed in more detail below.

Pre-existing medical conditions and risk factors may increase risks with estrogen administration, and should be considered to enable individualized discussions with patients regarding their unique risks and benefits of treatment. Available measures to reduce associated risks (see Table 7 and expanded discussion below) should be considered and discussed with patients, and, if possible, undertaken prior to or concurrently with the initiation of hormone therapy. In some cases, patients may wish to begin hormone therapy in the setting of ongoing increased risk, i.e., immitigable risk or having declined measures for risk mitigation. In these situations, a careful informed consent process should be undertaken which takes into consideration individual capacity to make an informed decision, the severity of potential harms from treatment, and the harms that may result from not pursuing treatment.

The initiation of feminizing hormone therapy should ideally be done in collaboration with relevant specialists who may already be involved in a patient's care. In some cases, a new referral may be helpful in informing decisions about risks and their mitigation. However, efforts should be taken to ensure that this does not cause undue delay. If accessibility to a specialist is limited, an e-consult can be both timely and beneficial.

There are a small number of contraindications to estrogen therapy:

- unstable ischemic cardiovascular disease;
- estrogen-dependent cancer;
- end-stage chronic liver disease;
- psychiatric conditions that limit the ability to provide informed consent; and
- hypersensitivity to one of the components of the formulation.

Table 7
Precautions with estrogen therapy and considerations in minimizing associated risks

Precaution to estrogen therapy	Considerations in minimizing associated risks
Strong family history of abnormal clotting	Rule out genetic clotting disorder, if affected see 'hypercoagulable state', consider transdermal route of administration, consider spironolactone as preferred anti-androgen
Metabolic syndrome	Dietary and medical management of component disorders, consider cardiac stress test, consider transdermal route of administration
Severe, refractory or focal migraine*	Consider referral to neurology, consider daily migraine prophylaxis, ensure all other cerebrovascular risk factors are optimized, consider transdermal route of administration, consider spironolactone as preferred anti-androgen
Seizure disorder	Consider referral to neurology, consult with a pharmacist re: possible estrogen interaction with anticonvulsant medication
Other cardiac disease	Consider referral to cardiology
Hyperprolactinemia	Determine etiology and manage as indicated, if prolactin > 80 mcg/L or symptomatic - rule out prolactinoma, refer to endocrinology as needed, consider spironolactone as preferred anti-androgen
History of benign intracranial hypertension	Consider referral to neurology/neurosurgery
Hepatic dysfunction	Dependent on etiology, e.g. minimize alcohol consumption, weight loss in NAFLD, consider referral to hepatology/gastroenterology, use transdermal, sublingual, or injectable route of administration, consider spironolactone as preferred anti-androgen
Strong family history of breast cancer	Refer to genetics/familial breast cancer program for further risk stratification and genetic testing as indicated
Prior history of estrogen-sensitive cancer	Refer to oncology
Autoimmune conditions (e.g. RA, MS, IBD)	Start low dose, titrate slowly in collaboration with any involved specialists
Personal or Family history of porphyria (rare)	Consider referral to porphyria clinic or internist with experience in porphyria
Stable ischemic cardiovascular disease*	Consider referral to cardiology, ensure optimal medical (including prophylactic antiplatelet agent(s) if indicated per national guidelines) and/or surgical management as indicated, risk factor optimization, use transdermal route of administration +/- lower dose, consider spironolactone as preferred anti-androgen

Precaution to estrogen therapy	Considerations in minimizing associated risks
Cerebrovascular disease*	Consider referral to neurology, ensure optimal medical management (including prophylactic antiplatelet agent(s) if indicated per current national guidelines) and risk factor optimization, use transdermal route of administration +/- lower dose
Hypercoagulable state or personal history of DVT or PE	Identify and minimize existent risk factors, prophylactic anti-coagulation if indicated per current national guidelines, consider referral to hematology/thrombosis clinic, use transdermal route of administration +/- lower dose, consider spironolactone as preferred anti-androgen
Marked hypertriglyceridemia	Identify and address barriers to optimal lipid control, refer to dietitian, minimize alcohol consumption, consider anti-lipemic pharmacologic therapy, consider endocrinology referral, use transdermal route of administration
Uncontrolled high blood pressure	Identify and address barriers to optimal BP control, use spironolactone as preferred anti-androgen, add additional antihypertensives as needed (avoid ACEs/ARBs with spironolactone), consider cardiac stress test, consider transdermal route of administration, consider referral to cardiology
Uncontrolled diabetes	Identify and address barriers to optimal glycemic control, refer to dietitian, encourage lifestyle modification, initiate antiglycemic agent(s) per national guidelines, consider cardiac stress test, consider transdermal route of administration
Smoker	Encourage and support smoking cessation, consider referral to smoking cessation program/offer NRT and/or bupropion/varenicline, or negotiate a decrease in smoking, consider cardiac stress test, use transdermal route of administration +/- lower dose, consider spironolactone as preferred anti-androgen, consider low-dose ASA prophylaxis

* Imparts moderate to high risk of an adverse outcome without risk mitigation

ACEs: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers; NRT: nicotine replacement therapy; NAFLD : non-alcoholic fatty liver disease; GI: gastroenterology; RA: rheumatoid arthritis; MS: multiple sclerosis; IBD: inflammatory bowel disease; DVT: deep vein thrombosis; PE: pulmonary embolism; BP: blood pressure; ASA: acetylsalicylic acid

SPECIFIC CONDITIONS: RISK MITIGATION AND LONG-TERM PREVENTIVE CARE

Venous thromboembolism (VTE)

Historically, studies on transfeminine patients have revealed a significant increase in thromboembolic events with estrogen administration at the highest risk during the first year of treatment. Potential variables affecting the risk of VTE in transfeminine patients include type, route and dose of estrogen; selection of anti-androgen; the use of progestin; and pre-existing risk factors.

Many of the patients in the original studies evaluating thromboembolic risk were taking ethinyl estradiol, which is now known to be significantly more thrombogenic than estradiol.[23] Studies on menopausal cis women have suggested increased thrombogenicity and CVD risk with the use of conjugated estrogens (Premarin) over estradiol.[33,34]

Studies on the risk associated with oral estradiol use in menopausal cis women have yielded variable results, with some suggesting no increased risk and others suggesting a 2.5 to 4-fold increased risk. Risk in this setting may also have been impacted by choice of co-administered progestin.[22,35] A recent retrospective study involving trans women taking a regimen of spironolactone and oral estradiol (4-8 mg/day) showed no increase of VTE over baseline risk in the general population.[36] A comparison of their results with those of Wierckx et al.,[37] which demonstrated a 5.1% increase in lifetime risk of VTE in trans women taking largely transdermal or oral estradiol in combination with cyproterone, prompted the authors to speculate on the potential role of cyproterone in conferring increased thrombogenic risk. Most recently, a large cohort study of 2,842 transfeminine patients in the U.S. who presented for care at Kaiser Permanente between 2006 and 2014 demonstrated an increased incidence of VTE, with two- and eight-year risk differences of 4.1 and 16.7 compared to cis men, and 3.4 and 13.7 risk differences compared to cis women. Despite the relatively large cohort size, detailed analysis by specific hormone regimens was precluded.[38]

Transdermal forms have been shown to have minimal effects on hemostatic variables and to confer minimal or no thrombotic risk in menopausal cis women, even in those with a prior history of thrombosis.[35] As discussed previously, sublingual and injectable formulations may also be associated with decreased VTE risk by bypassing first pass metabolism and the associated hepatic production of clotting factors, but how this balances with the potential impact of high-serum values observed shortly after administration is unknown.

Risk increases in patients who are over age 40, highly sedentary or obese, and particularly in smokers or those who have underlying thrombophilic disorders. Low-dose acetylsalicylic acid (ASA) prophylaxis can be considered for smokers, however there is no data to inform a risk-benefit analysis between VTE and bleeding.[39] Transdermal formulations should be used whenever possible in patients with risk factors. Routine screening for thrombophilic disorders prior to estrogen initiation is not recommended and should be restricted to those with a personal or strong family history of thromboembolic events.[40]

Deutsch's group presents helpful algorithms to address various scenarios of VTE history or risk factors and estrogen use.[12] The routine use of prophylactic ASA or anticoagulation is not recommended in transfeminine patients without another indication per national thrombosis guidelines.[41]

It is currently common practice to discontinue estrogen therapy 2–4 weeks prior to surgical procedures, including vaginoplasty, due to the assumed increased risk of VTE. The necessity of this practice has come into question by some experts who cite a lack of supportive evidence in addition to suspecting a strong association between hormone cessation and post-operative depression.[12] More research is needed to address this question. In the meantime, we encourage our patients to discuss

hormone cessation recommendations with their surgeon. In general, estrogen can be restarted post-operatively once a patient is ambulatory.

Cardiovascular disease and related metabolic risk factors

Studies in cis women demonstrating an increased risk of CV events with the use of estrogen gave rise to concerns about the extent to which estrogen preparations could cause harmful CV events in transgender women.[27,42] A 2010 Cochrane review of hormone replacement therapy in cis menopausal women found no increased all-cause mortality, cardiovascular-related mortality, non-fatal myocardial infarction (MI), angina, or need for angioplasty or bypass surgery. The same review demonstrated a small increase in stroke, limited to a subgroup of women who started hormone replacement therapy greater than ten years following menopause.[43]

The extrapolation from the use of estrogen in cis populations to trans populations is problematic for a number of reasons, including significant differences in the average age of initiation and associated risk factors at baseline, different hormone regimens and doses as well as differences in genetic makeup and natal hormonal milieu.

Studies in trans populations, however, have been limited to small prospective studies, and some larger retrospective cohort studies that did not account for significant risk factors, including tobacco use.[23,37,44,45] Furthermore, many of the studies on transfeminine patients do not distinguish between the dosage or form of oral estradiol used (ethinyl estradiol, conjugated equine estrogens or 17-β estradiol), the concomitant use of progesterone or the type of anti-androgen, which further complicates interpreting their data. Though also hampered by these limitations, it is noteworthy that the Kaiser Permanente cohort demonstrated rates of MI in transfeminine participants similar to those observed in cis men, with a very small increase noted in the rate of ischemic stroke.[38]

A large 2010 meta-analysis of transfeminine patients using feminizing hormones demonstrated an increase in triglyceride concentrations of 0.26 mmol/L, with no changes in any other lipid parameters or in blood pressure. Very few CV events were reported, and the authors concluded that data were insufficient to allow meaningful assessment of clinically important CV-related outcomes.[46]

A systematic review of 29 studies commissioned by the Endocrine Society in 2017 arrived at similar conclusions, reporting a statistically significant increase in triglycerides without changes in other lipid parameters, and very few cases of MI, stroke and CV-related mortality. Again, the evidence was noted to be of poor quality.[7]

The effect of feminizing hormones on blood sugar and diabetes type II (DMII) risk is also unclear. Some studies suggest an increase in insulin resistance and fasting glucose.[3,47,48] Higher rates of DMII have been observed in transfeminine patients compared to age-matched cisgender men and women,[37] but the degree to which hormone therapy is implicated versus other factors is unknown. The Endocrine Society guidelines state that there is limited evidence to determine whether estrogen has a beneficial or detrimental effect on blood sugar or DMII risk in transfeminine patients.[7]

Most experts and organizations take a similar approach regarding risk mitigation with estrogen: CV risk factors in transfeminine patients should be optimally managed, according to existing national guidelines, and a transdermal route of estrogen should be used preferentially in those with existing risk factors or high triglycerides.[7,12,28,49]

Optimal management of CV parameters can be reached prior to, or concurrently with, the administration of feminizing hormone therapy. They can be managed according to the guidelines if concerns arise during treatment.

While the assessment of baseline risk prior to the initiation of hormone therapy can be estimated by sex-based risk calculators using sex assigned

at birth (e.g., Framingham), risk calculations become more challenging after changes in the hormonal milieu. The UCSF Center for Excellence in Transgender Health suggests that, depending on the age of hormone initiation and duration of hormone exposure, providers may choose to use the risk calculator for sex assigned at birth, affirmed gender, or an average of both.[39] Prophylactic antiplatelet agents are not routinely recommended for primary prevention.

Osteoporosis and bone mineral density screening

Sex hormones affect bone mineral density (BMD), and the subsequent risk of osteoporosis. A hypogonadal state induces loss of bone in both cis men and cis women. In studies of older cis men, serum estradiol levels show a stronger association with the maintenance of BMD than testosterone levels.[50,51]

Although multiple studies have found a lower BMD in trans women prior to estrogen therapy when compared to age-matched cis men,[52–54] bone support appears to be adequate in transfeminine patients who are maintained on estrogen. Previous evidence has been conflicting, however a recent systematic review commissioned by the Endocrine Society found a statistically significant increase in BMD values at 12 and 24 months compared with baseline values before feminizing hormone therapy.[7]

In accordance with national recommendations for cis people, bone mineral density testing should be offered to all transfeminine patients over age 65, and screening to identify people at higher risk of osteoporosis (including those who smoke, are HIV-positive, have a high alcohol intake or a body weight < 60 kg) can begin at age 50. As in cis populations, the presence of certain high-risk conditions such as hyperparathyroidism or malabsorption syndrome warrant screening before age 50.[54]

High-risk scenarios unique to trans populations that should prompt earlier screening include patients who have undergone orchiectomy and have been on low-dose or no hormones for any significant length of time (i.e., > 2 years). Screening may also be considered for those who have been on anti-androgens or a GnRH analogue for a significant length of time without the co-administration of exogenous estrogen.

There are no studies to guide the interpretation of BMD results and fracture risk in trans people. Current tools (e.g., FRAX, CAROC) are age- and sex-based, and it is unclear whether better approximations are obtained using sex assigned at birth or affirmed gender. Some guidelines suggest that this decision may be made on an individual basis, depending on the age at which hormones are initiated. Alternatively, in some cases it may be reasonable to assess fracture risk using both sex calculators and using an intermediate value.[7] Our current practice is to interpret results in comparison to those that exist for both men and women, and some imaging centres (e.g., Women's College Hospital in Toronto) report results in this manner for patients who are identified as trans on the requisition by the ordering provider.

Despite reassuring data regarding risks, all transfeminine patients should ensure a daily intake of 1000 IU vitamin D and 1200 mg of calcium (total of diet + supplements). Weight-bearing exercise (i.e., exercise that involves moving the body against gravity) should also be encouraged. For those wanting to maintain muscle and bone strength but minimize muscle bulk development, weight lifting with high repetitions and lighter weights is suggested.

Hyperprolactinemia/prolactinoma

There is a theoretical increased risk of hyperprolactinemia and prolactinoma in transfeminine patients on feminizing hormone therapy. Elevations in serum prolactin are common and, while typically benign, there have been multiple case reports of prolactinoma in transfeminine patients following long-term

hormone therapy.[55–58] There remains no clear evidence, however, to suggest an increased risk compared to cis women.[12] Some point out concerns regarding the potential for estrogen to mask the symptoms of a prolactinoma given they are similar to the desired effects of estrogen.[3,24,59]

Thus, some guidelines recommend checking prolactin at baseline and monitoring every 1–2 years during treatment.[7] The recommended response to elevations include decreasing the estrogen dose and, if elevations are persistent or above a certain threshold, imaging of the sella turcica. Various arguments are emerging that these routine practices may be unnecessary. While the elevations in prolactin seen in transfeminine patients have historically been attributed to estrogen, recent studies implicate cyproterone as having a major role.[60,61]

These findings have prompted some to suggest that monitoring of prolactin is unnecessary if cyproterone is not being used.[61] Secondly, Deutsch's group points out that given the recommendation for expectant management of asymptomatic prolactinoma, such routine monitoring for hyperprolactinemia (and associated prolactinoma) would not have an impact on management[62] and could lead to needless harm and cost. As such, they recommend checking prolactin only in cases of symptoms, i.e., visual disturbances, excessive galactorrhea or new onset of headaches.[12]

Our current approach is to monitor prolactin at baseline, particularly in those with a history of hyperprolactinemia or those who use medications that may increase prolactin (e.g., antipsychotics), and then yearly if cyproterone is being used. If significant elevation (> 60–70) is noted on cyproterone, a trial switch to spironolactone should be considered prior to decreasing estrogen dose. Levels can be checked 6–8 weeks following any medication adjustments. Imaging can be considered in the setting of persistent elevations > 80 mcg/L, and should always be ordered if symptoms are present.

Breast cancer

Estrogens stimulate epithelial growth and the development of acini and lobules in the breasts of transgender women. How the risk of breast cancer in transfeminine patients compares with that of cis women or cis men has been a matter of debate. Evidence to date suggests that the risk of breast cancer in transfeminine patients is not higher and may potentially be lower than in cisgender women.[24,37,63,64,64,65]

Longer duration of feminizing hormone exposure (i.e., number of years taking estrogen), family history of breast cancer, obesity (BMI > 35), and the use of progestins likely increase the level of risk.[9] Those with a strong family history of breast and/or ovarian cancer who are considering estrogen should be referred to a familial breast cancer program and undergo genetic screening as indicated. It is unfortunately not known to what extent BRCA mutations influence the risk of developing breast cancer in transfeminine patients on estrogen, but the reasonable expectation of increased risk is important to take into account. A 2014 case report discusses the treatment of a BRCA 1 positive trans woman who declined prophylactic mastectomy and continued on estrogen therapy under informed consent.[66]

Transfeminine patients should receive counselling around breast self-awareness as is recommended for cis women. In general, annual clinical breast examination as a part of routine breast cancer screening is of questionable utility, but may be useful in transfeminine patients to assess the degree of breast development or to assess for implant complications if the patient has undergone breast augmentation.

A 2009 study which assessed the feasibility and acceptability of screening mammography in trans women found that screening was technically possible, nearly painless and of high personal importance.[67] However, the finding that transfeminine patients have a high prevalence of dense breasts—60% dense or very dense on mammography[67]—raises questions about

the sensitivity and specificity of mammography in trans compared to cis women.[26]

Recommendations for initiation and frequency of screening mammography in transfeminine patients vary between organizations. Our current practice is to perform mammography in transfeminine patients every two years if ≥ 50 years old AND on estrogen for ≥ 5 years total (i.e. years do not have to be consecutive), and to consider initiating screening at a younger age if additional risk factors are present. A Dutch retrospective cohort study presented at the 2018 Endocrine Society conference in Chicago found a comparable rate, but earlier age of onset of breast cancer in transfeminine patients when compared to cis women (average age 51 versus 61, respectively), prompting the question of a need for earlier screening in transfeminine patients.[65] More research to support this finding would be beneficial before revisions to the current recommendations for trans individuals are considered.

Transfeminine patients who have changed their OHIP sex marker to "female" can be screened as part of the organized Ontario Breast Screening Program and as such will receive correspondence letters for invitations, organized follow-up on abnormal results, and reminders.

When implants are present, the technical approach of a diagnostic mammogram rather than a screening mammogram is necessary.[67] In addition, routine imaging to screen for implant rupture may be recommended depending on the implant type. In the case of saline implants, rupture causes a visible deflation and thus diagnosis is clinical and routine imaging is not indicated. In the case of silicone implants, "silent" (non-visible) rupture can occur. Recommendations for screening vary between surgeons and implant manufacturers. Currently Gender Reassignment Surgery (GRS) Montreal recommends an annual ultrasound for silicone implants from the fifth year onward.[68] If a rupture is suspected but not confirmed by ultrasound, an MRI can be performed.

Prostate cancer

It is reasonable to assume that the risk of both benign prostatic hypertrophy and prostate cancer is significantly decreased by the androgen deprivation associated with feminizing hormone therapy and/or gonadectomy. Although rare, there have been cases of prostate cancer reported in transfeminine patients, generally occurring in those who started hormone therapy after the age of 50.[69] It is important to note that feminizing therapy will lower prostate-specific antigen (PSA) values even in the presence of prostate cancer, thus impacting its utility in this population. Some recommend a reduction in the upper limit of normal for PSA to 1 ng/L in transfeminine patients with suppressed testosterone.[70]

As with cis men, routine PSA screening is not recommended in transfeminine patients in the absence of significant risk factors. There is little evidence to support a role for annual digital rectal exam (DRE) in prostate cancer screening; however, it may be considered according to a provider's routine practice with cis men or if symptoms arise. Keep in mind that prostate volume is expected to decrease in the presence of feminizing therapy. In patients who have undergone vaginoplasty, the prostate remains in situ and may be palpated anteriorly via digital vaginal exam in a gender-affirming lithotomy position.

Liver and gallbladder

Estrogen may be associated with transient liver enzyme elevations and, rarely, clinical hepatotoxicity.[9] Baseline elevation in liver enzymes should be investigated and any existing hepatic disease optimized prior to or concurrently with the initiation of estrogen therapy. Spironolactone should be selected preferentially over cyproterone in those with hepatic disease or concomitant use of hepatotoxic medication and healthy renal function. Injectable, transdermal or sublingual routes are preferable in those with pre-existing

liver disease or use of hepatotoxic medication, given that they bypass first pass metabolism.

Chronic hepatitis C should not be considered a contraindication to feminizing hormone therapy, nor hormone therapy a contraindication to hepatitis C treatment. There is theoretical potential for interactions between estradiol and some interferon-free direct acting agent (DAA) treatment regimens for hepatitis C, which could increase serum concentrations of estrogen. Co-administration has not been studied and the clinical significance (if any) is not known. It is recommended that providers check for potential drug interactions using the University of Liverpool's HEP Drug Interactions Checker,[71] and/or choose treatment regimens and monitoring parameters in consultation with a pharmacist.

Estrogen use has been shown to increase the risk of cholelithiasis and subsequent cholecystectomy.[9]

Human immunodeficiency virus (HIV) and anti-retroviral (ARV) drugs

Transfeminine patients are disproportionately affected by HIV, particularly those of colour and those who do sex work. Canadian prevalence estimates are unavailable due to the lack of national surveillance and research on trans and non-binary populations,[72] however global estimates suggest a pooled worldwide prevalence of 19.1% amongst transgender women, and a 48 times greater risk of HIV infection compared with the general population.[73]

Due to sociocultural and structural barriers, trans people are more likely to present late for HIV care,[74] have lower rates of virologic suppression[75,76] and higher rates of HIV-related mortality.[77] The Toronto-based and community-driven Trans Women HIV Research Initiative (TWIRI) developed a model of intersectional stigma to illustrate the complex interplay of HIV-related stigma, sexism, racism and transphobia that creates barriers to care for trans women living with HIV.[78,79]

Although data are limited, there are no known significant drug-drug interactions between ARVs and spironolactone or cyproterone. Given that 25% of HIV-positive cis men are hypogonadal, androgen blockers may not be required in some cases, or required doses may be lower. The concomitant use of spironolactone and septra (for the prophylaxis of opportunistic infections) warrants caution due to risk of severe hyperkalemia.

Reported drug interactions between ARVs and estrogen are limited, and have been extrapolated from data related to the oral contraceptive pill. Concerns have been identified related to ethinyl estradiol in combination with older ARVs, including all protease inhibitors, efavirenz and nevirapine, as well as the boosters ritonavir and cobicistat. Currently, there are no known significant interactions between 17-β estradiol and ARVs, though again data are limited.[80] TWIRI is currently conducting studies to lay the groundwork for a larger pharmacokinetic study of drug-drug interactions between ARVs and feminizing hormone regimens.[81]

Some studies suggest that adherence to ARVs is positively impacted by the provision of gender-affirming hormone therapy in the clinical setting.[82] Providers should thus ideally be prepared to integrate ART with hormone therapy. Particular attention to risk reduction and screening for CVD and osteoporosis is warranted with the use of gender-affirming hormone therapy in HIV-positive patients. HIV infection increases the risk of human papillomavirus (HPV)-related oropharyngeal and anal malignancy, thus HPV vaccination is recommended (up to age 45) if not already received. HPV vaccination is publicly covered in Ontario via the catch-up program for adolescents up to grade 12 and for high risk groups 26 years of age and under including trans individuals whose sexual partner(s) include men who have sex with men (MSM).[83]

Pre-exposure prophylaxis should be offered to HIV-negative transfeminine patients with behavioural risk factors for infection as per Canadian guidelines.[84]

Seizure disorders and anticonvulsant therapy

Hormones appear to influence seizure occurrence by multiple mechanisms. Higher estrogen levels in particular are associated with an increased frequency of seizures in cisgender women.[85] Consultation with a neurologist can be considered in those with pre-existing seizure disorders. In addition, some anticonvulsant drugs impact estrogen metabolism through induction of the CYP450 isoenzyme, resulting in the accelerated conversion of estrogen to inactive metabolites. Of the common anticonvulsants used in Canada, phenobarbitol, phenytoin, carbamazepine and topiramate are all CYP450 inducers, whereas valproic acid, gabapentin and lamotrigine do not appear to interact with estrogen.[86] If a patient is on a CYP450-inducing anticonvulsant for a seizure disorder, neuropathic pain or mood stabilization, it is reasonable to consult a specialist or pharmacist to inquire about switching to a non-inducer or considering adjustments to estrogen dosages prior to initiation.

Sexual function and fatigue

Some transfeminine patients undergoing feminizing hormone therapy may experience loss of libido and/or sexual function. Though sexual desire and function are multi-faceted processes, having hormonal, anatomical and psychologic components, it is likely that androgen blockade and suppression play a significant role.

Should a patient report problematic sexual desire or function, all contributing aspects should be explored and considered. When appropriate, a trial of a decreased dose of anti-androgen or, if cyproterone is being used, a switch to spironolactone (often experienced as having less potent anti-androgen effects) can be considered. The addition of a progestin may also be trialled for low libido, following a discussion of potential risks/side effects and the lack of clear evidence for benefit (see section on progesterone, above). Loss of erectile function is common, and although may be welcome for some, others may wish to retain sexual function. Phosphodiesterase-5 (PDE-5) inhibitors (e.g., sildenafil or tadalafil) can be helpful for transfeminine patients wishing to maintain erectile function. Contraindications and precautions apply as per cis men.

The impact of gonadectomy (+/- vaginoplasty) has a variable impact on libido. As summarized by Wierckx et. al., some studies found no change or a decrease in sexual desire following surgery, while others observed an increase.[87] Nonetheless, it appears relatively consistent across studies that approximately one-third of post-operative transfeminine patients experienced significant distress as a result of low libido, and met the criteria for hypoactive sexual desire disorder (HSDD).[87–89]

Those who have undergone gonadectomy often have free and total testosterone levels that are below the normal range for ovulating cis women. Though studies investigating the relationship between libido and testosterone levels in both cis and transfeminine patients are limited, inconsistent and sometimes contradictory, weak evidence exists to suggest a potential benefit for low-dose transdermal testosterone supplementation to bring serum levels into the female range.[88,90]

A low-dose testosterone patch or low-concentration gel can be used. Dose ranges used in the treatment of sexual dysfunction in cis women may be used as a guide (typically 0.2–1mg of topical testosterone daily). This must be done carefully, with close monitoring for any signs of masculinization. Serum levels should also be monitored closely until a therapeutic dose is established. Serum levels within the female range are unlikely to have significant metabolic implications. This supplementation is contraindicated in the presence of prostate or other androgen-sensitive cancer.

Similarly, this intervention can be considered for post-op transfeminine patients experiencing significant fatigue, assuming a workup for other causes is negative or any contributing factors such as iron deficiency, hypothyroidism, sleep apnea or depression are optimally managed.

LONG-TERM FOLLOW-UP

The long-term follow-up of transfeminine patients on feminizing hormone therapy should involve (at least) annual preventive care visits. Preventive Care Checklists© endorsed by the College of Family Physicians of Canada exist for cisgender patients,[91] but use of these forms for trans patients is awkward and can lead to missed elements important in their comprehensive primary care. We have assembled recommendations for ongoing primary care of transfeminine patients into an adapted Preventive Care Checklist for transfeminine patients (see *Appendix D*), with accompanying explanations for trans-specific recommendations (see *Appendix E*) that can be accessed at the point of care. The use of these trans-specific forms assumes familiarity with the standard forms and their explanations. The standard forms contain graded evidence-based recommendations, which may or may not be the same for trans patients. Grades of evidence for individual recommendations have not been included on the adapted forms. The recommendations represent an effort to incorporate expert opinion, relevant research on cisgender populations and limited trans-specific evidence, with standard national and provincial primary care practices.

REFERENCES

1. De Sutter P. Reproductive options for transpeople: Recommendations for revision of the WPATH's Standards of Care. Int J Transgenderism. 2009;11(3):183.
2. Crowder C, Austin D. Age ranges of epiphyseal fusion in the distal tibia and fibula of contemporary males and females. J Forensic Sci. 2005 Sep;50(5):1001–7.
3. Gooren LJ, Giltay EJ, Bunck MC. Long-term treatment of transsexuals with cross-sex hormones: extensive personal experience. J Clin Endocrinol Metab. 2008 Jan;93(1):19–25.
4. Fung R, Hellstern-Layefsky M, Lega I. Is a lower dose of cyproterone acetate as effective at testosterone suppression in transgender women as higher doses? Int J Transgenderism. 2017 Apr 3;18(2):123–8.
5. Dittrich R, Binder H, Cupisti S, Hoffmann I, Beckmann MW, Mueller A. Endocrine treatment of male-to-female transsexuals using gonadotropin-releasing hormone agonist. Exp Clin Endocrinol Diabetes Off J Ger Soc Endocrinol Ger Diabetes Assoc. 2005 Dec;113(10):586–92.
6. Gava G, Cerpolini S, Martelli V, Battista G, Seracchioli R, Meriggiola MC. Cyproterone acetate vs leuprolide acetate in combination with transdermal oestradiol in transwomen: a comparison of safety and effectiveness. Clin Endocrinol (Oxf). 2016;85(2):239–46.
7. Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869–903.
8. Bienz M, Saad F. Androgen-deprivation therapy and bone loss in prostate cancer patients: a clinical review. BoneKEy Rep. 2015;4:716.
9. Feldman J, Safer J. Hormone therapy in adults: Suggested revisions to the sixth version of the Standards of Care. Int J Transgenderism. 2009 Aug 31;11(3):146–82.
10. Seal LJ, Franklin S, Richards C, Shishkareva A, Sinclaire C, Barrett J. Predictive markers for mammoplasty and a comparison of side effect profiles in transwomen taking various hormonal regimens. J Clin Endocrinol Metab. 2012 Dec;97(12):4422–8.
11. Ministry of Health and Long-term Care. ODB Formulary (search results: lupin-estradiol). Available at: https://www.formulary.health.gov.on.ca/formulary/results.xhtml?q=lupin-estradiol&type=2. Accessed October 1, 2019.
12. Deutsch M. Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people [Internet]. Centre of Excellence for Transgender Health. 2016. Available from: http://transhealth.ucsf.edu/protocols
13. Toorians AWFT, Thomassen MCLGD, Zweegman S, Magdeleyns EJP, Tans G, Gooren LJG, et al. Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. J Clin Endocrinol Metab. 2003 Dec;88(12):5723–9.
14. Asscheman H, Gooren LJ, Assies J, Smits JP, de Slegte R. Prolactin levels and pituitary enlargement in hormone-treated male-to-female transsexuals. Clin Endocrinol (Oxf). 1988 Jun;28(6):583–8.
15. Gooren LJ, Harmsen-Louman W, van Kessel H. Follow-up of prolactin levels in long-term oestrogen-treated male-to-female transsexuals with regard to prolactinoma induction. Clin Endocrinol (Oxf). 1985 Feb;22(2):201–7.
16. Levy A, Crown A, Reid R. Endocrine intervention for transsexuals. Clin Endocrinol (Oxf). 2003 Oct;59(4):409–18.
17. Price TM, Blauer KL, Hansen M, Stanczyk F, Lobo R, Bates GW. Single-dose pharmacokinetics of sublingual versus oral administration of micronized 17 beta-estradiol. Obstet Gynecol. 1997 Mar;89(3):340–5.
18. Düsterberg B, Nishino Y. Pharmacokinetic and pharmacological features of oestradiol valerate. Maturitas. 1982 Dec;4(4):315–24.
19. Sierra-Ramírez JA, Lara-Ricalde R, Lujan M, Velázquez-Ramírez N, Godínez-Victoria M, Hernádez-Munguía IA, et al. Comparative pharmacokinetics and pharmacodynamics after subcutaneous and intramuscular administration of medroxyprogesterone acetate (25 mg) and estradiol cypionate (5 mg). Contraception. 2011 Dec;84(6):565–70.
20. de Blok CJM, Klaver M, Wiepjes CM, Nota NM, Heijboer AC, Fisher AD, et al. Breast development in transwomen after 1 year of cross-sex hormone therapy: Results of a prospective multicenter study. J Clin Endocrinol Metab. 2018 01;103(2):532–8.
21. Fenway Health. Transgender Health Injection Guide [Internet]. Boston, MA: Fenway Health; 2015 p. 29. Available from: https://fenwayhealth.org/wp-content/uploads/2015/07/COM-1880-trans-health_injection-guide_small_v2.pdf
22. Canonico M, Plu-Bureau G, Lowe GDO, Scarabin P-Y. Hormone replacement therapy and risk of

venous thromboembolism in postmenopausal women: systematic review and meta-analysis. BMJ. 2008 May 31;336(7655):1227–31.

23. van Kesteren P, Asscheman H, Megens J, Gooren L. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clin Endocrinol (Oxf). 1997;47(3):337–43.
24. Wierckx K, Gooren L, T'Sjoen G. Clinical review: Breast development in trans women receiving cross-sex hormones. J Sex Med. 2014 May;11(5):1240–7.
25. Orentreich N, Durr NP. Proceedings: Mammogenesis in transsexuals. J Invest Dermatol. 1974 Jul;63(1):142–6.
26. Trans Care BC. Gender-affirming care for trans, Two-Spirit, and gender diverse patients in BC: A primary care toolkit [Internet]. Trans Care BC; 2017 Oct. Available from: http://www.phsa.ca/transgender/Documents/Primary%20Care%20Toolkit.pdf
27. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. JAMA. 2002 Jul 17;288(3):321–33.
28. Cavanaugh T, Hopwood R, Gonzalez A, Thompson J. The medical care of transgender persons [Internet]. Boston, MA: Fenway Health; 2015 Oct. Available from: https://www.lgbthealtheducation.org/publication/transgender-sod/
29. Bouman WP, Claes L, Marshall E, Pinner GT, Longworth J, Maddox V, et al. Sociodemographic variables, clinical features, and the role of preassessment cross-sex hormones in older trans people. J Sex Med. 2016 Apr;13(4):711–9.
30. Gooren L, Lips P. Conjectures concerning cross-sex hormone treatment of aging transsexual persons. J Sex Med. 2014 Aug;11(8):2012–9.
31. Free & Bioavailable Testosterone calculator [Internet]. [cited 2019 Feb 4]. Available from: http://www.issam.ch/freetesto.htm
32. Weinand J, Safer J. Hormone therapy in transgender adults is safe with provider supervision; A review of hormone therapy sequelae for transgender individuals. J Clin Transl Endocrinol. 2015;2(2):55–60.
33. Shifren JL, Rifai N, Desindes S, McIlwain M, Doros G, Mazer NA. A comparison of the short-term effects of oral conjugated equine estrogens versus transdermal estradiol on C-reactive protein, other serum markers of inflammation, and other hepatic proteins in naturally menopausal women. J Clin Endocrinol Metab. 2008 May;93(5):1702–10.
34. Ho JY-P, Chen M-J, Sheu WH-H, Yi Y-C, Tsai AC-W, Guu H-F, et al. Differential effects of oral conjugated equine estrogen and transdermal estrogen on atherosclerotic vascular disease risk markers and endothelial function in healthy postmenopausal women. Hum Reprod Oxf Engl. 2006 Oct;21(10):2715–20.
35. Canonico M, Oger E, Plu-Bureau G, Conard J, Meyer G, Lévesque H, et al. Hormone therapy and venous thromboembolism among postmenopausal women: impact of the route of estrogen administration and progestogens: the ESTHER study. Circulation. 2007 Feb 20;115(7):840–5.
36. Arnold JD, Sarkodie EP, Coleman ME, Goldstein DA. Incidence of venous thromboembolism in transgender women receiving oral Estradiol. J Sex Med. 2016;13(11):1773–7.
37. Wierckx K, Elaut E, Declercq E, Heylens G, De Cuypere G, Taes Y, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. Eur J Endocrinol. 2013 Oct;169(4):471–8.
38. Getahun D, Nash R, Flanders WD, Baird TC, Becerra-Culqui TA, Cromwell L, et al. Cross-sex hormones and acute cardiovascular events in transgender persons: A cohort study. Ann Intern Med. 2018 Aug 21;169(4):205–13.
39. The Center of Excellence for Transgender Health [Internet]. [cited 2019 Feb 4]. Available from: http://www.transhealth.ucsf.edu/
40. Ott J, Aust S, Promberger R, Huber JC, Kaufmann U. Cross-sex hormone therapy alters the serum lipid profile: a retrospective cohort study in 169 transsexuals. J Sex Med. 2011 Aug;8(8):2361–9.
41. Shatzel JJ, Connelly KJ, DeLoughery TG. Thrombotic issues in transgender medicine: A review. Am J Hematol. 2017 Feb;92(2):204–8.
42. Simon J, Lin F, Vittinghoff E, Bittner V, Res Grp HERS, Research group Heart and Estrogen-Progestin Replacement Study. The relation of postmenopausal hormone therapy to serum uric acid and the risk of coronary heart disease events: The Heart and Estrogen-Progestin Replacement Study (HERS). Ann Epidemiol. 2006;16(2):138–45.
43. Main C, Knight B, Moxham T, Gabriel Sanchez R, Sanchez Gomez LM, Roqué i Figuls M, et al. Hormone therapy for preventing cardiovascular disease in post-menopausal women. Cochrane Database Syst Rev. 2013 Apr 30;(4):CD002229.
44. Asscheman H, Giltay E, Megens J, de Ronde W, van Trontsenburg M, Gooren L. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol. 2011;164(4):635–42.
45. Dhejne C, Öberg K, Arver S, Landén M. An analysis of all applications for sex reassignment surgery in Sweden, 1960-2010: prevalence, incidence, and regrets. Arch Sex Behav. 2014 Nov;43(8):1535–45.
46. Elamin MB, Garcia MZ, Murad MH, Erwin PJ, Montori VM. Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses. Clin Endocrinol (Oxf). 2010 Jan;72(1):1–10.
47. Elbers JMH, Giltay EJ, Teerlink T, Scheffer PG, Asscheman H, Seidell JC, et al. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. Clin Endocrinol (Oxf). 2003 May;58(5):562–71.
48. Polderman KH, Gooren LJ, Asscheman H, Bakker A, Heine RJ. Induction of insulin resistance by androgens and estrogens. J Clin Endocrinol Metab. 1994 Jul;79(1):265–71.
49. Bourns A. Guidelines and protocols for hormone therapy and primary health care for trans clients [Internet]. Toronto: Sherbourne Health; 2015 p. 64. Available from: http://sherbourne.on.ca/wp-content/uploads/2014/02/Guidelines-and-Protocols-for-Comprehensive-Primary-Care-for-Trans-Clients-2015.pdf
50. Amin S, Zhang Y, Sawin CT, Evans SR, Hannan MT, Kiel DP, et al. Association of hypogonadism and estradiol levels with bone mineral density in elderly men from the Framingham study. Ann Intern Med. 2000 Dec 19;133(12):951–63.
51. Gennari L, Khosla S, Bilezikian JP. Estrogen and fracture risk in men. J Bone Miner Res Off J Am Soc Bone Miner Res. 2008 Oct;23(10):1548–51.
52. Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, et al. Preservation of volumetric bone density and geometry in trans women during cross-sex hormonal therapy: a prospective observational study. Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA. 2015 Jan;26(1):35–47.
53. Increase in lumbar spine Z-score after 10 years of cross-sex hormonal treatment in transwomen and transmen [Internet]. Endocrine Society. [cited 2019 Feb 4]. Available from: https://www.endocrine.org/meetings/endo-annual-meetings/abstract-details
54. Van Caenegem E, Taes Y, Wierckx K, Vandewalle S, Toye K, Kaufman J-M, et al. Low bone mass is prevalent in male-to-female transsexual persons before the start of cross-sex hormonal therapy and gonadectomy. Bone. 2013 May;54(1):92–7.
55. Gooren LJ, Assies J, Asscheman H, de Slegte R, van Kessel H. Estrogen-induced prolactinoma in a man. J Clin Endocrinol Metab. 1988 Feb;66(2):444–6.

56. Cunha FS, Domenice S, Câmara VL, Sircili MHP, Gooren LJG, Mendonça BB, et al. Diagnosis of prolactinoma in two male-to-female transsexual subjects following high-dose cross-sex hormone therapy. Andrologia. 2015 Aug;47(6):680–4.
57. Kovacs K, Stefaneanu L, Ezzat S, Smyth HS. Prolactin-producing pituitary adenoma in a male-to-female transsexual patient with protracted estrogen administration. A morphologic study. Arch Pathol Lab Med. 1994 May;118(5):562–5.
58. Serri O, Noiseux D, Robert F, Hardy J. Lactotroph hyperplasia in an estrogen treated male-to-female transsexual patient. J Clin Endocrinol Metab. 1996 Sep;81(9):3177–9.
59. Mueller A, Gooren L. Hormone-related tumors in transsexuals receiving treatment with cross-sex hormones. Eur J Endocrinol. 2008;159(3):197–202.
60. Nota NM, Dekker MJHJ, Klaver M, Wiepjes CM, van Trotsenburg MA, Heijboer AC, et al. Prolactin levels during short- and long-term cross-sex hormone treatment: an observational study in transgender persons. Andrologia. 2017 Aug;49(6).
61. Bisson JR, Chan KJ, Safer JD. Prolactin levels do not rise among transgender women treated with Estradiol and Spironolactone. Endocr Pract Off J Am Coll Endocrinol Am Assoc Clin Endocrinol. 2018 Jul;24(7):646–51.
62. Freda PU, Beckers AM, Katznelson L, Molitch ME, Montori VM, Post KD, et al. Pituitary incidentaloma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2011 Apr;96(4):894–904.
63. Brown GR, Jones KT. Incidence of breast cancer in a cohort of 5,135 transgender veterans. Breast Cancer Res Treat. 2015 Jan;149(1):191–8.
64. Gooren LJ, van Trotsenburg MAA, Giltay EJ, van Diest PJ. Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. J Sex Med. 2013 Dec;10(12):3129–34.
65. de Blok C, Wiepjes C, Nota N, van Engelen K. Breast cancer in transgender persons receiving cross-sex hormone treatment: Results of a nationwide cohort study. 2018 May [cited 2019 Feb 4]; Available from: https://www.endocrine.org/meetings/endo-annual-meetings/abstract-details
66. Colebunders B, T'Sjoen G, Weyers S, Monstrey S. Hormonal and surgical treatment in trans-women with BRCA1 mutations: a controversial topic. J Sex Med. 2014 Oct;11(10):2496–9.
67. Weyers S, Villeirs G, Vanherreweghe E, Verstraelen H, Monstrey S, Van den Broecke R, et al. Mammography and breast sonography in transsexual women. Eur J Radiol. 2010 Jun;74(3):508–13.
68. GRS Montreal. Screening recommendations for implant rupture. E-mail to Amy Bourns. 2018.
69. Gooren L, Morgentaler A. Prostate cancer incidence in orchidectomised male-to-female transsexual persons treated with oestrogens. Andrologia. 2014 Dec;46(10):1156–60.
70. Trum HW, Hoebeke P, Gooren LJ. Sex reassignment of transsexual people from a gynecologist's and urologist's perspective. Acta Obstet Gynecol Scand. 2015 Jun;94(6):563–7.
71. HEP Interactions [Internet]. University of Liverpool. [cited 2019 Feb 4]. Available from: https://www.hep-druginteractions.org/checker
72. Bauer GR, Hammond R, Travers R, Kaay M, Hohenadel KM, Boyce M. "I don't think this is theoretical; this is our lives": how erasure impacts health care for transgender people. J Assoc Nurses AIDS Care JANAC. 2009 Oct;20(5):348–61.
73. Baral SD, Poteat T, Strömdahl S, Wirtz AL, Guadamuz TE, Beyrer C. Worldwide burden of HIV in transgender women: a systematic review and meta-analysis. Lancet Infect Dis. 2013 Mar;13(3):214–22.
74. Stone VE. Optimizing the care of minority patients with HIV/AIDS. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 Feb 1;38(3):400–4.
75. Santos G-M, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. Sex Transm Infect. 2014 Aug;90(5):430–3.
76. Das M, Chu PL, Santos G-M, Scheer S, Vittinghoff E, McFarland W, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. PloS One. 2010 Jun 10;5(6):e11068.
77. San Francisco Department of Public Health. HIV Epidemiology Annual Report 2016 [Internet]. San Francisco: San Francisco Department of Public Health; 2017 p. 104. Available from: https://www.sfdph.org/dph/files/reports/rptshivaids/annual-report-2016-20170831.pdf
78. Logie CH, James L, Tharao W, Loutfy MR. HIV, gender, race, sexual orientation, and sex work: a qualitative study of intersectional stigma experienced by HIV-positive women in Ontario, Canada. PLoS Med. 2011 Nov;8(11):e1001124.
79. Lacombe-Duncan A. An Intersectional Perspective on Access to HIV-Related Healthcare for Transgender Women. Transgender Health. 2016;1(1):137–41.
80. Radix A, Sevelius J, Deutsch MB. Transgender women, hormonal therapy and HIV treatment: a comprehensive review of the literature and recommendations for best practices. J Int AIDS Soc [Internet]. 2016 Jul 17 [cited 2019 Feb 4];19(3Suppl 2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4949308/
81. Trans Women HIV Research Initiative. Characterizing trans women in Montreal and Toronto [Internet]. n.d. [cited 2019 Mar 7]. Available from: https://www.transwomenhivresearch.com/characterizing-trans-women-in-montreal-and-toronto/
82. Sevelius JM, Patouhas E, Keatley JG, Johnson MO. Barriers and facilitators to engagement and retention in care among transgender women living with human immunodeficiency virus. Ann Behav Med Publ Soc Behav Med. 2014 Feb;47(1):5–16.
83. Ministry of Health and Long-Term Care, Immunization Policy and Programs Unit. Clarification of eligibility criteria for public funding of the HPV vaccine in Ontario. E-mail to Amy Bourns. 2018.
84. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis | CMAJ [Internet]. [cited 2019 Feb 4]. Available from: http://www.cmaj.ca/content/189/47/E1448
85. Foldvary-Schaefer N, Falcone T. Catamenial epilepsy: Pathophysiology, diagnosis, and management. Neurology 2003;61(6):S2-S15
86. Carl JS, Weaver SP, Tweed E, Edgerton L. Effect of antiepileptic drugs on oral contraceptives. Am Fam Physician. 2008 Sep 1;78(5):634–5.
87. Wierckx K, Elaut E, Van Hoorde B, Heylens G, De Cuypere G, Monstrey S, et al. Sexual desire in trans persons: associations with sex reassignment treatment. J Sex Med. 2014 Jan;11(1):107–18.
88. Kronawitter D, Gooren LJ, Zollver H, Oppelt PG, Beckmann MW, Dittrich R, et al. Effects of transdermal testosterone or oral dydrogesterone on hypoactive sexual desire disorder in transsexual women: results of a pilot study. Eur J Endocrinol. 2009 Aug;161(2):363–8.
89. Elaut E, De Cuypere G, De Sutter P, Gijs L, Van Trotsenburg M, Heylens G, et al. Hypoactive sexual desire in transsexual women: prevalence and association with testosterone levels. Eur J Endocrinol. 2008 Mar;158(3):393–9.
90. A retrospective study on the use of androgen therapy in trans feminine patients to treat HSSD. EPATH conference; 2015 Mar 13; Ghent, Belgium.
91. Ridley J, Ischayek A, Dubey V, Iglar K. Adult health checkup: Update on the Preventive Care Checklist Form©. Can Fam Physician Med Fam Can. 2016 Apr;62(4):307–13.

Part III: Masculinizing hormone therapy

TESTOSTERONE

The cornerstone of hormone therapy for transmasculine patients is testosterone. The goal of treatment is virilization—the development of masculine secondary sexual characteristics. Generally, the desired androgenic effects of testosterone therapy include deepened voice, cessation of menses, clitoral growth, increased muscle mass, fat redistribution, and hair growth in androgen-dependent areas, including facial hair. Breast tissue may lose glandularity, but generally does not lose mass or hemi circumference.[1]

Voice changes and clitoral growth are irreversible changes. Fat redistribution and increased muscle mass are generally considered reversible effects, but some degree of redistribution may be irreversible. The cessation of menses is generally achievable within the first 3–6 months of therapy.

Fertility is decreased during testosterone administration, but should not be relied upon as contraception. While there may be an irreversible reduction in fertility, many transmasculine people have conceived healthy pregnancies following the discontinuation of testosterone (see *Fertility and birth control* section earlier in this document).

The effects of testosterone and their expected time courses are shown in Table 8. Typically, patients taking testosterone will experience masculinizing changes over a period of months to years. The timeframe of physiologic changes may be slightly slower with the use of transdermal preparations. The degree and rate of physical effects are also dependent on the dose administered,[2] as well as patient-specific factors such as age, ethnicity, genetics, body habitus and lifestyle.

Coarsening of body hair, as well as facial hair growth, begin soon after initiation of testosterone, but take a number of years to reach full expression. Clitoral growth usually begins in the first few months of therapy and may be accompanied by mild clitoral discomfort and increased spontaneous arousal.

If cessation of menses is not achieved within the first 6 months of therapy, testosterone dosage may need to be increased if not already at a maximum dose. In patients who prefer low-dose testosterone, or occasionally in patients using transdermal preparations, a progestin may be used, either in the form of a levonorgestrel-releasing intra-uterine system (IUS) (e.g., “Mirena”), or an injectable medroxyprogesterone acetate (MPA) (“Depo-Provera”).

Some patients may wish to have cessation of menses without virilization. For these individuals, the levonorgestrel-releasing IUS or injectable MPA can be used independently, without adding testosterone. While the use of MPA has been shown to affect bone accretion in adolescents, there is evidence to suggest that peak bone mass and future osteoporotic fracture risk are not affected.[3]

Alternatively, a GnRH analogue (leuprolide/"Lupron" or busrelin/"Suprefact") can be used to suppress menses *and* the expression of endogenous female hormones. GnRH analogues flood the pituitary gland's GnRH receptors, leading to a downregulation of the response to endogenous GnRH and sustained suppression of luteinizing hormone (LH) and follicle stimulating hormone (FSH) release. In the absence of stimulation by these gonadotropins, endogenous sex hormone production by the gonads ceases.

As such, GnRH analogues are commonly used for pubertal suppression in trans youth. Drawbacks include high cost, repeat (often painful) injections or frequent nasal spray dosing, and possible side-effects including headache, mood changes and weight gain. It should be noted that the administration of a GnRH analogue in the absence of exogenous hormone use, for a significant amount of time (i.e., > 2 years), can decrease bone mineral density. If providers lack experience with the use of GnRH analogues, we recommend consultation or communication with an endocrinologist or another experienced provider prior to initiation.

All patients with child-bearing potential (i.e., uterus and ova) who are considering testosterone should be counselled regarding its teratogenic impact (specifically hyper-androgenization of the fetus), regardless of current sexual practices. Patients should be aware of their ongoing risk of pregnancy, despite testosterone therapy or amenorrhea. It is important not to make assumptions about the type of sex a patient is having or may have. If a patient with child-bearing potential is having receptive penetrative genital sex with a partner who makes sperm, an effective method of birth control should be employed (see the *Fertility and birth control* section in part I of this document).

If unintended pregnancy does occur while on testosterone, patients should be counselled regarding their options, and testosterone therapy should be discontinued immediately if maintaining the pregnancy is desired or under consideration.

In Ontario, options for testosterone administration include injectable and transdermal preparations (patch or gel). Injectable formulations are most commonly used, due to superior efficacy and affordability. Testosterone undecanoate (IM depot or oral formulation) and "Testapel" (implantable subcutaneous testosterone-eluting pellet) are not currently available in Canada. Testosterone undecanoate is associated with a risk of pulmonary oil microembolism (POME), but none of the formulations of testosterone available in Canada are known to pose this risk. Table 9 outlines the formulations and recommended doses of testosterone therapy currently available.

Injection tips

- Testosterone cypionate is compounded in cottonseed oil, while testosterone enanthate is compounded in sesame oil, making both formulations non-irritating but quite viscous.
- Warming the vial in the palm of the hand for a few moments will reduce viscosity.
- Generally, testosterone is drawn up with larger-gauge needles (18–20G) and then injected intramuscularly with medium-gauge needles (22–23G) or subcutaneously with smaller-gauge needles (25–26G). This can be adjusted to manage client discomfort as needed—smaller gauge needles may mean longer injections, but less pain.
- Needle lengths are determined by body habitus and route of administration.
- The use of a 1 ml syringe can improve accuracy when drawing up smaller doses of injectable testosterone and will decrease the force required to press the plunger of the syringe upon injection, compared to a 3 ml syringe.

Table 8
Effects and expected time course of masculinizing hormones

Effect	Expected onset[a]	Expected maximum effect[a]
Skin oiliness/acne	1-6 months	1-2 years
Facial/body hair growth	3-6 months	4-5 years
Scalp hair loss	6-12 months[b]	Variable
Increased muscle mass/strength[c]	6-12 months	2-5 years
Body fat redistribution	1-6 months	2-5 years
Cessation of menses	1-6 months	n/a
Clitoral enlargement	3-6 months	1-2 years
Vaginal atrophy	1-6 months	1-2 years
Deepened voice	6-12 months	1-2 years

a Estimates represent published and unpublished clinical observations[4–7]
b Highly dependent on age and inheritance; may be minimal
c Significantly dependent on amount of exercise

Adapted from Hembree et al., *The Endocrine Treatment of Gender-Dysphoric/ Gender Incongruent Persons: An Endocrine Society Guideline*[8]

Injectable testosterone is funded by the Ontario Drug Benefit (ODB) program for gender affirmation with an Exceptional Access Program (EAP) request.[9] We suggest that providers submit EAP requests for both testosterone cypionate and testosterone enanthate, so that delays in access do not result when one formulation is on back order or not locally available. (See *Appendices N and O* for samples).

The advantage of transdermal preparations is the relatively steady state of testosterone delivery, as opposed to the periodicity associated with injectables. Some reported drawbacks include local reactions, higher cost, fear of skin-to-skin transmission, problems with the adhesion of patches and an unpleasant odour with gel.[10] Although more expensive and not covered through ODB for the purposes of gender affirmation, transdermal formulations are often covered by private drug plans.

Patches should be applied to a flat, clean, dry and undamaged area of skin on the back, stomach, upper arm or thigh. Gel should be applied to the upper arms, shoulders and/or abdomen (the axillary gel formulation Axiron™ is unfortunately no longer being manufactured). If a gel formulation is used, patients should be counselled regarding the risk of inadvertent exposure to others who come into contact with the patient's skin. This is of particular importance for patients who care for young children and/or have intimate partners who are pregnant or considering pregnancy. Testosterone gel should be allowed to dry prior to getting dressed, and the site of application should remain dry for at least two hours (to allow for absorption into the dermis). Thorough hand washing should be performed following application, and gloves worn if the gel is applied by someone else.

While intramuscular injection is the most common means of administering parenteral testosterone, subcutaneous (SC) delivery has also been used with clinical efficacy and is very well tolerated. Proponents describe less discomfort for patients, a decreased rate of injection site complications and an increased capacity for self-injection. A study in adult trans men demonstrated achievement of amenorrhea in 51 of 53 pre-menopausal participants with careful dose adjustment of SC testosterone cypionate. Of 63 total participants, 61 had testosterone levels within the male range on a dose of 100 mg weekly or less (median dose 75–80 mg). The same study reported that all 22 patients who had switched from IM to SC injections had a mild (n=2) or marked (n=22) preference for the SC route.[10]

Pharmacokinetic studies to date, though small, suggest that the SC route of testosterone is associated with a greater half-life compared to IM, with a comparable trough level and total drug exposure (area under the curve).[11,12] Based on these studies' findings, some suggest a 10–15% dose reduction in testosterone when switching from IM to SC. A subsequent testosterone level can be obtained to ensure that desired levels are maintained.

While the IM route remains better studied and often more familiar to both patients and providers, we feel that enough evidence exists to suggest reasonable safety and efficacy for the SC route and so are comfortable offering this as an option for our patients.

If patients want to self-inject, it is important to instruct them on technique for safe injection and sharps disposal. Directly observing a patient self-inject is helpful for the correction of any problems with technique and to reassure patients that they are injecting correctly. A written step-by-step guide on self-injection for patients is available from Fenway Health.[13]

Some surgeons have advocated for the topical application of testosterone to the clitoris as an adjunct to growth prior to metoidioplasty (surgical reconstruction of the hypertrophied clitoris to create a phallus). There is no definitive evidence for this practice and as such we do not routinely recommend it; however, if undertaken, the applied dose should be subtracted from the patient's total testosterone dosage.[14]

No reduction in testosterone dosing is required following bilateral or unilateral oophorectomy with hysterectomy,[15] however some patients may choose to lower their dose due to the absence of concerns regarding the return of menses. Consideration should be given to bone mineral density in agonadal patients on low-dose testosterone (see the *Osteoporosis and bone mineral density screening* section below.)

SPECIAL CONSIDERATIONS FOR OLDER TRANSMASCULINE PATIENTS

There is little information in the literature to guide recommendations for the initiation or maintenance of masculinizing hormone regimens in older transmasculine patients. Unique considerations in older populations include changes in endogenous hormone levels; physiologic changes that may affect response to medications; a higher burden of existing medical conditions; and multiple concurrent medications leading to the increased potential for drug interactions.

It is not uncommon for trans patients to seek to initiate hormone therapy at older ages,[16] though there is evidence to suggest that transmasculine patients may generally seek treatment at an earlier age on average than transfeminine patients.[4] In one centre, 71 of 74 patients over 50 seeking gender-affirming hormone therapy during a period of 30 months identified as trans women versus only three who identified as trans men.[16]

Testosterone treatment in hypogonadal cis men is often continued into old age, and there is no upper age limit to this treatment.[17] Adverse outcomes in cis populations have largely highlighted issues with prostate cancer risk, which is not a concern in

transmasculine patients. Increases in hematocrit and overt polycythemia are more commmon in older cis men than younger cis men,[18] and can be expected to also be the case for older transmasculine patients. As discussed further below, the impact of testosterone on cardiovascular outcomes is minimal and is likely highly dependent on pre-existing risk factors. Modifiable risk factors that may be present in older transmasculine patients should be managed according to existing national guidelines.

With appropriate monitoring and risk management, there is no reason not to initiate testosterone therapy in a patient simply due to older age, and no compelling argument to require discontinuation at any age.[19] Several studies have shown that testosterone levels in many cis men fall gradually and to a modest degree between the ages of 40 and 79 (an average of 0.4% per year in one study)[20] and may fall more markedly after the age of 80.[21] However, due to the variability of this decline,[22] the upper limit of normal total testosterone (< 28.8 nmol/L at Lifelabs) is not stratified by age in adults, and there is no normal "andropausal range" akin to the menopausal range for estrogen in cis women.

Therefore, as transmasculine patients age, dose reductions can be discussed and considered in accordance with patients' goals. Some guidelines suggest considering complete discontinuation for patients over 50, however those without gonads may experience symptoms of hypogonadism, along with potential bone mineral density loss. Those with or without gonads may be expected to experience reduced muscle mass, body hair and libido,[15] though in some cases the irreversible changes induced by testosterone may be sufficient to maintain a presentation that is consistent with a patient's needs.

As with all trans patients, decisions about hormone therapy at an advanced age should be individualized, following a thorough discussion of risks and benefits.

MONITORING AND DOSE ADJUSTMENTS

As with treatment for transfeminine patients, monitoring should be done at 3, 6 and 12 months after starting therapy. Some clinicians prefer to see patients monthly until an effective dose is established. Follow-up visits should include a functional inquiry, a targeted physical exam, bloodwork, and health promotion and disease prevention counselling. The suggested tasks for each of these follow-up visits are summarized and expanded upon in Appendix C.

Functional inquiry should include noted positive or negative impacts on overall well-being, mood/mental health and energy levels (including fluctuation). It is useful to inquire about changes in libido and how the patient is managing any change. Inquiry regarding physiological changes should include discussing menstruation. There may be some irregular bleeding or spotting in the first few months of treatment. However, once sustained cessation is achieved, any vaginal bleeding without explanation (e.g., missed dose(s) or lowered dose of testosterone) warrants a workup for endometrial hyperplasia or cancer.

Clients should be reminded about the importance of adequate calcium and vitamin D intake and encouraged to participate in regular, moderate physical activity. With regular exercise, lean muscle mass tends to begin to increase soon after treatment begins. Clients should be advised to increase resistance in weightlifting slowly, since there has been evidence of tendon rupture with testosterone administration. This is likely a result of the rapid increase of muscle mass without the ability for compensatory changes in the tendons.

Examination should be focused, and minimally include blood pressure and weight. Bloodwork should be completed according to Table 10, with more frequent monitoring as needed if concerns are identified. Hemoglobin and hematocrit (via complete blood count (CBC) should be followed due to the risk for polycythemia (male reference ranges should be used for the upper limit of normal). Liver enzymes, fasting glucose or glycosylated

hemoglobin (Hba1c), as well as lipids, should be checked at least once between 6 and 12 months, or potentially earlier if concerns were identified prior to initiation. The need for ongoing monitoring of liver enzymes should be guided by individual risk.

Table 9
Formulations and recommended doses of testosterone for masculinizing hormone therapy

	Starting/low dose	Maximum dose	Cost per unit	Approx. cost per 4 weeks
Testosterone enanthate (IM/SC)	20–50 mg q weekly or 40–100 mg q2 weeks	100 mg q weekly or 200 mg q2 weeks	5 mL vial (each contains 200 mg/mL x 5 mL = 1000 mg): $73.50	$14–$29 (covered by ODB with EAP request)
Testosterone cypionate (IM/SC)[a]			10 mL vial (each contains 100 mg/mL x 10 mL = 1000 mg): $64	$13–$26 (covered by ODB with EAP request)
Testosterone patch (transdermal)[b]	2.5–5mg daily	5–10 mg daily	60 x 2.5 mg patches: $164 30 x 5 mg patches: $169	$76.50–$315
Testosterone gel 1% (transdermal)	2.5–5 g daily (2–4 pumps, equivalent to 25–50 mg testosterone)	5–10 g daily (4–8 pumps, equivalent to 50–100 mg testosterone)	30 x 2.5 g sachets: $67 30 x 5 g sachets: $110 2 pump bottles[c]: $175	Sachets: $62–$205 Bottles: $81–$327

a Testosterone enanthate is compounded in sesame oil, and testosterone cypionate is compounded in cottonseed oil; patients with allergy to either of these compounds should use the alternative agent

b Androderm brand, per drug monograph the 12.2 mg patch delivers 2.5 mg/day while the 24.3 mg patch delivers 5 mg per day

c Each pump bottle provides 60 pumps, 1 pump = 1.25 g of gel, equivalent to 12.5 mg of testosterone

* Price quotes provided by www.pharmacy.ca. The prices listed above are accurate as of June 2018 and represent the price of the generic brand of medication unless otherwise indicated (ranging from low dose to maximum dose). Prices include a usual and customary dispensing fee of $9 99, which may vary from pharmacy to pharmacy.

Note: Testosterone (in all forms) is considered a controlled substance in Canada; prescriptions should be written in accordance with provincial requirements for controlled substances.

Titration of doses will generally occur in the early phases of treatment. For example, with injectable testosterone, a starting dose of 30 mg injected weekly could be increased by 10–20 mg every 4 to 6 weeks. Speed of titration will depend on lab results, patient goals, response and side effects.

Some patients will intentionally seek testosterone levels midway between the male and female range. For patients seeking maximum masculinization, the target dose will bring the testosterone level into the physiologic male range. It is important to keep in mind, however, that clinical effects

are the goal of therapy, not specific lab values. If a patient is happy with the rate and degree of masculinization, there is no need to increase the dose to achieve a certain range.

If levels are at the lower end of the male range and patients are concerned about slow progress, or low energy, libido, mood or breakthrough bleeding, the dose can be slowly increased with close monitoring. Once the midpoint of the male reference range is attained, additional benefit is questionable. After the first year of treatment, hormone levels can be monitored yearly in the absence of metabolic shifts such as substantial weight gain, concerns regarding regression of virilization, or the emergence of symptoms potentially related to hormone levels (e.g., cyclic symptoms such as migraines or pelvic cramping/bleeding).[23]

When monitoring injectable testosterone, some clinicians prefer to check serum levels at trough (i.e., just before the next injection is due) while others prefer mid-cycle. The former adds convenience for patients who prefer to come into clinic for their injections. There may be utility in varying the timing of bloodwork to gather information regarding serum levels throughout the cycle (peak, mid-cycle and trough), especially if a patient is reporting cyclic symptoms or breakthrough bleeding. In such cases, wide fluctuations should prompt consideration of increasing the frequency of injections or switching to a route with less periodicity.[23]

Supraphysiologic levels should be avoided due to the increased risk of adverse events and side effects, as well as the potential for the aromatization of excess testosterone into estrogen. Dose adjustment is warranted if supraphysiologic doses are measured at mid-cycle or trough. Since changes to the integument occur with testosterone administration, patients on a transdermal formulation may require ongoing titration in order to obtain or maintain physiologic changes. Some transmasculine patients may require titration of topical testosterone to the extent that they need to apply upwards of 6 or more pumps of gel daily. If patients are finding this cumbersome or that they are "running out" of surface area, some compounding pharmacies can create a higher concentration of gel (e.g., 5% rather than the standard 1%) so that the volume applied is less. Note that specific details and dosing of compounded formulations should be discussed with the compounding pharmacist.

If the sex marker associated with the patient's health card has not been changed, the reference ranges reported from the laboratory will refer to the sex assigned at birth. Reference ranges vary between laboratories, so it is important to refer to reference ranges for the affirmed gender from the laboratory. These can often be found on laboratory websites or obtained by request from the lab. For those using LifeLabs in Ontario, their male and female reference ranges for hormone levels are listed in *Appendix J*.

Ideally, labs would be able to report reference ranges in a patient's affirmed gender, regardless of their OHIP sex marker, or to report both male and female reference ranges with a patient's results. There are currently logistical and systemic barriers to this practice in Ontario labs, though efforts are underway to make improvements in laboratories' direct service to trans patients, as well as amendments to reference range reporting.

PRECAUTIONS AND RISK MITIGATION WITH TESTOSTERONE THERAPY

Providers may have concerns about the safety of testosterone, particularly with respect to metabolic impacts, cardiovascular (CV) events and malignancies. As more evidence emerges in transgender populations, fears of a significant impact on morbidity and mortality in transmasculine patients are being set aside. Following a recent comprehensive review of the literature, Weinand and Safer conclude that the compiled evidence suggests that masculinizing therapy for transgender individuals is safe without a large risk of adverse events when followed carefully for a few well-documented medical concerns,[24] which will be reviewed in more detail below.

Pre-existing medical conditions and risk factors may impart increased risks with testosterone administration and should be considered in order to enable individualized discussions with patients regarding the risks and benefits of treatment. Measures available to reduce associated risks (see Table 11 and expanded discussion below) should be considered and discussed with patients, and, if possible, undertaken prior to or concurrently with the initiation of hormone therapy. In some cases, patients may wish to begin hormone therapy in the setting of ongoing increased risk, i.e., immitigable risk or having declined measures for risk mitigation. In such situations, a careful informed consent process should be followed which takes into consideration: individual capacity to make an informed decision, the severity of potential harms from treatment, and the harms that may result from not treating.

Initiating testosterone should ideally be done in collaboration with relevant specialists who may already be involved in a patient's care. In some cases, a new referral may be helpful in informing decisions about risks and their mitigation. However, efforts should be taken to ensure that this does not cause undue delay. If access to a specialist is limited, an e-consult can be both timely and beneficial.

There are a small number of contraindications to testosterone therapy:

- pregnancy or breastfeeding;
- active, known sex hormone-sensitive cancer (eg. breast, endometrial);
- unstable ischemic cardiovascular disease;
- poorly controlled psychosis or acute homicidality;
- psychiatric conditions that limit the ability to provide informed consent; and
- hypersensitivity to one of the components of the formulation.

Table 10
Recommended bloodwork for monitoring masculinizing hormone therapy

In this table, smaller and lighter grey "x"s indicate parameters that are measured under particular circumstances

Test	Baseline	3 months	6 months	12 months[c]	Yearly	According to guidelines for cis patients, or provider discretion
CBC[a]	X	X	X	X	X	
ALT/AST	X		X[d]			X
Fasting Glucose/ Hba1c	X		X[d]			X
Lipid profile	X		X[d]			X
Total Testosterone	X	X	X	X	X	
LH[b]	x			x	x	
Other	Hep B, C, pregnancy test					
	Consider: HIV, syphilis and other STI screening as indicated, frequency depending on risk					

a Male reference ranges should be used for Hb/Hct (lower limit of female range can be used if menstruating)

b Post-gonadectomy only: elevated LH may have implications regarding bone mineral density (See Osteoporosis and bone mineral density screening)

c During first year of treatment only

d Once at either 6 or 12-month mark

Note: Individual parameters should be considered more frequently if concerns are identified or existing risk factors are present.

Table 11
Precautions with testosterone therapy and considerations in minimizing associated risks

Precaution to testosterone therapy	Considerations in minimizing associated risks
Stable ischemic cardiovascular disease	consider referral to cardiology, ensure optimal medical (including prophylactic antiplatelet agent(s) if indicated per national guidelines) and/or surgical management as indicated, optimize risk factors, consider transdermal route of administration, and/or low dose/slow titration with monitoring
Uncontrolled high blood pressure	identify and address barriers to optimal BP control, initiate antihypertensive(s) as needed, consider cardiac stress test, consider low dose/slow titration with monitoring, consider referral to cardiology
Uncontrolled diabetes	identify and address barriers to optimal glycemic control, refer to dietitian, encourage lifestyle modification, initiate antiglycemic agent(s) per national guidelines, consider endocrinology referral, consider cardiac stress test, consider low dose/slow titration with monitoring
Uncontrolled dyslipidemia	identify and address barriers to optimal lipid control, refer to dietitian, initiate antilipemic pharmacologic therapy per national guidelines, consider endocrinology referral, consider cardiac stress test, consider low dose/slow titration with monitoring
Hepatic dysfunction	dependent on etiology, e.g., minimize alcohol consumption, weight loss in NAFLD, consider referral to hepatology/gastroenterology, consider low dose/slow titration with monitoring
Polycythemia	identify etiology and address contributing factors, consider referral to hematology, consider transdermal route of administration and/or low dose/slow titration with monitoring
History of DVT/PE or hypercoagulable state	identify and minimize existent risk factors, prophylactic anti-coagulation if indicated per current national guidelines, consider referral to hematology/thrombosis clinic, consider transdermal route of administration, and/or low dose/slow titration with with close monitoring for polycythemia

Precaution to testosterone therapy	Considerations in minimizing associated risks
Chronic respiratory disease that may be worsened by erythrocytosis/ polycythemia	consider transdermal route of administration, and/ or low dose/slow titration with monitoring, consider referral to respirology
Severe/ uncontrolled sleep apnea	initiate CPAP or oral device, refer to dietitian and encourage lifestyle changes if overweight, monitor for changes in CPAP pressure requirements
Androgen-sensitive epilepsy	refer to neurology
Smoker	encourage and support smoking cessation, consider referral to smoking cessation program/offer NRT and/ or bupropion/varenicline, or negotiate a decrease in smoking, consider cardiac stress test
Migraines	consider daily migraine prophylaxis, consider transdermal route of administration
Inter-menstrual bleeding/ menorrhagia	work up per national guidelines,[25] gynaecology referral as needed
Oligo-/ Amenorrhea	identify etiology (e.g. PCOS, rule out pregnancy), consider pelvic ultrasound (transvaginal if possible), consider progesterone-induced menstrual bleed prior to testosterone initiation
Autoimmune conditions (e.g., RA, MS, IBD)	consider low dose/slow titration with monitoring in collaboration with any involved specialists

BP: blood pressure; NAFLD: non-alcoholic fatty liver disease; DVT: deep vein thrombosis; PE: pulmonary embolus; CPAP: continuous positive airway pressure; NRT: nicotine replacement therapy; RA: Rheumatoid arthritis; MS: multiple sclerosis; IBD: inflammatory bowel disease

SPECIFIC CONDITIONS: RISK MITIGATION AND LONG-TERM PREVENTIVE CARE

Cardiovascular disease and related metabolic risk factors

There are well-known differences in CV risk between cis men and women. In addition, increased risk is suggested in women with polycystic ovarian syndrome (a hyper-androgenic state). Overall, studies of testosterone therapy for hypogonadal cis men remain conflicting and inconclusive: while multiple large studies have suggested no increased risk, others have suggested an increased risk in CV events and/or subclinical atherosclerosis. Together, these findings have contributed to concerns about the impact of testosterone on CV risk in transmasculine patients.However, multiple studies in transmasculine patients have been reassuring. For example, a large long-term cohort study out of the Netherlands found no increased risk for CV mortality in trans men.[26]

A meta-analysis conducted by Elamin et al. in 2010 and the Endocrine Society's systematic review in 2016 both demonstrated a statistically significant rise in triglycerides (TGs) and low-density lipoprotein (LDL) levels, as well as a decrease in high-density lipoprotein (HDL) levels, with testosterone administration in trans men. However, the clinical significance of these changes was debatable, and the overall evidence regarding CV outcomes was insufficient to allow meaningful conclusions.[8,27]

Studies regarding the effect of testosterone on insulin resistance have shown mixed results, with some studies reporting an increase in insulin resistance[28] while others have suggested no impact.[29,30] A 2013 case-control study demonstrated an increased prevalence of diabetes mellitus type II (DMII) in trans men at baseline compared with control cisgender men and women, as well as a small increase in incidence over a 7-year period, however the number of cases was low. The authors suggest that the discrepancy may have been related to lifestyle differences rather than testosterone administration.[31]

The risk of hypertension among transmasculine patients using testosterone is also unclear, since data have been inconclusive. It appears that testosterone therapy likely leads to a small increase in blood pressure that is statistically significant, but may not be clinically significant. For example, Elamin et al.'s meta-analysis revealed an average increase in systolic blood pressure of 1.74 mmHg.[27]

Overall, the data seems to suggest that the CV and metabolic risks associated with testosterone in transmasculine patients are at most minimal, and have likely been overestimated in the past. However, patients with risk factors such as PCOS or existing dyslipidemia may be at increased risk of further abnormalities with testosterone administration.

Most experts and organizations take a similar approach regarding CV risk mitigation with testosterone: CV risk factors in transmasculine patients should be optimally managed according to existing national guidelines. Optimal management of CV parameters can be attained prior to or concurrently with the administration of masculinizing hormone therapy, and managed per guidelines if concerns emerge during treatment.

While the assessment of baseline risk prior to the initiation of hormone therapy can be estimated by sex-based risk calculators (e.g., Framingham) using sex assigned at birth, risk calculations become more challenging following alterations in the hormonal milieu. The University of California, San Francisco (UCSF) Center for Excellence in Transgender Health suggests that, depending on the age of hormone initiation and duration of hormone exposure, providers may choose to use the risk calculator for sex assigned at birth, affirmed gender, or an average of both.[15] The use of prophylactic antiplatelet agents is not generally recommended for primary

prevention, and a decision to prescribe should be made in accordance with national guidelines.[33]

Obstructive sleep apnea

Sleep apnea may be worsened or unmasked by testosterone therapy.[17] Those with risk factors and/or suggestive signs or symptoms of sleep apnea should be screened via sleep study. As continuous positive airway pressure (CPAP) requirements may change with masculinizing therapy, they should be reassessed periodically via sleep study following testosterone initiation.

Hepatic dysfunction

Transient elevation of liver enzymes may occasionally occur with testosterone therapy and generally spontaneously resolves unless another cause of hepatic dysfunction is present.

According to the Endocrine Society,[8] past concerns regarding liver toxicity with testosterone have been alleviated with more recent reports that indicate minimal risk of serious liver disease. Liver enzymes should be checked at baseline. However, recommendations for ongoing monitoring vary between protocols. We recommend liver enzymes be checked between 6-12 months, with more frequent and ongoing monitoring depending on individual risk factors, concomitant medications and previous results.

Chronic liver disease, including chronic hepatitis C, does not constitute a contraindication to testosterone.[23] No known drug interactions exist between testosterone and treatment regimens for hepatitis C.[34]

Polycythemia

Testosterone increases renal erythropoietin production, which in turn induces increased marrow production of red blood cells. Associated amenorrhea also impacts hemoglobin/hematocrit levels, so an increase in red cell mass and concentration are expected with testosterone therapy. No action is required unless hemoglobin/hematocrit results exceed the male range (as mentioned above, if the OHIP sex marker has not been changed, reported reference ranges may not be applicable).

If levels exceed the male range, adjustments are recommended because the associated higher blood viscosity may lead to an increased risk of adverse vascular events—particularly in those with other risk factors, such as smoking or sleep apnea. This may necessitate a dose reduction, but adjustments to minimize periodicity may also resolve the problem. This can be achieved by increasing the dosing frequency (for example 100 mg once weekly, rather than 200 mg every two weeks), or by switching to a transdermal formulation. Transdermal formulations can be used preferentially in those with a history of or major risk factors for polycythemia.[35]

Psychiatric effects

The peaks and troughs of serum testosterone associated with the injectable route may lead to fluctuations in energy and mood. Some transmasculine patients may report significant fatigue and lower mood as serum levels fall leading up to the next injection. In such cases, it may be useful to vary the timing of bloodwork to gather information about serum levels throughout the cycle (peak, mid-cycle and trough). Wide fluctuations should prompt consideration of increased frequency of injections or a route with less periodicity.

There have been some concerns regarding negative psychiatric effects with testosterone use.
A small number of case reports note an increase in psychiatric symptoms including mania in cis men, particularly in those with a history of bipolar disorder. Observational data in trans populations have noted increased aggression, hypersexuality and occasionally psychotic symptoms. Adverse effects were often associated with higher doses or supraphysiologic serum levels of testosterone.[2]

The first prospective study of the impact of testosterone on mental health in trans men demonstrated no increase in hypomania or psychotic symptoms three months after testosterone initiation.[36] Several studies demonstrate improved psychological functioning in multiple domains with testosterone initiation in transgender men.[36–38]

Overall, there is no convincing evidence that testosterone administration is associated with the onset or worsening of mental health conditions.[15] Nonetheless, it is prudent to exercise some caution in patients with bipolar disorder or psychotic disorders, particularly when sub-optimally managed. Transdermal preparations result in a steady serum testosterone level and are preferred in patients prone to mood or other psychiatric disturbances.

Vaginal bleeding and endometrial cancer

There has been some debate regarding the impact of testosterone on the endometrium and risk of endometrial cancer. PCOS, which is associated with higher levels of circulating endogenous androgens, has been associated with an increased risk of endometrial cancer.[39] The local aromatization of testosterone to estrogen, thereby creating a uterine environment of unopposed estrogen, has been postulated to be a mechanism by which an increased risk might occur.[40]

There is one case report of endometrial cancer in a transgender man reported in the literature,[41] and we have had one case at our centre (unpublished). Retrospective long-term studies have revealed no cases.[4,26,42] Histopathologic studies have had variable findings, with some showing a tendency toward an atrophic endometrium,[43–45] some showing no change,[46,47] and two small studies suggesting a tendency toward a proliferative endometrium and hyperplasia.[48,49] Taken in sum, the evidence to date does not suggest an increased risk of endometrial cancer with testosterone administration.

Nonetheless, when initiating testosterone, unexplained frequent, irregular or heavy bleeding may indicate existing pathology and should be investigated prior to or concurrently with testosterone, especially in the presence of other risk factors for endometrial hyperplasia and cancer. Unaddressed pathology (including benign causes) may at the very least complicate the attainment of cessation of menses with testosterone.

For patients who are experiencing oligo- or amenorrhea at baseline, workup is suggested prior to testosterone administration, including a pregnancy test when indicated by sexual history. Alternatives to traditional workup in those who may experience transvaginal imaging or procedures as overly invasive include watchful waiting for amenorrhea at 6 months following testosterone initiation, transabdominal ultrasonography or progesterone challenge[23]—though the latter may also be emotionally difficult. In some cases, a referral to a culturally competent gynecologist may be helpful.

A pelvic or transabdominal ultrasound may reveal previously unknown PCOS and can provide an estimate of the endometrial thickness. Some have suggested a potential benefit with the induction of a menstrual period for such patients prior to starting testosterone, with the rationale that it is preferable to start out with a thinner lining and may hasten the cessation of menses. However, once again, this may be emotionally difficult for some.

Routine screening for endometrial cancer in transmasculine patients on testosterone is not recommended. However, once sustained menstrual cessation is achieved, any vaginal bleeding without explanation (e.g., missed dose(s) or lowered dose of testosterone) warrants workup including endometrial biopsy for endometrial hyperplasia or cancer.

Pelvic pain

The differential diagnosis for chronic pelvic pain (> 6 months) in transmasculine patients is broad. Causes to consider in transmasculine patients include vaginitis, cystitis, STIs, post-surgical sequelae, and musculoskeletal and psychologic causes. Obedin-Maliver explores the approach to chronic pelvic pain in transmasculine patients in depth as part of the UCSF Center For Excellence in Transgender Care's primary care guidelines.[23]

Some transmasculine patients may report pelvic pain secondary to uterine cramping associated with cyclic testosterone dosing and/or following orgasm. The mechanism of this pain is poorly understood. Anti-inflammatory doses of non-steroidal anti-inflammatories (NSAIDs) are often effective. Prevention or reduction of post-orgasmic pain may be attained through the administration of an NSAID approximately one hour prior to sexual activity. Clients may also obtain some relief by adjusting testosterone route or frequency to minimize serum peaks and troughs. Definitive management with hysterectomy may also be an option, especially if other motivating factors for this procedure are present (see the *Supporting patients with transition-related surgeries* section in Part I of this document).

Atrophic changes

Testosterone therapy may result in atrophy and dryness of vaginal tissues, particularly following oophorectomy. This may lead to discomfort or dyspareunia in patients who wish to have receptive frontal (vaginal) sex. This may sometimes be improved with topical estrogen therapy as in postmenopausal cis women. Some systemic absorption does occur but is not likely sufficient to interfere with physiologic masculinization if testosterone is maintained. Local lubricants and moisturizers may also be helpful.

Osteoporosis and bone mineral density screening

Sex hormones are well known to impact bone mineral density (BMD), and the subsequent risk of osteoporosis. A hypogonadal state induces loss of bone in both cis men and cis women. Serum estradiol levels show a stronger association with maintenance of BMD than do testosterone levels. It is likely that the aromatization of testosterone to estrogen contributes significantly to bone density in cis men.[19]

Baseline BMD prior to testosterone administration in trans men has been found in one study to be in the expected range for sex assigned at birth.[50] Studies to date show either no change in BMD with testosterone over time,[51,52] or have shown an increase.[53,54] A recent systematic review commissioned by the Endocrine Society found no statistically significant change at 12 and 24 months compared with baseline values before initiating masculinizing hormone therapy.[8]

In accordance with national recommendations for cis individuals, BMD testing should be offered to all transmasculine patients over age 65, and screening to identify people at higher risk of osteoporosis (including those who smoke, are HIV+, have a high alcohol intake or have a body weight < 60 kg) can begin at age 50. As in cis populations, the presence of certain high-risk conditions such as hyperparathyroidism or malabsorption syndrome warrant screening before age 50.[55] Clients who have undergone oophorectomy and have been on low-dose or no exogenous testosterone for any significant length of time (i.e., > 2 years) are also be considered to be at high risk.

One small study suggested that LH level may be associated with BMD in patients who have undergone gonadectomy—that is, if LH is elevated, the patient may not be achieving adequate hormonal support for bone maintenance.[56] Thus in transmasculine patients, BMD testing may additionally be considered in agonadal patients with elevated LH.

There are no studies to guide the interpretation of BMD results and fracture risk in trans people. Current tools (e.g., FRAX, CAROC) are age- and sex-based, and it is unclear whether better approximations are obtained using sex assigned at birth or affirmed gender. The Endocrine Society guidelines suggest that this decision may be made on an individual basis, depending on the age at which hormones are initiated. Alternatively, in some cases it may be reasonable to assess fracture risk using both sex calculators and using an intermediate value.[8] Our current practice is to interpret results in comparison to both men and women, and some imaging centres (e.g., Women's College Hospital in Toronto) report results in this manner for patients who are identified as trans on the requisition by the ordering provider.

Despite reassuring data regarding risks, all transmasculine patients should ensure a daily intake of 1000 IU vitamin D and 1200 mg of calcium (total of diet and supplements). Moderate and gradual weight-bearing exercise (i.e., exercise that involves moving the body against gravity) should also be encouraged.

Breast cancer

Testosterone therapy is not thought to significantly increase the risk of breast cancer in transmasculine patients.[8] Transmasculine patients who have undergone chest reconstruction in fact likely have a significantly lower risk than cis women since there is much less tissue present in which malignancy could develop, though there is residual breast tissue, particularly in the axillary regions. There are, however, several reports of trans men developing breast cancer on testosterone, even after chest reconstruction.[57–60]

For those who have undergone chest reconstruction and are presenting with physical concerns, chest and axillary lymph node examination should be performed to assess for abnormalities in the remaining tissue. If an abnormality is detected post-surgically by the patient or by physical exam, ultrasound is recommended as an initial investigation, given that mammography would be technically very difficult. Focused MRI may also be useful to investigate chest abnormalities in transmasculine patients who have undergone chest reconstruction.

In the absence of other significant risk factors, no routine screening investigations are needed post-chest reconstruction. Transmasculine patients who have not undergone chest reconstruction should follow the same guidelines for screening mammography as cis women. Breast/chest self-awareness should be encouraged for all transmasculine patients.

Cervical cancer and Pap tests

Testosterone does not appear to increase the risk of cervical cancer, however transmasculine patients are at risk and are often underscreened.[61] Transmasculine patients with a cervix should be screened with Papanicolaou (Pap) tests following the guidelines for cis women. Human papillomavirus (HPV) vaccination should be offered to patients under age 45. HPV vaccination is publicly covered in Ontario for trans individuals 26 years of age and under whose sexual partner(s) include men who have sex with men (MSM).[62]

Pap testing may be emotionally difficult and/or painful for transmasculine patients. Several strategies may be employed to minimize the discomfort that can be associated with this examination (see Tips for Providing Paps to Trans men,[63] and Cervical Cancer Screening for Patients on the Female-to-Male Spectrum: A Narrative Review and Guide for Clinicians).[78]

Barring contraindications, topical 2% lidocaine jelly may be applied vaginally 5–10 minutes prior to the procedure in those who find speculum examination painful due to atrophic changes. The use of vaginal estrogens for 1 week prior to the exam may also be helpful. To minimize histological misinterpretation, it is important to note on the cytology requisition

that a patient is on testosterone, as well as their menstrual status. Inadequate samples are more common in patients on testosterone and repeat may be required.[61] The use of both brush and broom may increase yield in patients with atrophic changes.[65]

Ovarian cancer

Analogous to concerns of an increased risk for ovarian cancer in cis women with elevated androgen levels, it has been postulated that testosterone therapy in transmasculine patients may increase risk. There have been a small number of reports of ovarian cancer in transgender men.[64,66] Small histologic studies have shown hyperplasia of the ovarian stroma and an increase in fibrous collagen content with testosterone administration, but no evidence of polycystic ovary morphology,[44,67] whereas one recent study did report multifollicular ovaries.[47] Overall, there is no evidence to suggest an increased risk of ovarian cancer in transmasculine patients on testosterone,[24] and thus no cause to perform oophorectomy in transmasculine patients solely for the purpose of the primary prevention.

Human immunodeficiency virus (HIV) and anti-retroviral (ARV) drugs

In comparison to transfeminine patients, there are few studies estimating HIV prevalence amongst transmasculine patients, likely reflecting a lower prevalence. However, transgender men, particularly those who have sex with men (TMSM), share a number of risk factors for HIV infection with transfeminine individuals, and there are indications that risks are increasing.[15]

In addition to social and structural risks, there are a number of factors that may put transmasculine patients at risk of HIV infection. Like transfeminine patients, some transmasculine patients may engage in sex work and survival sex.[68] Additionally, TMSM are often sexually active with cis men who have sex with men (MSM), some of whom are at high risk of HIV. High-risk behaviours in transmasculine patients may be impacted by the effects of testosterone on sex drive and expansion of sexual interests, as well as a desire to integrate into MSM communities.[69] The atrophic effect of testosterone on frontal (vaginal) tissues may increase transmission risks,[70] while the impact of genital reconstructive surgeries on transmission risk is unknown.

Due to sociocultural and structural barriers, transgender people in general are more likely to present late for HIV care,[71] have lower rates of virologic suppression[72,73] and higher rates of HIV-related mortality.[74] Studies suggest that adherence to anti-retroviral therapy (ART) is associated with the gender-affirming provision of hormone therapy in the clinical setting.[70] Providers should thus ideally be prepared to integrate ART with hormone therapy. Though data are limited, there are no reported interactions between testosterone and ARVs. In HIV-positive patients, particular attention to risk reduction and screening for CVD as well as osteoporosis is warranted with the use of gender-affirming hormone therapy.

Pre-exposure prophylaxis should be offered to HIV-negative transmasculine patients with behavioural risk factors for infection as per Canadian guidelines,[75] however it should be noted that risk assessment tools (e.g., HIV Risk Incidence Index for Men Who Have Sex with Men [HIRI-MSM][76]) do not account for unique considerations in TMSM and thus may not accurately reflect risk.

Acne

Many transmasculine patients will experience a significant increase or worsening of acne upon initiation of testosterone. This may be limited to the face, or may also involve the chest and back; in a minority of patients the acne may be severe. Acne is generally worse in the first year of hormone therapy, peaking in severity at 6 months.[6] Acne may be managed as for cisgender patients. Severe acne may also improve by changing the formulation, route, and/or frequency of testosterone. Dose

reductions need only be considered once all treatments and alternatives have been exhausted.[14]

Hair loss

Androgenic alopecia may occur as a result of testosterone therapy and, as in cis men, is often genetically determined. Thinning is also related to the duration of therapy.[6] Finasteride may be used to treat androgenic alopecia in transmasculine patients by blocking the conversion of testosterone to dihydroydrotestosterone (DHT).[i] Clients considering this option should be counselled that this may impact facial hair growth, and the potential negative impact on other aspects of masculinization early in transition are unknown. Minoxidil may alternatively be used as a topical agent applied to the scalp.[14]

LONG-TERM FOLLOW-UP

The long-term follow-up of transmasculine patients on masculinizing hormone therapy should involve (at least) annual preventive care visits. Preventive Care Checklists© endorsed by the College of Family Physicians of Canada exist for cis gender patients,[77] but use of these forms for trans patients is awkward and can lead to missed elements important in their comprehensive primary care. We have assembled recommendations for the ongoing primary care of transmasculine patients into an adapted Preventive Care Checklist for Transmasculine Patients (see *Appendix F*), with accompanying explanations for trans-specific recommendations (see *Appendix G*) that can be accessed at the point of care. The use of these trans-specific forms assumes familiarity with the standard forms and their explanations. The standard forms contain graded, evidence-based recommendations—which may or may not be the same for trans patients. Grades of evidence for individual recommendations have not been included on the adapted forms. The recommendations represent an effort to incorporate expert opinion, relevant research on cisgender populations and limited trans-specific evidence, with standard national and provincial primary care practices.

i The typical dose of finasteride for alopecia is 1 mg per day. For those paying out of pocket, it is much more affordable to prescribe the 5 mg tablet and have the patient carefully split the tablet and take 1/4 tab daily

References

1. Futterweit W, Schwartz IS. Histopathology of the breasts of 12 women receiving long-term exogenous androgen therapy. Mt Sinai J Med N Y. 1988 Sep;55(4):309–12.
2. Feldman J, Safer J. Hormone therapy in adults: Suggested revisions to the sixth version of the Standards of Care. Int J Transgenderism. 2009 Aug 31;11(3):146–82.
3. Kaunitz AM. Depot medroxyprogesterone acetate for contraception: Efficacy, side effects, metabolic impact, and benefits [Internet]. UpToDate. 2018. Available from: https://www.uptodate.com/contents/depot-medroxyprogesterone-acetate-for-contraception-efficacy-side-effects-metabolic-impact-and-benefits
4. Gooren LJ, Harmsen-Louman W, van Kessel H. Follow-up of prolactin levels in long-term oestrogen-treated male-to-female transsexuals with regard to prolactinoma induction. Clin Endocrinol (Oxf). 1985;22(2):201–207.
5. Toorians AWFT, Thomassen MCLGD, Zweegman S, Magdeleyns EJP, Tans G, Gooren LJG, et al. Venous thrombosis and changes of hemostatic variables during cross-sex hormone treatment in transsexual people. J Clin Endocrinol Metab. 2003 Dec;88(12):5723–9.
6. Wierckx K, Van Caenegem E, Schreiner T, Haraldsen I, Fisher AD, Toye K, Kaufman JM, T'Sjoen G. Cross-sex hormone therapy in trans persons is safe and effective at short-time follow-up: results from the European network for the investigation of gender incongruence. J Sex Med. 2014;11(8):1999–2011.
7. AsschemanH, Gooren LJ, Assies J, Smits JP, de Slegte R. Prolactin levels and pituitary enlargement in hormone-treated male-tofemale transsexuals. Clin Endocrinol (Oxf). 1988;28(6):583–588.
8. Hembree WC, Cohen-Kettenis PT, Gooren L, Hannema SE, Meyer WJ, Murad MH, et al. Endocrine treatment of gender-dysphoric/gender-incongruent persons: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2017 Nov 1;102(11):3869–903.
9. Government of Ontario. Central Forms Repository - Request for an Unlisted Drug Product - Exceptional Access Program [Internet]. n.d. [cited 2019 Feb 5]. Available from: http://www.forms.ssb.gov.on.ca/mbs/ssb/forms/ssbforms.nsf/
10. Spratt DI, Stewart II, Savage C, Craig W, Spack NP, Chandler DW, et al. Subcutaneous injection of Testosterone is an effective and preferred alternative to intramuscular injection: Demonstration in female-to-male transgender patients. J Clin Endocrinol Metab. 2017 01;102(7):2349–55.
11. Wilson DM, Kiang TKL, Ensom MHH. Pharmacokinetics, safety, and patient acceptability of subcutaneous versus intramuscular testosterone injection for gender-affirming therapy: A pilot study. American Journal of Health-System Pharmacy 2018;75(6):351-358.
12. McFarland J, Craig W, Clarke NJ, Spratt DI. Serum Testosterone Concentrations Remain Stable Between Injections in Patients Receiving Subcutaneous Testosterone. Journal of the Endocrine Society 2017;1(8):1095-1103.
13. Fenway Health. Transgender Health Injection Guide [Internet]. Boston, MA: Fenway Health; 2015 p. 29. Available from: https://fenwayhealth.org/wp-content/uploads/2015/07/COM-1880-trans-health_injection-guide_small_v2.pdf
14. Gorton N, Buth J, Spade D. Medical therapy and health maintenance for transgender men: A guide for healthcare providers [Internet]. San Francisco, CA: Lyon Martin Women's Health Services; 2005. Available from: https://www.nickgorton.org/Medical%20Therapy%20and%20HM%20for%20Transgender%20Men_2005.pdf
15. The Center of Excellence for Transgender Health [Internet]. [cited 2019 Feb 4]. Available from: http://www.transhealth.ucsf.edu/
16. Bouman WP, Claes L, Marshall E, Pinner GT, Longworth J, Maddox V, et al. Sociodemographic variables, clinical features, and the role of preassessment cross-sex hormones in older trans people. J Sex Med. 2016 Apr;13(4):711–9.
17. Bhasin S, Cunningham GR, Hayes FJ, Matsumoto AM, Snyder PJ, Swerdloff RS, et al. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2010 Jun;95(6):2536–59.
18. Haddad RM, Kennedy CC, Caples SM, Tracz MJ, Boloña ER, Sideras K, et al. Testosterone and cardiovascular risk in men: a systematic review and meta-analysis of randomized placebo-controlled trials. Mayo Clin Proc. 2007 Jan;82(1):29–39.
19. Gooren L, Lips P. Conjectures concerning cross-sex hormone treatment of aging transsexual persons. J Sex Med. 2014 Aug;11(8):2012–9.
20. Wu FCW, Tajar A, Pye SR, Silman AJ, Finn JD, O'Neill TW, et al. Hypothalamic-pituitary-testicular axis disruptions in older men are differentially linked to age and modifiable risk factors: the European Male Aging Study. J Clin Endocrinol Metab. 2008 Jul;93(7):2737–45.
21. Handelsman DJ, Yeap B, Flicker L, Martin S, Wittert GA, Ly LP. Age-specific population centiles for androgen status in men. Eur J Endocrinol. 2015 Dec;173(6):809–17.
22. Travison TG, Vesper HW, Orwoll E, Wu F, Kaufman JM, Wang Y, et al. Harmonized reference ranges for circulating testosterone levels in men of four cohort studies in the United States and Europe. J Clin Endocrinol Metab. 2017 01;102(4):1161–73.
23. Deutsch M. Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people [Internet]. Centre of Excellence for Transgender Health. 2016. Available from: http://transhealth.ucsf.edu/protocols
24. Weinand J, Safer J. Hormone therapy in transgender adults is safe with provider supervision; A review of hormone therapy sequelae for transgender individuals. J Clin Transl Endocrinol. 2015;2(2):55–60.
25. Singh S, Best C, Dunn S, Leyland N, Wolfman WL. Abnormal uterine bleeding in pre-menopausal women. J Obstet Gynaecol Can. 2013 May;35(5):473–5.
26. van Kesteren P, Asscheman H, Megens J, Gooren L. Mortality and morbidity in transsexual subjects treated with cross-sex hormones. Clin Endocrinol (Oxf). 1997;47(3):337–43.
27. Elamin MB, Garcia MZ, Murad MH, Erwin PJ, Montori VM. Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analyses. Clin Endocrinol (Oxf). 2010 Jan;72(1):1–10.
28. Polderman KH, Gooren LJ, Asscheman H, Bakker A, Heine RJ. Induction of insulin resistance by androgens and estrogens. J Clin Endocrinol Metab. 1994 Jul;79(1):265–71.
29. Elbers JMH, Giltay EJ, Teerlink T, Scheffer PG, Asscheman H, Seidell JC, et al. Effects of sex steroids on components of the insulin resistance syndrome in transsexual subjects. Clin Endocrinol (Oxf). 2003 May;58(5):562–71.
30. Meriggiola MC, Armillotta F, Costantino A, Altieri P, Saad F, Kalhorn T, et al. Effects of testosterone undecanoate administered alone or in combination with letrozole or dutasteride in female to male transsexuals. J Sex Med. 2008 Oct;5(10):2442–53.

31. Wierckx K, Elaut E, Declercq E, Heylens G, De Cuypere G, Taes Y, et al. Prevalence of cardiovascular disease and cancer during cross-sex hormone therapy in a large cohort of trans persons: a case-control study. Eur J Endocrinol. 2013 Oct;169(4):471–8.
32. Amin S, Zhang Y, Sawin CT, Evans SR, Hannan MT, Kiel DP, et al. Association of hypogonadism and estradiol levels with bone mineral density in elderly men from the Framingham study. Ann Intern Med. 2000 Dec 19;133(12):951–63.
33. Bell AD, Roussin A, Cartier R, Chan WS, Douketis JD, Gupta A, et al. The use of antiplatelet therapy in the outpatient setting: Canadian Cardiovascular Society Guidelines Executive Summary. Can J Cardiol. 2011 Apr;27(2):208–21.
34. HEP Interactions [Internet]. University of Liverpool. [cited 2019 Feb 4]. Available from: https://www.hep-druginteractions.org/checker
35. Dobs AS, Meikle AW, Arver S, Sanders SW, Caramelli KE, Mazer NA. Pharmacokinetics, efficacy, and safety of a permeation-enhanced testosterone transdermal system in comparison with bi-weekly injections of testosterone enanthate for the treatment of hypogonadal men. J Clin Endocrinol Metab. 1999 Oct;84(10):3469–78.
36. Keo-Meier C, Herman L, Reisner S, Pardo S, Sharp C, Babcock J. Testosterone treatment and MMPI-2 improvement in transgender men: A prospective controlled study. J Consult Clin Psychol. 2015;83(1):143–56.
37. Gómez-Gil E, Zubiaurre-Elorza L, Esteva I, Guillamon A, Godás T, Cruz Almaraz M, et al. Hormone-treated transsexuals report less social distress, anxiety and depression. Psychoneuroendocrinology. 2012 May;37(5):662–70.
38. Colton Meier S, Fitzgerald K, Pardo S, Babcock J. The effects of hormonal gender affirmation treatment on mental health in female-to-male transsexuals. J Gay Lesbian Ment Health. 2011 Jul 1;15(3):281–99.
39. Cattrall FR, Healy DL. Long-term metabolic, cardiovascular and neoplastic risks with polycystic ovary syndrome. Best Pract Res Clin Obstet Gynaecol. 2004 Oct;18(5):803–12.
40. Futterweit W. Endocrine therapy of transsexualism and potential complications of long-term treatment. Arch Sex Behav. 1998 Apr;27(2):209–26.
41. Urban RR, Teng NNH, Kapp DS. Gynecologic malignancies in female-to-male transgender patients: the need of original gender surveillance. Am J Obstet Gynecol. 2011 May;204(5):e9–12.
42. Schlatterer K, Yassouridis A, von Werder K, Poland D, Kemper J, Stalla GK. A follow-up study for estimating the effectiveness of a cross-gender hormone substitution therapy on transsexual patients. Arch Sex Behav. 1998 Oct;27(5):475–92.
43. Miller N, Bédard YC, Cooter NB, Shaul DL. Histological changes in the genital tract in transsexual women following androgen therapy. Histopathology. 1986 Jul;10(7):661–9.
44. Grynberg M, Fanchin R, Dubost G, Colau J, Brémont-Weil C, Frydman R, et al. Histology of genital tract and breast tissue after long-term testosterone administration in a female-to-male transsexual population. Reprod Biomed Online. 2009;20(4):553–8.
45. Perrone AM, Cerpolini S, Maria Salfi NC, Ceccarelli C, De Giorgi LB, Formelli G, et al. Effect of long-term testosterone administration on the endometrium of female-to-male (FtM) transsexuals. J Sex Med. 2009 Nov;6(11):3193–200.
46. Mueller A, Kiesewetter F, Binder H, Beckmann MW, Dittrich R. Long-term administration of testosterone undecanoate every 3 months for testosterone supplementation in female-to-male transsexuals. J Clin Endocrinol Metab. 2007 Sep;92(9):3470–5.
47. Loverro G, Resta L, Dellino M, Edoardo DN, Cascarano MA, Loverro M, et al. Uterine and ovarian changes during testosterone administration in young female-to-male transsexuals. Taiwan J Obstet Gynecol. 2016 Oct;55(5):686–91.
48. Futterweit W, Deligdisch L. Histopathological effects of exogenously administered testosterone in 19 female to male transsexuals. J Clin Endocrinol Metab. 1986 Jan;62(1):16–21.
49. Mikhaĭlichenko VV, Fesenko VN, Khmelnitskiĭ NV, Ozhiganova IN, Novikov AI, Korolev VV, et al. Morphological and functional changes of organs of female and male reproductive systems at change of sex. Urologiia. 2013 Jun;(3):18–23.
50. Van Caenegem E, Wierckx K, Taes Y, Schreiner T, Vandewalle S, Toye K, et al. Body composition, bone turnover, and bone mass in trans men during testosterone treatment: 1-year follow-up data from a prospective case-controlled study (ENIGI). Eur J Endocrinol. 2015 Feb;172(2):163–71.
51. Mueller A, Haeberle L, Zollver H, Claassen T, Kronawitter D, Oppelt PG, et al. Effects of intramuscular testosterone undecanoate on body composition and bone mineral density in female-to-male transsexuals. J Sex Med. 2010 Sep;7(9):3190–8.
52. Levy A, Crown A, Reid R. Endocrine intervention for transsexuals. Clin Endocrinol (Oxf). 2003 Oct;59(4):409–18.
53. Turner A, Chen TC, Barber TW, Malabanan AO, Holick MF, Tangpricha V. Testosterone increases bone mineral density in female-to-male transsexuals: a case series of 15 subjects. Clin Endocrinol (Oxf). 2004 Nov;61(5):560–6.
54. Nota NM, Dekker MJHJ, Klaver M, Wiepjes CM, van Trotsenburg MA, Heijboer AC, et al. Prolactin levels during short- and long-term cross-sex hormone treatment: an observational study in transgender persons. Andrologia. 2017 Aug;49(6).
55. Papaioannou A, Morin S, Cheung AM, Atkinson S, Brown JP, Feldman S, et al. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. CMAJ. 2010 Nov 23;182(17):1864–73.
56. van Kesteren P, Lips P, Gooren L, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. Clin Endocrinol (Oxf). 1998;48(3):347–54.
57. Brown GR, Jones KT. Incidence of breast cancer in a cohort of 5,135 transgender veterans. Breast Cancer Res Treat. 2015 Jan;149(1):191–8.
58. Gooren LJ, van Trotsenburg MAA, Giltay EJ, van Diest PJ. Breast cancer development in transsexual subjects receiving cross-sex hormone treatment. J Sex Med. 2013 Dec;10(12):3129–34.
59. Gooren L, Bowers M, Lips P, Konings IR. Five new cases of breast cancer in transsexual persons. Andrologia. 2015 Dec;47(10):1202–5.
60. de Blok C, Wiepjes C, Nota N, van Engelen K. Breast cancer in transgender persons receiving cross-sex hormone treatment: Results of a nationwide cohort study. 2018 May [cited 2019 Feb 4]; Available from: https://www.endocrine.org/meetings/endo-annual-meetings/abstract-details
61. Peitzmeier SM, Khullar K, Reisner SL, Potter J. Pap test use is lower among female-to-male patients than non-transgender women. Am J Prev Med. 2014 Dec;47(6):808–12.
62. Ministry of Health and Long-Term Care, Immunization Policy and Programs Unit. Clarification of eligibility criteria for public funding of the HPV vaccine in Ontario. E-mail to Amy Bourns. 2018.
63. Tips For Providing Paps to Trans Men [Internet]. [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/tips-for-providing-paps-to-trans-men/
64. Dizon DS, Tejada-Berges T, Koelliker S, Steinhoff M, Granai CO. Ovarian cancer associated with testosterone supplementation in a female-to-male transsexual patient. Gynecol Obstet Invest. 2006;62(4):226–8.
65. Davis-Devine S, Day SJ, Anderson A, French A, Madison-Henness D, Mohar N, et al. Collection of the BD SurePath Pap Test with a broom device plus endocervical brush

improves disease detection when compared to the broom device alone or the spatula plus endocervical brush combination. CytoJournal. 2008 Feb 12;6:4.

66. Hage JJ, Dekker JJ, Karim RB, Verheijen RH, Bloemena E. Ovarian cancer in female-to-male transsexuals: report of two cases. Gynecol Oncol. 2000 Mar;76(3):413–5.
67. Ikeda K, Baba T, Noguchi H, Nagasawa K, Endo T, Kiya T. Excessive androgen exposure in female-to-male transsexual persons of reproductive age induces hyperplasia of the ovarian cortex and stroma but not polycystic ovary morphology. Hum Reprod. 2013;28(2):453–61.
68. Scheim A, Bauer G. Sex and gender diversity among transgender persons in Ontario, Canada: Results from a respondent-driven sampling survey. J Sex Res. 2015;52(1):1–14.
69. Nguyen Q. HIV Primary Care for LGBTQ2S Patients. In: Caring for LGBTQ2S People: A Clinical Guide. University of Toronto Press; in press.
70. Sevelius J. Feature: 'There's No Pamphlet for the Kind of Sex I Have': HIV-Related Risk Factors and Protective Behaviors Among Transgender Men Who Have Sex With Nontransgender Men. Journal of the Association of Nurses in AIDS Care 2009;20(5):398-410.
71. Stone VE. Optimizing the care of minority patients with HIV/AIDS. Clin Infect Dis Off Publ Infect Dis Soc Am. 2004 Feb 1;38(3):400–4.
72. Santos G-M, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. Sex Transm Infect. 2014 Aug;90(5):430–3.
73. Das M, Chu PL, Santos G-M, Scheer S, Vittinghoff E, McFarland W, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. PloS One. 2010 Jun 10;5(6):e11068.
74. San Francisco Department of Public Health. HIV Epidemiology Annual Report 2016 [Internet]. San Francisco: San Francisco Department of Public Health; 2017 p. 104. Available from: https://www.sfdph.org/dph/files/reports/rptshivaids/annual-report-2016-20170831.pdf
75. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2017 Nov 27;189(47):E1448–58.
76. Smith DK, Pals SL, Herbst JH, Shinde S, Carey JW. Development of a clinical screening index predictive of incident HIV infection among men who have sex with men in the United States. J Acquir Immune Defic Syndr. 2012 Aug;60(4):421–7.
77. Ridley J, Ischayek A, Dubey V, Iglar K. Adult health checkup: Update on the Preventive Care Checklist Form©. Can Fam Physician Med Fam Can. 2016 Apr;62(4):307–13.
78. Potter, J., Peitzmeier, S. M., Bernstein, I., Reisner, S. L., Alizaga, N. M., Agénor, M., & Pardee, D. J. (2015). Cervical Cancer Screening for Patients on the Female-to-Male Spectrum: a Narrative Review and Guide for Clinicians. Journal of general internal medicine, 30(12), 1857–1864. doi:10.1007/s11606-015-3462-8

Conclusion

Having now read through our introduction to trans and non-binary communities as well as the basics of primary care for transfeminine and transmasculine patients, it is our hope that you finish your review of the Guidelines feeling better equipped to care for your trans and non-binary patients. Even if you do not have any in your care yet that you are aware of, with demand continuing to increase for gender-affirming care, it's possible—or even likely—that you will before long.

As you continue your journey of increasing your clinical and cultural competency in providing gender-affirming care, you can and should make use of the many resources, references and peer support networks available to you. Once your knowledge and experience grows, you may even in turn find yourself ready and eager to contribute to communities of practice committed to gender-affirming care.

Feedback

Feedback about the Guidelines, whether on clinical information, language use or any other feedback, should be directed to Rainbow Health Ontario, a program of Sherbourne Health, at info@rainbowhealthontario.ca.

Acknowledgements

Thank you to all those who contributed informally to this update through numerous emails, phone calls, and hallway conversations, including Faith Chaput, Michael Richardson, Corey Doughty, Mona Loutfy, and the members of the Sherbourne Health LGBT2SQ clinical team and the Rainbow Health Ontario program staff. Special thanks to Rebecca Hammond for contributing her expertise and strengthening this document's approach to language. Thanks to all of the medical and allied health providers and community members whose contributions have been essential in developing this body of experiential knowledge, particularly Dr. Kate Greenaway, Dr. Leslie Shanks, and Vlad Wolanyk who authored previous versions of the Guidelines. As always, a heartfelt thank you to all the patients who have allowed us the privilege of being involved in their care and who have taught us so much about authenticity, resilience, and the strength of the human spirit.

APPENDIX A:
Hormone Planning Period Checklist

The following is a tool to assist in undertaking planning visits with new (or newly transitioning) trans patients in primary care settings who wish to initiate hormone therapy. This checklist is for patients who have completed puberty. If they have not, consider providing care under the guidance of an expert, or referral to a specialized centre or another provider with expertise in this area. For providers wishing to grow their expertise in this area, RHO is expecting to offer training in caring for pubertal trans children and youth as of spring 2020.

NOTE: A "No" response does not necessarily preclude a patient from being a candidate for hormone therapy however it does indicate an area that may need ongoing attention

ITEM	YES / DONE	NO	COMMENTS
PATIENT HISTORY			
Discussion of rationale for planning period			
General medical intake & medical history			
Obtain/Review records from previous providers			
Exploration of gender identity and expression			
BASELINE DATA			
Vitals (incl BP, Ht, Wt)			
Focused physical exam (+/- Breast inspection/ measurement in transfeminine patients)			
Bloodwork (liver enzymes, lipids, fasting glu or a1c, complete blood count, hormone levels, +/- renal function – See Tables 6 & 10)			
Health screening commensurate to age/risk			

ITEM	YES / DONE	NO	COMMENTS
PATIENT EDUCATION, PREPARATION & SUPPORTS			
Articulation of transition goals, (including interest in transition-related surgeries)			
Reasonable expectations expressed			
Risks + side effects, and potential benefits (expected changes both reversible & irreversible) associated with treatment discussed and patient understanding demonstrated (See Appendices K-M for checklists)			
Effects on fertility and options for preservation discussed, early referral for preservation if desired			
Pregnancy risk/options for contraception discussed & implemented if needed			
Possesses capacity to consent			
Potential costs (e.g. medication, hair removal, fertility preservation) reviewed and considered			
Psychosocial preparation and supports discussed			
Medication options/routes reviewed			
EAP form submission (patients on ODB wishing to start testosterone)			
RISK MANAGEMENT			
Absence of contraindications			
Precautions optimally managed or management plan in place			
If present, mental health conditions reasonably well-managed or management plan in place			

ITEM	YES / DONE	NO	COMMENTS
If smoker, smoking cessation counselling done			
DIFFERENTIAL DIAGNOSIS			
Other possible diagnoses ruled out			
Meets criteria for Gender Dysphoria/Gender Incongruence			
Intersex condition ruled out or taken into consideration			
FINAL / NEXT STEPS			
Choose initial hormone regimen			
Discuss/arrange follow up			

APPENDIX B:

hormone monitoring summary for transfeminine patients (collaborative PCP and nursing team)

	Baseline	Month 3, 6, 12	Annual
Review	Contraindications and precautions to feminizing therapies, Old records, Mental Health,[A] Education/Lifestyle counselling,[B] Psychosocial,[C] Bone health, Health Maintenance[D]	Review of hormone effects, Spontaneous arousal, Mental Health,[A] Education/ Lifestyle counselling,[B] Psychosocial[C]	See Preventive Care Checklist for Transfeminine Patients and Accompanying Explanations (Appendices D & E)
Focused physical exam	Include BP, height, weight, +/- breast inspection/ measurement(s)*	BP, weight, +/-breast inspection/ measurement(s) at 12 months*	
Lab	See Guidelines for gender-affirming primary care with trans and non-binary patients, Part II		
Other	Consider HPV, Hep A, B and routine vaccinations as indicated		

* For those who may have interest in MOHLTC-covered breast augmentation surgery, breast inspection at baseline and 12 months with particular attention to Tanner stage. Chest circumference at the fullest part of the breast and areolar diametre may be helpful in determining the presence or absence of breast growth, or may be of interest to some patients (See *Part I - Physical Exam and Baseline Investigations*)

A. Mental Health:

- Screen for symptoms of depression (including suicidality), anxiety disorders, self-harm, and other mental health concerns
- Inquire re: current experience of gender dysphoria and body image
- Screen for disordered eating
- Assess patient interest in surgical treatments if not previously undergone
- Inquire re: libido/changes in libido

B. Education/Lifestyle Counselling:

- Review healthy eating and general nutrition
- Adequate Calcium Intake – ensure a minimum intake of 1200 mg of Calcium daily (total: diet + supplements)
- Adequate Vitamin D – ensure 1000 IU of vitamin D daily
- Hormone Adherence – missed doses of estrogen may impact bone health if post-orchiectomy, while extra doses may lead to supratherapeutic serum levels
- Regular, moderate physical activity – encourage weight-bearing exercise for osteoporosis prevention as well as aerobic exercise
- Alcohol and other substances – inquire re: problematic use of substances including hormones without a

prescription; estrogen affects the metabolism of alcohol by the liver - we suggest using the same safe-drinking guidelines for transfeminine patients as for cis women (see Canada's Low-risk Alcohol Drinking Guidelines[1])

- Smoking – cessation, stage of readiness, motivational interviewing, etc
- STI Prevention – transfeminine patients may be at high risk of STIs depending on behavioural factors; safer sex counselling is recommended (for patient-centred handout materials, see *Brazen 2.0: a Trans women's Safer Sex Guide*[2])
- Review the signs and symptoms of DVT and PE if risk factors present

C. Psychosocial:

- An effort should be made to assess the impact of transition/trans identity on employment, housing, family, relationships, and economic well-being
- Social Supports – specific attention should be given to assessing the extent of a patient's social supports, creating an opportunity to suggest additional resources if needed
- Name change/identification – assess patient need/desire to change name and/or gender marker on identification and offer support for this process (See *Part I: Changing Sex Designation on Government ID, and Appendices Q and R*)

D. Health Maintenance:

- Immunization history
- STI/HIV risk assessment and screening as indicated, frequent screening (i .e. every 3 months) for those at high risk, consider indications for HIV PrEP
- TB skin test as indicated

1. The Canadian Centre on Substance Use and Addiction [Internet]. Ottawa: The Canadian Centre on Substance Use and Addiction; [updated 2018]. Canada's low risk alcohol drinking guidelines; [2012] [cited 2019 Feb 7]. Available from: http://www.ccsa.ca/Resource%20Library/2012-Canada-Low-Risk-Alcohol-Drinking-Guidelines-Brochure-en.pdf
2. Brazen 2.0: Trans women's safer sex guide [Internet]. Toronto: The 519 Church Street Community Centre and CATIE; 2017 p. 34. Available from: www.the519.org/media/download/3246

APPENDIX C:

hormone monitoring summary for transmasculine patients (collaborative PCP and nursing team)

	Baseline	Month 3, 6, 12	Annual
Review	Contraindications and precautions to testosterone, Old records, Mental Health[A], Education/Lifestyle counselling[B], Psychosocial[C], Health Maintenance[D]	Hormone effects, Cessation of menses, Mental Health[A], Education/ Lifestyle counselling[B], Psychosocial[C]	See Preventive Care Checklist for Transmasculine Patients and Accompanying Explanations (Appendices F & G)
Exam	Focused PE with PAP[E] if indicated, Include BP, height, weight	BP, weight	
Lab	Pregnancy test prior to 1st dose, See Guidelines for gender-affirming primary care with trans and non-binary patients, Part III.		
Other	Consider HPV, Hep A, B and routine vaccinations as indicated		

A. Mental Health:

- Screen for mood changes including irritability/anger, depressive symptoms (including suicidality), self-harm, anxiety, +/- hypomania/mania and psychotic symptoms in those with underlying predisposition
- Inquire re: current experience of gender incongruence/dysphoria and body image
- Screen for disordered eating
- Assess patient interest in surgical treatments if not previously undergone
- Inquire re: libido/changes in libido

B. Education/Lifestyle Counselling:

- Review health eating and general nutrition
- Adequate Calcium Intake – ensure a minimum intake of 1200 mg of Calcium daily (diet + supplements)
- Adequate Vitamin D – ensure 1000 IU of vitamin D daily
- Hormone Adherence – missed doses of testosterone may impact bone health if post-oophorectomy, while extra doses may lead to supratherapeutic levels
- Regular, moderate physical activity – encourage weight-bearing exercise for osteoporosis prevention; to avoid tendon rupture, weight loads used in strength training should be increased gradually with an emphasis on repetitions and stretching
- Safe sex practices/STI counselling – transmasculine patients may be at high risk of STIs depending on behavioural factors; safer sex counselling is recommended (for patient-

centred handout materials, see *PRIMED2: The Back Pocket Guide for Trans men & the Men Who Love Them*[1])

- Potential for pregnancy/need for birth control – transmasculine patients on testosterone may become pregnant even if menstrual suppression has been achieved and should be counselled in this regard; given that testosterone is a teratogen, reliable birth control should be instituted where pregnancy is a risk based on sexual activity
- Smoking – cessation, stages of readiness, motivational interviewing, etc
- Alcohol and other substances – inquire re: problematic use of substances including non-prescribed hormones or anabolic steroids; we recommend that transmasculine patients follow the safe drinking guidelines as for cis women[2]

C. Psychosocial:

- An effort should be made to assess the impact of transition/trans identity on employment, housing, family, relationships, and economic well-being
- Social Supports – specific attention should be given to assessing the extent of a patient's social supports, creating an opportunity to suggest additional resources if needed
- Name change/identification – assess patient need/desire to change name and/or gender marker on identification and offer support for this process (See Part 1: Changing Sex Designation on Government ID, and Appendices Q & R)

D. Health Maintenance:

- Immunization history
- STI/HIV risk assessment and screening as indicated, frequent screening (i.e. every 3 months) for those at high risk
- TB skin test as indicated

E. Pap

- Follow cervical cancer screening guidelines as for cis women if the cervix is present
- Several strategies may be employed to minimize the discomfort/trauma associated with this examination for some transmasculine patients (see Tips for Providing Paps to Trans men)[3]
- Barring contraindications, topical 2% lidocaine jelly may be applied vaginally 5-10 minutes prior to the procedure in those who find speculum examination painful due to atrophic changes

1. PRIMED2: A sex guide for trans men into men [Internet]. Toronto: CATIE; 2015. Available from: http://librarypdf.catie.ca/PDF/ATI-20000s/24654.pdf
2. The Canadian Centre on Substance Use and Addiction [Internet]. Ottawa: The Canadian Centre on Substance Use and Addiction; [updated 2018]. Canada's low risk alcohol drinking guidelines; [2012] [cited 2019 Feb 7]. Available from: http://www.ccsa.ca/Resource%20Library/2012-Canada-Low-Risk-Alcohol-Drinking-Guidelines-Brochure-en.pdf
3. Potter, M. Rainbow Health Ontario [Internet] Toronto: Rainbow Health Ontario; [updated 2018]. Tips for providing paps to trans men; [updated 2015] [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/tips-for-providing-paps-to-trans-men/

APPENDIX D:

preventative care checklist for transfeminine patients

For annual health assessments of transfeminine patients, applying to patients who were assigned male at birth and have a gender identity that is female or on the feminine spectrum, who may or may not have accessed hormonal and/or surgical treatments for gender dysphoria/gender incongruence.

Prepared by: Dr. A. Bourns · Adapted from the Preventive Care Checklist Form © 2016

(see Ridley, J, Ischayek, A., Dubey, V., Iglar, K., *Adult health Checkup: Update on the Preventive Care Checklist Form*© Canadian Family Physician, 2016 Apr; 62:307-313)

Please note: **Bold** = transgender-specific considerations, see Explanation Sheet for detailed recommendations

Unbolded items should be followed according to the most recent update to the original Preventive Care Checklist©

IDENTIFYING DATA:

Name:_____

Tel:_____

DOB:_____

Age:_____

Date of Examination:_____

MEDICAL TRANSITION HISTORY:

Androgen Blocker:

☐ Spironolactone ☐ Cyproterone ☐ N/A

Estrogen: ○ Yes ○ No

If Yes, Start Date:_____

Orchiectomy: ○ Yes ○ No

Vaginoplasty: ○ Yes ○ No

Breast Aug: ○ Yes ○ No

CURRENT CONCERNS

LIFESTYLE/HABITS/PSYCHOSOCIAL:

Diet:_____

Fat/Cholesterol_____

Fiber_____

Calcium _____

Sodium_____

Exercise:_____

Work/Education:_____

Poverty:_____

Social supports:_____

Family:_____

Relationships:_____

Sexual History:_____

Family Planning/Contraception:_____

Name change/identification:_____

Sleep:_____

Smoking:_____

Alcohol:_____

Safe Guidelines ≤10/week, ≤2/day

Drugs:_____

MENTAL HEALTH

Screen for:

Depression	○ Positive	○ Negative
Suicidal Ideation	○ Positive	○ Negative
Self-harm	○ Positive	○ Negative
Anxiety	○ Positive	○ Negative
Persistent Gender Dysphoria	○ Positive	○ Negative
Experiences/Impacts of transphobia	○ Positive	○ Negative

UPDATE CUMULATIVE PATIENT PROFILE

- ☐ Family History
- ☐ Medications
- ☐ Hospitalizations/Surgeries
- ☐ Allergies

FUNCTIONAL INQUIRY

	Normal	Remarks:
HEENT:	☐	_____
CVS:	☐	_____
Resp:	☐	_____
Breasts:	☐	_____
GI:	☐	_____
GU:	☐	_____
Sexual Function:	☐	_____
MSK:	☐	_____
Neuro:	☐	_____
Derm:	☐	_____
Constitutional Sx:	☐	_____

PHYSICAL EXAMINATION:

Physical examination, as required, taking into consideration pre-existing conditions and presenting complaints

BP _____ HT _____
WT _____ BMI _____

☐ Or See EMR Vitals

May include:

Breasts _____

Tanner stage _____
Breast circumference _____
Areolar diametre _____

Genitourinary _____
Ano-rectum _____

EDUCATION/COUNSELLING

Behavioural

- ☐ adverse nutritional habits
- ☐ dietary advice on fat/cholesterol
- ☐ **adequate calcium intake (1200 mg daily diet + supp)**
- ☐ **adequate vitamin D (1000 IU daily**)
- ☐ **hormone adherence**
- ☐ **regular, moderate physical activity**
- ☐ avoid sun exposure, use protective clothing
- ☐ **safe sex practices/STI counselling/PrEP indications**

Overweight (BMI 25-29) or Obese (BMI 30-39)

- ☐ Overweight (BMI 25-29)
- ☐ Obese (BMI 30-39)
  - ☐ structured behavioural interventions for weight loss
  - ☐ **screen for mental health contributors**
  - ☐ multidisciplinary approach

Underweight

- ☐ **Underweight (BMI<18)**
  - ☐ screen for eating disorders

Smoking

- ☐ smoking cessation
- ☐ nicotine replacement therapy/other medications
- ☐ dietary advice on fruits and green leafy vegetables
- ☐ referral to validated smoking cessation program

Alcohol & other substances

- ☐ case finding for problematic substance use
- ☐ counselling for problematic substance use
- ☐ **referral for substance abuse treatment**
- ☐ **provide naloxone kit if indicated**

Elderly

- ☐ cognitive assessment (if concerns)
- ☐ fall assessment (if history of falls)
- ☐ **advanced care planning**

Oral hygeine

- ☐ brushing/flossing teeth
- ☐ fluoride (toothpaste/supplement)
- ☐ tooth scaling and prophylaxis
- ☐ smoking cessation

Personal safety

- ☐ hearing protection
- ☐ noise control programs
- ☐ seat belts
- ☐ **injection safety**
- ☐ **bathroom safety**

Parents with children

- ☐ poison control prevention
- ☐ smoke detectors
- ☐ non-flammable sleepwear
- ☐ hot water thermostat settings (<54°C)

LABS / INVESTIGATIONS

≤64 YEARS	≥65 YEARS
☐ **Mammogram (estrogen ≥5 years total and avg risk: age 50-64 q2 yrs)**	☐ **Mammogram (estrogen ≥5 years total and avg risk age: 65-74 q2 yrs**
☐ Fecal immunochemical test (FIT) (age 50-64 q2 yrs) OR ☐ Sigmoidoscopy OR ☐ Colonoscopy	☐ Fecal immunochemical test (FIT) (up to 74 yrs q2 yrs) OR ☐ Sigmoidoscopy OR ☐ Colonoscopy
☐ **GC/CT/Syphilis/HIV/HBV/HCV screen (high risk)**	☐ **GC/CT/Syphilis/HIV/HBV/HCV screen (high risk)**
☐ **Bone Mineral Density if at risk**	☐ Bone Mineral Density
	☐ Audioscope (or inquire/whispered voice test)
Consider Anal Pap if history of receptive anal sex, q2-3 yrs or yearly if HIV+ (age range not defined)	

ANNUAL TRANS BLOODWORK (ALL AGES, ASSUMING 12 MONTHS ON HORMONE THERAPY)

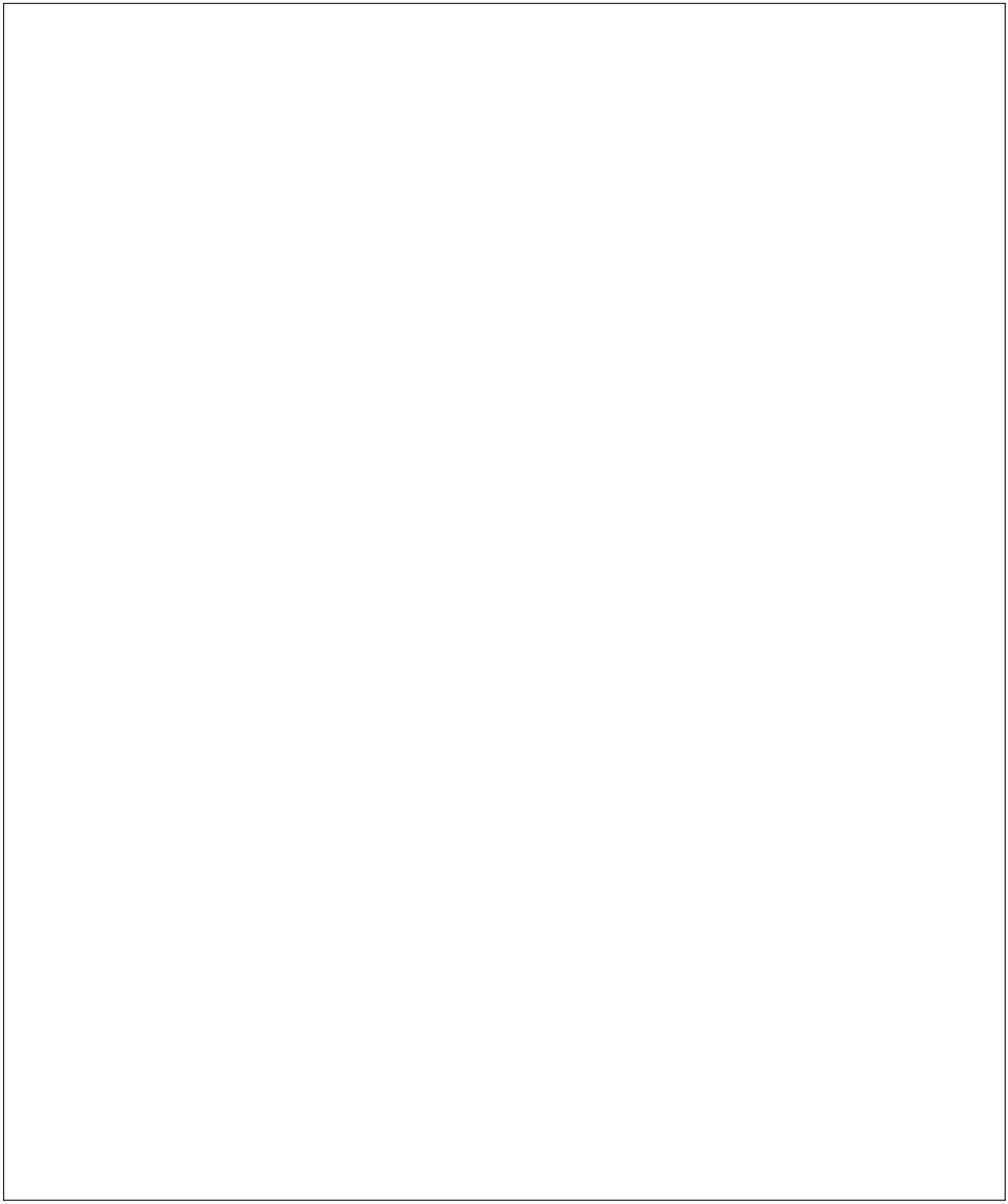
Lab Test	Indication
☐ CBC*	on cypro or first year on hormone therapy
☐ Cr, lytes**	on spiro or first year on cypro
☐ ALT+/-AST	on estrogen or cypro
☐ Lipid Profile	at 12 mos, then per routine guidelines
☐ Hba1c or FPG	at 12 mos, then per routine guidelines
☐ Estradiol	on estrogen
☐ Prolactin	on cypro
☐ Total testosterone	on antiandrogen

*Hb/Hct - use female reference for LLN and male reference for ULN
**Cr - use male reference range for ULN

IMMUNIZATIONS

≤64 YEARS	≥65 YEARS
☐ Tetanus vaccine q10 yrs	☐ Tetanus vaccine q10 yrs
☐ Influenza vaccine q1 yr	☐ Influenza vaccine q1 yr
☐ Acellular pertussis vaccine	☐ Pneumococcal vaccine
☐ Varicella vaccine (2 doses)	☐ Acellular pertussis vaccine
☐ **Human papillomavirus vaccine (consider up to age 45 yrs, publicly covered ≤26 yrs if sexually active with MSM)**	☐ Varicella vaccine (2 doses))
☐ Measles/mumps/rubella vaccine	☐ Herpes zoster vaccine (publicly covered 65-70yrs)
☐ Meningococcal vaccine	
☐ Herpes zoster vaccine (consider ≥60 yrs)	
☐ **Hepatitis A/Hepatitis B** ☐ **Hep A immunity** ☐ **Hep B immunity**	

ASSESSMENT AND PLANS



APPENDIX E:
accompaniment to the preventive care checklist for transfeminine patients

EXPLANATIONS FOR TRANS-SPECIFIC RECOMMENDATIONS

Note: This form has been adapted with permission from Dr. V. Dubey from the CFPC-endorsed Preventive Care Checklist Form©. The use of these trans-specific forms assumes familiarity with the original forms and their explanations. The original form contains graded evidence-based recommendations,[1] which may or may not be applicable to transgender patients. Unbolded recommendations should be followed as per the original forms. The specific recommendations herein represent an effort to incorporate expert opinion and limited trans-specific evidence with standard National and Provincial primary care practices in a practical format that can be accessed at the point-of-care.

MEDICAL TRANSITION HISTORY

Establishment of a patient's status regarding gender-related treatments and timing of these treatments at the outset of a preventive care assessment allows for patient-centred tailoring of counselling, education, physical examination, and screening recommendations.

LIFESTYLE/HABITS/PSYCHOSOCIAL

An effort should be made to assess the impact of transition/trans identity, experiences of transphobia and impact on employment, housing, family, relationships, and economic well-being.

Social Supports – specific attention should be given to assessing the extent of a patient's social supports, creating an opportunity to suggest additional resources if needed.

Sexual History – delineating the types of sex that a patient is having and with whom will direct the indicated type and frequency of STI screening.

Family Planning/Contraception – transfeminine patients planning to undergo hormonal treatment and/or gonadectomy should be counselled regarding the option for fertility preservation, those who have not undergone gonadectomy and are on hormonal therapy should be counselled regarding the variable effect on fertility and the need for contraception if sexually active with a partner who may become pregnant. (See *Guidelines for gender-affirming primary care with trans and on-binary patients, Part 1*, and *RHO's Reproductive Options Fact Sheet*[2] and the LGBTQ Parenting Network's 'Fertility Preservation for People Who Produce Sperm'[3])

Name change/identification – assess patient need/desire to change name and/or sex marker on identification and offer support for this process (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part I*, and *Appendices P and Q*)

Alcohol – estrogen affects the metabolism of alcohol by the liver and has been associated with elevation in liver enzymes, thus we suggest using the same safe-drinking guidelines for transfeminine individuals as for cis women (i.e. max 10 drinks a week with no more than 2 drinks a day most days, see Canada's Low-risk Alcohol Drinking Guidelines).[4]

FUNCTIONAL INQUIRY

An effort should be made to use language consistent with a patient's gender identity; if unsure - consider asking the patient how they refer to their gendered body parts.

Mental Health – inquire re: experiences/impacts of transphobia; screen for depressive symptoms, anxiety (particularly social anxiety), and self-harm; suicidal ideation and attempts are particularly high in the trans population[5] and should be specifically inquired about; inquire re: current level of gender dysphoria and body image, (re-)assess patient interest in transition-related surgeries if not undergone.

Breasts – inquire re: breast pain (can be normal in early phases of feminization), and nipple discharge (bilateral/non-bloody discharge can be considered normal in early phases, otherwise may be indicative of hyperprolactinemia or local breast disease); if implants present consider inquiry re: symptoms of capsular contracture or rupture (pain, loss of contour, deflation).

GU – inquiry re: urinary symptoms is relevant regardless of genital operative status: spironolactone can cause urinary frequency; the prostate remains post-vaginoplasty; vaginoplasty may lead to urinary complications including increased frequency of UTIs, stricture, fistula; if post-op vaginoplasty; inquire re: vaginal discharge, pruritus, pelvic pain. Odour/discharge is most frequently due to sebum, dead skin, or keratin debris (skin graft) – routine douching with soapy water is usually adequate to maintain hygiene. Imbalances in neovaginal flora may also occur – cleansing/douching with a solution of 25% povidine iodine in water for 2-3 days may be helpful and if symptoms persist; a 5-day course of vaginal metronidazole is reasonable;[6] STIs, granulation tissue, and other neovaginal lesions should also be considered in the differential.

Sexual Function – if patient has not undergone vaginoplasty, inquire re: erectile dysfunction and if present, whether this is of concern for the patient (PDE-5 inhibitors may be considered in patients wishing to maintain erectile function); if the patient has undergone vaginoplasty, inquire re: problems with dilation, dyspareunia, post-coital bleeding, and ability to achieve orgasm (also see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part II: Sexual Function and Fatigue*).

Constitutional Symptoms – fatigue in the absence of other associated symptoms suggesting another cause may be due to testosterone levels below the physiologic female range (also see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part II: Sexual Function and Fatigue*).

EDUCATION/COUNSELLING

Review S/Sx DVT/PE/Stroke – consider periodic review of the signs and symptoms of DVT, PE, and stroke for transfeminine patients on hormone therapy who have additional risk factors.

Adequate Calcium Intake – all transfeminine patients on hormone therapy should ensure a minimum intake of 1200 mg of Calcium daily (total: diet + supplements).

Adequate Vitamin D – all transfeminine patients on feminizing hormone therapy should take 1000 IU of vitamin D daily.

Hormone Adherence – poor hormone adherence may impact bone health if post-orchiectomy, while extra doses may lead to risks associated with high serum levels of estrogen.

Regular, moderate physical activity – some transfeminine individuals may tend to avoid exercise for fear of unwanted muscle development; encourage aerobic exercise as well as high-repetition weight-bearing exercise for osteoporosis prevention.

Safe sex practices/STI counselling - transfeminine patients may be at high risk of STIs depending

on behavioural factors; inquire re: sexual practices and risks including sex work; safer sex counselling, frequent screening (i.e. every 3 months) and an assessment of indications for HIV PrEP[7] are indicated for those at high risk. For patient-centred handout materials, see *Brazen 2.0: Trans women's Safer Sex Guide*.[8]

Overweight/Obese – obesity may increase the thromboembolic and metabolic risks associated with estrogen therapy, weight loss counselling should be emphasized; screen for eating disorders (more prevalent in LGBT2SQ populations, particularly amongst youth).

Underweight - screen for disordered eating – persistent gender dysphoria/incongruence may be associated with a desire to maintain a thinner body habitus in order to hide indicators of natal sex, which may have negative health impacts; strategizing around other ways to address persistent gender dysphoria/incongruence may be helpful.

Smoking – smoking greatly increases the thromboembolic risks associated with estrogen therapy, smoking cessation should be emphasized.

Alcohol and other substances – substance use is more prevalent in members of the LGBT2SQ community; inquire re: problematic use of substances including hormones without a prescription; if referral to a substance abuse program is indicated, consider an LGBT2SQ-specific or LGBT2SQ-positive program such as Rainbow Services at CAMH. Offer safer smoking and injection kits when indicated for harm reduction. A naloxone kit and instructions on use should be offered to all patients who are at risk of opioid overdose, as well as friends and family of those at risk.[9]

Advanced care planning – A discussion regarding advanced care planning is recommended at least once for Canadians ≥65.[10] Trans and gender diverse patients may have particular needs in ensuring that their gender identity and expression are respected and a respectful decision-maker is chosen (See '*Creating End of Life Documents for Trans Individuals: An Advocate's Guide*').[11]

Injection safety – for patients who self-inject estrogen: confirm dose, review aseptic injection technique, inquire re: rotating injections sites, injection site reactions, and pre-injection anxiety; consider review of route options (IM vs. SC injectable, oral, transdermal), ensure safe sharps disposal; counsel re: risks of injecting non-medical silicone (i.e. 'pumping' to enhance body shape) including chronic inflammation, disfigurement, pulmonary complications, sepsis, and death.

Bathroom safety - finding a bathroom that feels comfortable and safe can frequently be a source of stress for trans individuals. Resources such as *Refuge Restrooms*[12]can assist trans people in locating gender neutral bathrooms. For those who may be experiencing urinary frequency due to spironolactone, timing of administration can be adjusted if safe bathroom access is a concern.

PHYSICAL EXAMINATION

Breasts – Evidence to date suggests that the risk of breast cancer in transfeminine individuals is not higher than in cis women and may potentially be lower than in cis women, however both benign and malignant breast disease can occur in transfeminine patients on hormone therapy (also see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part II: Breast Cancer*); annual routine clinical breast exams in transfeminine patients with or without implants are of questionable utility but may be useful to assess the degree of breast development or to detect implant complications respectively. Transfeminine patients should receive counselling around breast self-awareness as is recommended for cis women.

For those who may have interest in MOHLTC-covered breast augmentation surgery, **breast inspection** at baseline and 12 months following hormone initiation is recommended, with particular attention to Tanner stage. **Measurements** such

as chest circumference at the fullest part of the breast and nipple-areolar diametre may be helpful in determining the presence or absence of breast growth, or may be of interest to some patients (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part I: Physical Exam and Baseline Investigations*).

Genitourinary – In patients who have not undergone orchiectomy, testicular examination may reveal testicular atrophy in the setting of feminizing therapy but is not routinely needed. For those who have undergone vaginoplasty, we do suggest annual (starting 1 year post-op) neovaginal speculum examination to detect any abnormalities such as granulation tissue (which may be treated with silver nitrate), active hair follicles (which may be tweezed or if extensive, cauterized under local anesthetic), warts, abnormal discharge, or malignancy; vault smears are not generally recommended as their utility in detecting dysplasia or metaplasia in keratinized epithelium is not established; neovaginal tissue created from colon can be screened for malignancy by direct visual inspection; in the extremely rare case that a neo-cervix has been surgically created, Pap guidelines may be followed as for cis women; if examination of the prostate is indicated, the prostate may be palpated along the anterior wall of the neovagina by digital examination in the lithotomy position.

Ano-rectum – for those who engage in receptive anal sex, visual examination of the perianal region for any evidence of anal warts or other anorectal problems such as hemorrhoids should be considered–particularly those who are HIV+. Additionally consider DRE for detection of internal lesions. HIV+ patients with physical findings consistent with warts or other HPV-related changes should also be referred for HRA.

LABS/INVESTIGATIONS

Mammography – consider mammography in transfeminine patients on hormone therapy every 2 years if aged 50-74 AND on estrogen for ≥5 years total (i.e. years do not need to be consecutive), consider initiating screening at a younger age if additional risk factors are present (i.e. estrogen + progestin for > 5 yrs, family history), consider obtaining expert opinion regarding the need for annual mammography with MRI for those aged 30-69 with family history suggestive of hereditary breast cancer; the presence of breast implants necessitates diagnostic mammography rather than routine screening mammography; additional imaging modalities (ultrasound, MRI) may be recommended by implant manufacturers or a patient's surgeon at regular intervals to detect silent rupture of silicone implants. GRS Montreal currently recommends annual ultrasounds from the 5th year onward to screen for silent rupture in silicone implants, while suggesting clinical exam only (without imaging) for monitoring of saline implants given that rupture causes visible deflation.

GC/CT/Syphilis/HIV/HBV/HCV screen – consider STI detection from the following sites as indicated: throat, urethra, neovagina, anorectum, and serum.

Yearly trans bloodwork – bloodwork should be tailored to the patient's hormone regimen, risk factors and pre-existing conditions; screening for DMII and dyslipidemia should be performed at baseline and 1 year following hormone therapy initiation, and otherwise according to routine guidelines for cis patients; Framingham calculation will be less reliable with exogenous hormone use - depending on the age of hormone initiation and duration of hormone exposure providers may choose to use the risk calculator for sex assigned at birth, affirmed gender, or an average of both;[6] for management of elevated prolactin levels see *Part II 'Hyperprolactinemia/Prolactinoma'*.

Note: For patients on anti-androgen +/- estrogen:

- Hb/Hct - use the female reference for lower limit of normal and male reference for upper limit of normal
- Cr - use male reference range for upper limit of normal

BMD screening – exogenous estrogens appear to effectively maintain bone mass in transfeminine patients although they may have lower BMD than age-matched cis-men at baseline. In accordance with national recommendations, perform bone mineral density testing in all transfeminine patients over age 65. BMD should be considered earlier in those at high risk, such as those who, for a significant period of time (i.e. >2 yrs):

- have been on low-dose or no hormones and are agonadal
- have been on anti-androgens without the co-administration of exogenous estrogen
- have been on a GnRH analogue without exogenous estrogen (See '*Part III: Osteoporosis and BMD Screening*')

Note: frequency of follow-up BMD screening will depend on the results of the initial scan.

Anal Pap screening – for those who have a history of receptive anal sex, consider anal pap every 2-3 years or yearly in those who are HIV+ (if local HRA for the follow up of abnormal results is available). See the Canadian Cancer Society's Colon cancer screening guidelines for gay and bisexual men for more information.

IMMUNIZATIONS

Hepatitis A/Hepatitis B – transfeminine patients may be at higher risk of Hepatitis A/B depending on behavioural risks, if behavioural risk factors are present, the patient may qualify for publicly funded vaccination similarly to MSM.

HPV – consider HPV vaccination x 3 doses in transfeminine patients up to the age of 45, tailor to risk; vaccination can be publicly covered in Ontario via the catch-up program for adolescents up to grade 12 and ≤26 years old for those who are sexually active with MSM.

CFPC – College of Family Physicians of Canada,
STI - sexually transmitted infection,
RHO – Rainbow Health Ontario,
GU - genitourinary,
UTI – urinary tract infection,
PDE-5 – phosphodiesterase-5,
DVT – deep vein thrombosis, PE – pulmonary embolus,
IU – international units,
HIV - human immunodeficiency virus,
LGBT2SQ - lesbian, gay, bisexual, trans, queer, and 2 spirit,
CAMH – Centre for Addiction and Mental Health,
IM - intramuscular,
SC - subcutaneous,
MRI- magnetic resonance imaging,
DRE - digital rectal exam,
HRA - high resolution anoscopy,
GC – gonococcus,
CT – chlamydia trachomatis,
HBV – hepatitis B virus,
HCV - Hepatitis C virus,
DMII - Diabetes mellitus type II,
Hb - hemoglobin,
Hct - hematocrit,
Cr - creatinine,
BMD – bone mineral density,
HPV – human papillomavirus,
MSM - men who have sex with men

1. Ridley J, Ischayek A, Dubey V, Iglar K. Adult health checkup: Update on the Preventive Care Checklist Form©. Can Fam Physician Med Fam Can. 2016; 62(4):307–13.
2. RHO Fact Sheet: Reproductive options for trans people [Internet]. Toronto: Rainbow Health Ontario; 2012 p. 9. Available from: https://www.rainbowhealthontario.ca/wp-content/uploads/woocommerce_uploads/2012/09/RHO_FactSheet_REPRODUCTIVEOPTIONSFORTRANSPEOPLE_E.pdf
3. LGBTQ Parenting Network [Internet]. Toronto: Sherbourne Health; [updated 2018]. Fertility preservation for trans people who produce sperm; [2018] [cited 2019 Feb 8]. Available from: http://lgbtqpn.ca/wp-content/uploads/2018/07/Fertility-Preservation-for-Trans-People-who-Produce-Sperm-Version-2.0-Sept-2017.pdf
4. The Canadian Centre on Substance Use and Addiction [Internet]. Ottawa: The Canadian Centre on Substance Use and Addiction; [updated 2018]. Canada's low risk alcohol drinking guidelines; [2012] [cited 2019 Feb 7]. Available from: http://www.ccsa.ca/Resource%20Library/2012-Canada-Low-Risk-Alcohol-Drinking-Guidelines-Brochure-en.pdf
5. Bauer G, Pyne J, Francino M, Hammond R. La Suicidabilite parmi les personnes trans en Ontario : Implications en travail social et en justice sociale. Serv Soc. 2013; 59(1):35–62.
6. Deutsch M. Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people [Internet]. Centre of Excellence for Transgender Health. 2016. Available from: http://transhealth.ucsf.edu/protocols
7. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2017; 189(47):E1448–58.

8. Brazen 2.0: Trans women's safer sex guide [Internet]. Toronto: The 519 Church Street Community Centre and CATIE; 2017 p. 34. Available from: www.the519.org/media/download/3246
9. Ontario Ministry of Health and Long-Term Care [Internet]. Toronto: Ontario Ministry of Health and Long-Term Care [updated 2018]. Naloxone - Drugs and Devices; [date unknown] [cited 2019 Feb 8]. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/naloxone/
10. Speak Up [Internet]. Ottawa: Canadian Hospice Palliative Care Association; [updated 2019] [cited 2019 Feb 7]. Available from: http://www.advancecareplanning.ca/
11. National Resource Center on LGBT Aging [Internet]. New York: National Resource Center on LGBT Aging; [updated 2019]. Creating end-of-life documents for trans individuals: An advocate's guide; [October 2014] [cited 2019 Feb 7]. Available from: https://www.lgbtagingcenter.org/resources/resource.cfm?r=694
12. REFUGE Restrooms [Internet]. REFUGE Restrooms; [updated 2019] [cited 2019 Feb 7]. Available from: https://www.refugerestrooms.org/about

APPENDIX F:

preventive care checklist for transmasculine patients

For annual health assessments of transmasculine patients, applying to patients who were assigned female at birth and have a gender identity that is male or on the masculine spectrum, who may or may not have accessed hormonal and/or surgical treatments for gender dysphoria/ gender incongruence.

Prepared by: Dr. A. Bourns · Adapted from the Preventive Care Checklist Form © 2016

(see Ridley, J, Ischayek, A., Dubey, V., Iglar, K., Adult health Checkup: Update on the Preventive Care Checklist Form© Canadian Family Physician, 2016 Apr; 62:307-313)

Please note: **Bold** = transgender-specific considerations, see Explanation Sheet for detailed recommendations

Unbolded items should be followed according to the most recent update to the original Preventive Care Checklist©

IDENTIFYING DATA:

Name:_____

Tel:_____

DOB:_____

Age:_____

Date of Examination:_____

MEDICAL TRANSITION HISTORY:

Testosterone:	○ Yes	○ No
If Yes, Start Date:_____		
Chest Reconstruction:	○ Yes	○ No
TAH:	○ Yes	○ No
BSO:	○ Yes	○ No

Genital Reconstruction

Clitoral Release:	○ Yes	○ No
Meta:	○ Yes	○ No
Phallo:	○ Yes	○ No

CURRENT CONCERNS

LIFESTYLE/HABITS/PSYCHOSOCIAL:

Diet:_____

- Fat/Cholesterol_____
- Fibre_____
- **Calcium**_____
- Sodium_____
- Exercise:_____

Work/Education:_____

Poverty:_____

Social supports:_____

- Family:_____
- Relationships:_____

Sexual History:_____

Family Planning/Contraception:_____

Name change/identification:_____

Sleep:_____

Smoking:_____

Alcohol:_____

Safe Guidelines ≤10/week, ≤2/day

Drugs:_____

MENTAL HEALTH

Screen for:

Depression	○ Positive	○ Negative
Suicidal Ideation	○ Positive	○ Negative
Self-harm	○ Positive	○ Negative
Anxiety	○ Positive	○ Negative
Persistent Gender Dysphoria	○ Positive	○ Negative
Experiences/Impacts of transphobia	○ Positive	○ Negative

UPDATE CUMULATIVE PATIENT PROFILE

- ☐ Family History
- ☐ Medications
- ☐ Hospitalizations/Surgeries
- ☐ Allergies

FUNCTIONAL INQUIRY

	Normal	Remarks:
HEENT:	☐	_____
CVS:	☐	_____
Resp:	☐	_____
Chest:	☐	_____
GI:	☐	_____
GU/PV bleeding:	☐	_____
Sexual Function:	☐	_____
MSK:	☐	_____
Neuro:	☐	_____
Derm:	☐	_____
Constitutional Sx:	☐	_____

PHYSICAL EXAMINATION:

Physical examination, as required, taking into consideration pre-existing conditions and presenting complaints

BP _____ HT _____

WT _____ BMI _____

☐ Or See EMR Vitals

May include:

Chest _____

Pelvic/pap _____

Ano-rectum _____

Derm _____

EDUCATION/COUNSELLING

Behavioural

- ☐ adverse nutritional habits
- ☐ dietary advice on fat/cholesterol
- ☐ **adequate calcium intake (1200 mg daily diet + supp)**
- ☐ **adequate vitamin D (1000 IU daily)**
- ☐ **hormone adherence**
- ☐ **regular, moderate physical activity**
- ☐ avoid sun exposure, use protective clothing
- ☐ **safe sex practices/STI counselling/PrEP indications**
- ☐ **review potential for pregnancy/ assess need for birth control**
- ☐ **assess need for folic acid** (0.4-0.8 mg)

Overweight (BMI 25-29) or Obese (BMI 30-39)

- ☐ Overweight (BMI 25-29)
- ☐ Obese (BMI 30-39)
  - ☐ structured behavioural interventions for weight loss
  - ☐ **screen for mental health contributors**
  - ☐ multidisciplinary approach

Underweight

- ☐ **Underweight (BMI<18)**
  - ☐ **screen for eating disorders**

Smoking

- ☐ smoking cessation
- ☐ nicotine replacement therapy/other medications
- ☐ dietary advice on fruits and green leafy vegetables
- ☐ referral to validated smoking cessation program

Alcohol & other substances

- ☐ case finding for problematic substance use
- ☐ counselling for problematic substance use
- ☐ **referral for substance abuse treatment**
- ☐ **provide naloxone kit if indicated**

Elderly

- ☐ cognitive assessment (if concerns)
- ☐ fall assessment (if history of falls)
- ☐ **advanced care planning**

Oral hygeine

- ☐ brushing/flossing teeth
- ☐ fluoride (toothpaste/supplement)
- ☐ tooth scaling and prophylaxis
- ☐ smoking cessation

Personal safety

- ☐ hearing protection
- ☐ noise control programs
- ☐ seat belts
- ☐ **injection safety**
- ☐ **bathroom safety**

Parents with children

- ☐ poison control prevention
- ☐ smoke detectors
- ☐ non-flammable sleepwear
- ☐ hot water thermostat settings (<54°C)

LABS / INVESTIGATIONS

≤64 YEARS	≥65 YEARS
☐ Mammography (q2 yrs age 50-74 if no chest reconstruction)	☐ Mammography (q2 yrs age 50-74 if no chest reconstruction)
☐ **Cervical cytology** (q3 yrs if ever sexually active and 21-69 yrs)	☐ **Cervical cytology** (q3 yrs if ever sexually active and up to 69 yrs)
☐ Fecal immunochemical test (FIT) (age 50-64 q2 yrs)	☐ Fecal immunochemical test (FIT) (up to 74 yrs q2 yrs)
OR ☐ Sigmoidoscopy OR ☐ Colonoscopy	OR ☐ Sigmoidoscopy OR ☐ Colonoscopy
☐ **GC/CT/Syphilis/HIV/HBV/HCV screen (high risk)**	☐ **GC/CT/Syphilis/HIV/HBV/HCV screen (high risk)**
☐ **Bone Mineral Density if at risk**	☐ Bone Mineral Density
	☐ Audioscope (or inquire/whispered voice test)
Consider Anal Pap if history of receptive anal sex, q2-3 yrs or yearly if HIV+ (age range not defined)	

ANNUAL TRANS BLOODWORK (ALL AGES, ASSUMING 12 MONTHS ON HORMONE THERAPY)

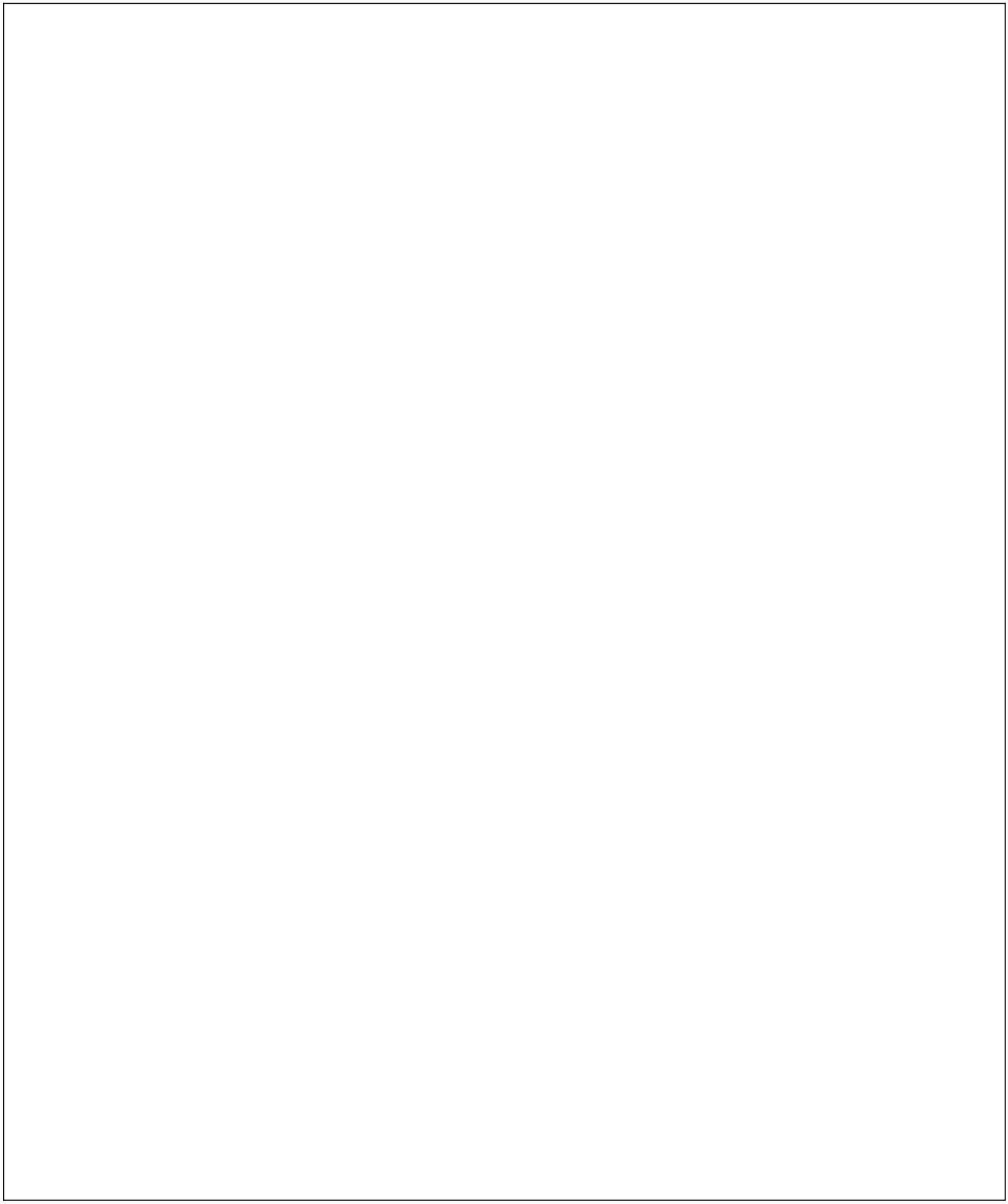
Lab Test	Indication
☐ CBC*	yearly
☐ ALT+/-AST	per provider discretion
☐ Total testosterone	yearly
☐ LH	yearly if agonadal
☐ Lipid Profile	at 12 mos, then per routine guidelines
☐ Hba1c or FPG	at 12 mos, then per routine guidelines

*use male reference range for ULN Hb/Hct

IMMUNIZATIONS

≤64 YEARS	≥65 YEARS
☐ Tetanus vaccine q10 yrs	☐ Tetanus vaccine q10 yrs
☐ Influenza vaccine q1 yr	☐ Influenza vaccine q1 yr
☐ Acellular pertussis vaccine	☐ Pneumococcal vaccine
☐ Varicella vaccine (2 doses)	☐ Acellular pertussis vaccine
☐ **Human papillomavirus vaccine (consider up to age 45 yrs, publicly covered** ≤26 yrs if sexually active with MSM)	☐ Varicella vaccine (2 doses)
☐ Measles/mumps/rubella vaccine	☐ Herpes zoster vaccine (publicly covered 65-70yrs)
☐ Meningococcal vaccine	
☐ Herpes zoster vaccine (consider ≥60 yrs)	
☐ **Hepatitis A/Hepatitis B** ☐ **Hep A immunity** ☐ **Hep B immunity**	

ASSESSMENT AND PLANS



APPENDIX G:
accompaniment to preventive care checklist for transmasculine patients

EXPLANATIONS FOR TRANS-SPECIFIC RECOMMENDATIONS

Note: This form has been adapted with permission from Dr. V. Dubey from the CFPC-endorsed Preventive Care Checklist Form©. The use of these trans-specific forms assumes familiarity with the original forms and their explanations. The original form contains graded evidence-based recommendations,[1] which may or may not be applicable to transgender patients. Unbolded recommendations should be followed as per the original forms. The specific recommendations herein represent an effort to incorporate expert opinion and limited trans-specific evidence with standard National and Provincial primary care practices in a practical format that can be accessed at the point-of-care

MEDICAL TRANSITION HISTORY

Establishment of a patient's status regarding gender-related treatments and timing of these treatments at the outset of a preventive care assessment allows for patient-centred tailoring of counselling, education, physical examination, and screening recommendations

LIFESTYLE/HABITS/PSYCHOSOCIAL

An effort should be made to assess the impact of transition/transgender identity, experiences of transphobia and impact on employment, housing, family, relationships, and economic well-being

Social Supports – specific attention should be given to assessing the extent of a patient's social supports, creating an opportunity to suggest additional resources if needed

Sexual History – delineating the types of sex that the patient is having and with whom will direct the indicated type and frequency of STI screening

Family Planning/Contraception – transmasculine patients considering hormonal treatment and/or gonadectomy should be counselled regarding the option for fertility preservation (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part I - Fertility and Birth Control*, and RHO's Reproductive Options Fact Sheet and the LGBTQ Parenting Network's 'Fertility Preservation for People Who Produce Sperm'[2])

See also potential for pregnancy/need for birth control below.

Name change/identification – assess patient need/desire to change name and/or sex marker on identification and offer support for this process (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part I - Changing Sex Designation on Government ID*, and *Appendices Q and R*)

Alcohol – due to presumed smaller liver size compared with cis men, we suggest that transmasculine patients, regardless of exogenous hormone use, follow the safe-drinking guidelines for cis women (i e maximum 10 drinks a week with no more than 2 drinks a day most days, see *Canada's Low-risk Alcohol Drinking Guidelines*)[3]

Sleep – testosterone therapy may worsen or unmask obstructive sleep apnea,[4] consider inquiring re: symptoms of sleep apnea; in those with sleep apnea, CPAP requirements may change with masculinizing hormone therapy and should be monitored

FUNCTIONAL INQUIRY

An effort should be made to use language consistent with a patient's gender identity; if unsure, consider asking the patient how they refer to their body parts

Mental Health – inquire re: experiences and impacts of transphobia; screen for mood disturbances including irritability, anger, and depression, as well as anxiety (particularly social anxiety) and self-harm; suicidal ideation and attempts are particularly high in the trans population[5] and should be specifically inquired about; inquire regarding symptoms of hypomania, mania, or psychotic symptoms in patients on testosterone who have underlying psychiatric disorders that include such symptoms; inquire re: current level of gender dysphoria and body image, (re-)assess patient interest in transition related surgeries if not undergone

Chest – inquire regarding skin changes, lumps/bumps and nipple discharge regardless of surgical status, if patient has undergone chest reconstruction, consider asking about scarring and patient satisfaction with surgical outcome (in some cases, revisions can be considered to optimize cosmetic appearance); if patient has not undergone chest reconstruction consider asking about binding (the practice of compressing chest tissue to create a flatter appearance) and any associated MSK, dermatologic, or respiratory symptoms; encourage the use of a product designed specifically for the purpose of chest binding (several commercial brands are available, for a comparison see '*Chest Binding 101*')[6] and discourage the use of other products such as tensors or duct tape; binding frequency (#days/week), and to a lesser extent binding intensity (#hours/day) have been found to be positively correlated with negative effects, suggesting that 'days off' and/or shortened duration of binding may minimize complications);[7] most manufactures recommend maximum use of 8 hours per day. Some private insurance companies will cover the cost of a commercial binder as a medical device with a prescription.

GU/PV Bleeding – inquire about symptoms of vaginal atrophy (if on testosterone), vaginal bleeding, discharge, and pelvic pain. Problematic symptoms due to vaginal atrophy often respond to topical estrogen; pelvic pain may be associated with cyclic testosterone dosing – changing the frequency/route of testosterone and/or the use of NSAIDs can be helpful (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part III - Pelvic Pain*)

NB: any unexplained vaginal bleeding once full menstrual cessation has been achieved on testosterone warrants a full work-up for endometrial hyperplasia/malignancy

Sexual Function – inquire regarding libido/hypersexual behaviour, dyspareunia (as indicated by surgical status and sexual activity), and post-orgasmic uterine cramping

Derm – inquire re: acne and androgenic alopecia, both of which may be managed as in cis patients

EDUCATION/COUNSELLING

Adequate Calcium Intake – all transmasculine patients on testosterone should ensure a minimum intake of 1200 mg of Calcium daily (diet + supplements)

Adequate Vitamin D – all transmasculine patients on testosterone should take 1000 IU of vitamin D daily

Hormone Adherence – missed doses of testosterone may impact bone health if post-oophorectomy, while extra doses may lead to a host of problems associated with supratherapeutic testosterone levels

Regular, moderate physical activity – weight-bearing exercise helps in osteoporosis prevention; to avoid tendon rupture in transmasculine individuals on testosterone weight loads used in strength training should be increased gradually with an emphasis on repetitions and stretching

Safe sex practices/STI counselling – transmasculine patients may be at high risk of STIs depending on behavioural factors; inquire re: sexual practices and risks including sex work; safer sex counselling, frequent screening (i.e. every 3 months) and an assessment of indications for HIV PrEP[8] are indicated for those at high risk. For patient-centred handout materials, see *PRIMED*[2]*: A Sex Guide for Trans Men into Men*[9]

Potential for pregnancy/need for birth control – transmasculine patients on testosterone (who have not undergone hysterectomy) may become pregnant even if menstrual suppression has been achieved and should be counselled in this regard; given that testosterone is a teratogen, reliable birth control should be instituted where pregnancy is a risk based on sexual activity; signs and symptoms of pregnancy can be reviewed, as well as options and resources should unplanned pregnancy occur

Need for folic acid – transmasculine patients not on testosterone and in whom pregnancy is possible based on sexual activity, as well as for those who are hoping to achieve pregnancy, folic acid recommendations are the same as for cis women

Overweight/Obese – screen for mental health contributors – persistent gender dysphoria may be associated with a desire to maintain a larger body habitus in order to hide indicators of sex assigned at birth, which may have negative health impacts; strategizing around other ways to address persistent gender dysphoria may be helpful; barriers to physical activity can also include an avoidance of gyms/locker rooms which the provider may help strategize around; screening for eating disorders is also warranted (see below)

Underweight – eating disorders are more common in LGBT2SQ populations, particularly amongst youth; screening is warranted in those presenting with BMI<18 or other related signs/symptoms

Smoking – tobacco use can worsen polycythemia (Hb/Hct above male range) which can be associated with testosterone administration, and increases the risk of CVD and thromboembolic events

Alcohol and other substances – substance use is more prevalent in members of the LGBT2SQ community; inquire re: problematic use of substances including testosterone without a prescription and anabolic steroids; if referral to substance abuse program is indicated, consider an LGBT2SQ-specific or LGBT2SQ-positive program such as *Rainbow Services at CAMH*. Offer safer smoking and injection kits when indicated for harm reduction. A naloxone kit and instructions on use should be offered to all patients who are at risk of opioid overdose, as well as friends and family of those at risk[10]

Advanced care planning – A discussion regarding advanced care planning is recommended at least once for Canadians ≥65.[11] Trans and gender diverse patients may have particular needs in ensuring that their gender identity and expression are respected and a respectful decision-maker is chosen (*See Creating End of Life Documents for Trans Individuals: An Advocate's Guide*)[12]

Injection safety – for patients who self-inject testosterone: confirm dose, review aseptic injection technique, inquire re: rotating injection sites, injection site reactions, and pre-injection anxiety; consider conversation re: SC vs. IM injection vs. transdermal route options, ensure safe sharps disposal

Bathroom safety – finding a bathroom that feels comfortable and safe can frequently be a source of stress for trans individuals. Resources such as *Refuge Restrooms*[13] can assist trans people in locating gender neutral bathrooms

PHYSICAL EXAMINATION

Chest – testosterone therapy is not thought to increase the risk of breast cancer; for transmasculine individuals who have not undergone chest reconstruction, clinical chest (i.e. breast) exam

is of questionable utility but can be considered according to a provider's common practice with cis women; transmasculine individuals who have undergone chest reconstruction are at low risk and chest and axillary lymph node exam are of questionable utility but may be considered to assess for abnormalities in the remaining breast tissue; if an abnormality is noted in this case, ultrasound +/- MRI is indicated as mammography is technically difficult or may be impossible

Pelvic/Pap – follow cervical cancer screening guidelines as for cis women if the cervix is present; there is no evidence to support the performance of a bimanual exam but if uterus and/or ovaries are present this can be considered according to the clinician's routine practice with cis women, and may be helpful in determining the appropriate width/length of speculum to use; several strategies may be employed to minimize the discomfort/trauma associated with speculum examination for some transmasculine individuals (*see Tips for Providing Paps to Trans men*).[14] Barring contraindications, topical 2% lidocaine jelly may be applied vaginally 5-10 minutes prior to the procedure in those who find speculum examination painful due to atrophic changes. The pre-procedural administration of low-dose lorazepam or the use of vaginal estrogens for 1 week prior to the exam may also be helpful

Ano-rectum – for those who engage in receptive anal sex, visual examination of the perianal region for any evidence of anal warts or other anorectal problems such as hemorrhoids should be considered; particularly those who are HIV+. Additionally consider DRE for detection of internal lesions. HIV+ patients with physical findings consistent with warts or other HPV-related changes should also be referred for HRA

Derm – examine for acne and androgenic alopecia

LABS/INVESTIGATIONS

Mammography – for transmasculine patients who have not undergone chest reconstruction, follow guidelines as for cis women; mammography is not required following chest reconstruction; for all transmasculine patients, if a strong family history of breast cancer is present, follow the same guidelines as for cis women regarding indications for referral to a high risk screening program/genetic assessment

GC/CT/Syphilis/HIV/HBV/HCV screen – consider STI detection from the following sites as indicated: throat, urethra, vagina, ano-rectum, and serum. NB: Self-collected frontal (vaginal) swabs may be more sensitive for diagnosing GC and CT than provider-collected swabs and first-catch urine[15] and may help minimize discomfort for trans patients

Cervical cytology – see Pelvic/Pap above, if patient is on testosterone, ensure to note this on the cytology requisition in order to minimize histological misinterpretation; inadequate samples are more common in patients on testosterone and repeat may be required - the use of both brush and broom may increase yield in patients with atrophic changes[16]

Yearly trans bloodwork – yearly investigations listed are for those currently on testosterone; bloodwork should be tailored to the patient's hormone regimen, risk factors and pre-existing conditions; screening for DMII and dyslipidemia should be performed at baseline and 1 year following hormone therapy initiation; and otherwise according to routine guidelines for cis patients. Framingham calculation will be less reliable with exogenous hormone use - depending on the age of hormone initiation and duration of hormone exposure providers may choose to use the risk calculator for sex assigned at birth, affirmed gender, or an average of both.[17]

> **Note**: For patients on testosterone male reference ranges should be used for Hb/Hct, however the lower limit of the female range can be used if menstruating

BMD – there is no evidence to suggest that testosterone therapy negatively impacts BMD; in accordance with national recommendations, perform bone mineral density testing in all transmasculine patients over age 65

BMD should be considered earlier in those at high risk, such as those who, for a significant period of time (i.e. >2 yrs):

- have been on low-dose or no hormones and are agonadal
- have been on a GnRH analogue without exogenous estrogen

BMD testing may additionally be considered in agonadal transmasculine patients with elevated LH.[18] (*See 'Part III Osteoporosis and BMD Screening'*)
Note: frequency of BMD screening will depend on the results of the initial scan

Anal Pap screening – for those who have a history of receptive anal sex, consider anal pap every 2-3 years or yearly in those who are HIV+ (if local HRA for the follow up of abnormal results is available). See the Canadian Cancer Society's *Colon cancer screening guidelines for gay and bisexual men* for more information

IMMUNIZATIONS

Hepatitis A/Hepatitis B – transmasculine patients may be at higher risk of Hep A/B depending on behavioural risks, trans MSM qualify for publicly funded vaccination

HPV – consider HPV vaccination in transmasculine patients up to age 45; publicly covered ≤26 yrs if sexually active with MSM

CFPC – College of Family Physicians of Canada,
STI – sexually transmitted infection,
RHO – Rainbow Health Ontario,
CPAP – continuous positive airway pressure,
MSK – musculoskeletal,
GU – genitourinary,
PV – per vagina,
NSAIDs – non-steroidal anti-inflammatories,
IU – international units,
Hb - Hemoglobin,
Hct - Hematocrit,
LGBT2SQ – lesbian, gay, bisexual, trans, queer, and two-spirit,
BMI – body mass index,
CVD – cardiovascular disease,
CAMH – Centre for Addiction and Mental Health ,
MRI – magnetic resonance imaging,
DRE - digital rectal exam, HRA - high resolution anoscopy,
HIV – human immunodeficiency virus,
GC – gonococcus,
CT – chlamydia trachomatis,
HBV – Hepatitis B virus, HCV – Hepatitis C virus,
DMII - diabetes mellitus type II,
Hb - hemoglobin, Hct - hematocrit,
BMD – bone mineral density,
LH – luteinizing hormone,
MSM – men who have sex with men,
HPV – human papillomavirus,
MSM - men who have sex with men

1. Ridley J, Ischayek A, Dubey V, Iglar K. Adult health checkup: Update on the Preventive Care Checklist Form©. Can Fam Physician Med Fam Can. 2016; 62(4):307–13.22. RHO Fact Sheet: Reproductive options for trans people [Internet]. Toronto: Rainbow Health Ontario; 2012 p. 9. Available from: https://www.rainbowhealthontario.ca/wp-content/uploads/woocommerce_uploads/2012/09/RHO_FactSheet_REPRODUCTIVEOPTIONSFORTRANSPEOPLE_E.pdf
2. LGBTQ Parenting Network [Internet]. Toronto: Sherbourne Health; [updated 2018]. Fertility preservation for trans people who produce sperm; [2018] [cited 2019 Feb 8]. Available from:
3. The Canadian Centre on Substance Use and Addiction [Internet]. Ottawa: The Canadian Centre on Substance Use and Addiction; [updated 2018]. Canada's low risk alcohol drinking guidelines; [2012] [cited 2019 Feb 7]. Available from: http://www.ccsa.ca/Resource%20Library/2012-Canada-Low-Risk-Alcohol-Drinking-Guidelines-Brochure-en.pdf
4. Matsumoto AM, Sandblom RE, Schoene RB, Lee KA, Giblin EC, Pierson DJ, et al. Testosterone replacement in hypogonadal men: effects on obstructive sleep apnoea, respiratory drives, and sleep. Clin Endocrinol (Oxf). 1985; 22(6):713–21..
5. Bauer G, Pyne J, Francino M, Hammond R. La Suicidabilite parmi les personnes trans en Ontario : Implications en travail social et en justice sociale. Serv Soc. 2013; 59(1):35–62.
6. TransGuys.com; [updated 2019]. Chest Binding 101 - FTM - Updated for 2017; [2010] [cited 2019 Feb 7]. Available from: https://transguys.com/features/chest-binding
7. Peitzmeier S, Gardner I, Weinand J, Corbet A, Acevedo K. Health impact of chest binding among transgender adults: a community-engaged, cross-sectional study. Culture, Health & Sexuality 2017;19(1):64-75
8. Tan DHS, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, et al. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ. 2017; 189(47):E1448–58.
9. PRIMED2: A sex guide for trans men into men [Internet]. Toronto: CATIE; 2015. Available from: http://librarypdf.catie.ca/PDF/ATI-20000s/24654.pdf
10. Ontario Ministry of Health and Long-Term Care [Internet]. Toronto: Ontario Ministry of Health and Long-Term Care [updated 2018]. Naloxone - Drugs and Devices; [date unknown] [cited 2019 Feb 8]. Available from: http://www.health.gov.on.ca/en/pro/programs/drugs/naloxone/

11. Speak Up [Internet]. Ottawa: Canadian Hospice Palliative Care Association; [updated 2019] [cited 2019 Feb 7]. Available from: http://www.advancecareplanning.ca/
12. National Resource Center on LGBT Aging [Internet]. New York: National Resource Center on LGBT Aging; [updated 2019]. Creating end-of-life documents for trans individuals: An advocate's guide; [October 2014] [cited 2019 Feb 7]. Available from: https://www.lgbtagingcenter.org/resources/resource.cfm?r=694
13. REFUGE Restrooms [Internet]. REFUGE Restrooms; [updated 2019] [cited 2019 Feb 7]. Available from: https://www.refugerestrooms.org/about
14. Potter, M. Rainbow Health Ontario [Internet] Toronto: Rainbow Health Ontario; [updated 2018]. Tips for providing paps to trans men; [updated 2015] [cited 2019 Feb 4]. Available from: https://www.rainbowhealthontario.ca/resources/tips-for-providing-paps-to-trans-men
15. Korownyk C, Kraut RY, Kolber MR. Vaginal self-swabs for chlamydia and gonorrhea. Can Fam Physician. 2018; 64(6):448.
16. Davis-Devine S, Day SJ, Anderson A, French A, Madison-Henness D, Mohar N, et al. Collection of the BD SurePath Pap Test with a broom device plus endocervical brush improves disease detection when compared to the broom device alone or the spatula plus endocervical brush combination. CytoJournal. 2008; 6:4.
17. Deutsch M. Centre of Excellence for Transgender Health [Internet]. San Francisco: University of California; [updated 2019]. Guidelines for the primary and gender-affirming care of transgender and gender nonbinary people; 2016 [cited 2019 Jan 31]. Available from http://transhealth.ucsf.edu/trans?page=guidelines-home
18. van Kesteren P, Lips P, Gooren LJ, Asscheman H, Megens J. Long-term follow-up of bone mineral density and bone metabolism in transsexuals treated with cross-sex hormones. Clin Endocrinol (Oxf). 1998; 48(3):347–54.

APPENDIX H:
glossary of terms

The following are definitions intended as useful references for this resource and for your work with trans and non- binary patients. As language is constantly evolving and seldom universally agreed upon, it is key to mirror back language people use to express their lived experience and understanding of self.

ASSUMED CIS: Previously known as **passing.** Passing is being identified as belonging to a group with more privilege and power, for instance someone who is non-disabled, white and cisgender. A trans person is "assumed cis" when they move through the world on an everyday basis with few/ no persons being aware they are trans. When one is assumed to be **cis**, the social, economic, safety and other risks associated with **cis sexist** discrimination and **transphobic** violence are decreased, thus conferring **conditional cis privilege.** Given such benefits, getting to a point where one is "assumed cis" may be a goal of one's transition, but this is not always the case. "Passing" should not be used as it implies that one is being mistaken for something they are not; it also has a particular historical meaning related to race and skin colour.

BINDING: For **transmasculine individuals**, the process of flattening one's **chest** to disguise one's "breasts." This can be done utilizing a few different things from undershirts intended for this end to lower back supports. Using an ace bandage is discouraged as it may constrict breathing. Some **transmasculine** individuals and **non-binary** people don't bind at all, some layer clothing to help hide their chests, some bind only on certain occasions and some bind all of the time.

BOTTOM SURGERY: A type of **transition-related surgery (TRS).** These are a variety of genital modification procedures, typically vaginoplasty for **transfeminine** individuals and metaoidioplasty or phalloplasty for **transmasculine individuals.**

BUTCH: A masculine form of **gender expression.** A masculine-identified person of any gender identity.

CHEST: The most common term used by **transmasculine individuals** to describe this part of their anatomy, regardless of whether they have had **top surgery** It is always important to use gender-affirming language (or at least gender-neutral language) with body parts that have a strong gender attachment.

CIS: Having a non-trans gender identity. You may also sometimes see "cissexual" or "cisgender." Thus, non-**transmasculine** individuals are "cis men" and non-**transfeminine** individuals are "cis women" It is preferable (and more accurate) to use "cis" than to use terms such as "bio", "genetic" or "real." It is also preferable to use "cis" rather than only using "woman" or "man" to describe non-trans persons. If cis is not used as a descriptor for non-trans persons, then such persons may be presumed to be the more "normal" or "valid" instantiation of that particular gender, thus contributing to **cissexism.**

CIS PRIVILEGE: The privileges afforded to those who are **cis.** In health care settings, some common experiences that reflect cis privilege include: as a patient, not worrying that providers will see their gender as less "real" or "valid" if they read through their chart and learn about their medical history; not being concerned about having tests rejected because of the "wrong" sex marker being on one's health card, and; not having to worry about questions concerning their gender distracting from care they may need that has nothing to do with gender.

CISNORMATIVITY: The assumption that all people are **cis**, i.e. that those assigned male at birth always grow up to be men and those assigned female at birth always grow up to be women. Cisnormative assumptions are so prevalent that they are difficult at first to even recognize. For example, in health care

settings cisnormativity associates "women's health" with things such as Pap tests and contraception when, in fact, these things are relevant to many men, specifically **transmasculine** individuals.

CISSEXISM: The thoughts and actions resulting from the belief that **cis** bodies or identities are more "real" or "valid" than **trans** ones. This is distinct from **transphobia** (which denotes hatred and fear towards trans persons).

COMING OUT: Usually in reference to one's **sexual orientation** or **gender identity.** It involves disclosing something about one's identity that would not otherwise be known. One only has to "come out" when a heteronormative or **cisnormative** assumption (i.e. that one is "heterosexual" or "**cissexual**") has been made about them.

CONDITIONAL CIS PRIVILEGE: The privilege experienced by **trans** persons who are often **assumed cis** in their everyday life. Such privilege is conditional on their trans identity or history not being known or revealed. Formerly referred to as "**passing privilege.**"

CROSS-DRESSER: Someone who wears clothes of another gender/sex but whose **gender identity** does not differ from the one assigned to them at birth. Most commonly, this term has been used to describe men wearing women's clothes on a part-time basis, however some may cross-dress more frequently or all of the time. Cross-dressing may not have a fetishistic or sexual association. Some persons who practice cross-dressing may one day decide to undergo **transition.**

DIFFERENCES OF SEX DEVELOPMENT (DSD): A term used to describe the various conditions experienced by those who are intersex. Preferred by some to using "**intersex**" (regional variations exist). Also preferred over the more pathologizing term "disorders of sex development." Persons with DSD may be **cis** or **trans** depending on how their gender identity relates to the one assigned to them at birth. "Intersex" relates to someone's biology—it does not tell us anything about a person's sexual orientation or gender identity.

DRAG: The performance of one or multiple genders theatrically. "Drag queens" are men performing as women; "drag kings" are women performing as men. Some persons who practice drag may one day decide to undergo gender transition.

"E": Slang for Estrogen.

FEMME: A form of **gender expression.** A feminine identified person of any **gender identity.**

FTM: An older term to describe **transmasculine individuals**. It has fallen out of favour given its implied binary limitations and the fact that it conflates sex and **gender identity**.

GENDER AFFIRMING SURGERY (GAS): See **transition-related surgeries (TRS).**

GENDER DYSPHORIA: May refer specifically to the DSM-5 diagnosis and/or to the experience of distress associated with having one's current gender presentation misaligned with their internal **gender identity.** Through a **medical transition, legal transition** and/or **social transition**, gender dysphoria can usually be alleviated.

GENDER EXPRESSION: The social expression of gender. Often described as being on a spectrum between **masculine** and **feminine.** Often related to, but sometimes distinct from, **gender identity.** For example, some **trans** or **cis** women may identity as **butch** or have a masculine presentation, and some cis or **transmasculine** individuals may be feminine or identity as **femme.**

GENDER IDENTITY: A person's internal self-awareness of being a boy/man, girl/woman, something in between these, or something other altogether.

GENDER INCONGRUENCE: May refer specifically to the WHO ICD-11 diagnosis and/or to the experience of having one's internal **gender identity** misaligned

with their sex assigned at birth. Differs from the diagnosis and concept of **gender dysphoria** in that there is no requirement for or implied experience of significant distress or impairment.

GENDER NON-CONFORMITY: When someone expresses themselves in ways that are perceived to deviate from what is socially associated with and expected from the sex they were assigned at birth.

GENDER ROLE EXPERIENCE (GRE): Previously known as the **Real Life Test** or **Real Life Experience.** According to World Professional Association of Transgender Health's Standards of Care Version 7 it is the period of time during which a trans person is required to live full time in the role of the gender they identify with prior to accessing **bottom surgery** (i.e. genital (re)constructive procedures). It is not required, and potentially dangerous, for persons to undergo a GRE prior to taking **hormone treatment** or having **top surgery.**

GENDERQUEER: A person whose **gender identity** does not align with binary gender categories such as "man/woman" or "boy/girl." Genderqueer persons often identify as a fluid gender that does not fit the male/female gender binary.

HORMONE TREATMENT: The medical management of **trans** persons with sex hormones. For **transmasculine individuals**, this is typically testosterone; for **transfeminine** individuals this may include estrogen and/or anti-androgens.

INTERSEX CONDITIONS: A subset of the "**differences of sex development**" or "disorders of sex development," in which chromosomal sex is inconsistent with genital sex, or in which the genital or gonadal sex is not classifiable as either male or female. Some individuals who report their identity as "intersex" do not have a verifiable intersex condition."[1]

LEGAL TRANSITION: The various legal identity and document changes to affirm and validate one's gender identity. This includes legal names and changes in documents and pieces of identification, such as health card, birth certificate, passport, driver's license, school transcripts, etc.

MEDICAL TRANSITION: The process of seeking and receiving various medical interventions including, but not limited to hormone therapy (including anti-androgens for **transfeminine** individuals), **transition-related surgeries** and other related surgeries (including hair transplants), and hair removal (e.g. electrolysis).

MTF: An older term to describe **transfeminine** individuals. It has fallen out of favour given its implied binary limitations and the fact that it conflates sex and gender identity.

NON-BINARY: Umbrella term for anyone who does not identify with static, binary gender identities. Includes persons who may identify as having a gender on the spectrum between girl/woman and boy/man (e.g. genderqueer), as being multiple genders, as having a constantly shifting gender, or as not having a gender altogether.

NON-DISCLOSURE: A term that applies to **trans** persons who are **assumed cis** and who choose to not share that they are trans with others. May be specific to some situations (e.g. work, sex) or applicable to all situations. Also sometimes referred to as being "stealth." Often protective as it avoids having to face **cissexist** discrimination or **transphobic** violence that can occur if others know one is trans.

NON-OP: Trans individuals not seeking any **transition-related surgery(ies).**

PACKING: The process of creating a bulge in one's crotch that leads others to believe that one may possess a penis.

PASSING: See **assumed cis**.

PASSING PRIVILEGE: See **conditional cis privilege.**

PRE-OP: Trans individuals who are seeking, but who have not undergone, one or more **transition-related surgery(ies).**

POST-OP: Trans individuals who have undergone one or more **transition-related surgery(ies).**

QUEER: A term commonly used to describe persons with non-heterosexual **sexual orientations.** More common in younger generations than terms such as "gay" or "lesbian" because of the binary nature of these older terms. Due to the historical use of queer as a derogatory term, some (particularly older adults) may continue to experience this word as offensive.

REAL LIFE TEST (RLT) OR REAL LIFE EXPERIENCE: See **Gender Role Experience (GRE)**.

SEX: Describes one's phenotype, often determined by genital configuration. Referred to in terms of "male" or "female." Due to **cisnormativity**, often conflated with **gender identity.**

SEXUAL ORIENTATION: Refers to the group(s) of persons that someone may desire intimate emotional and/or sexual relationships with. Examples of sexual orientations include, straight, queer, lesbian, gay, bisexual, pansexual, and asexual Everyone, **cis** or **trans**, has a sexual orientation (e.g. trans persons can be bisexual, queer, or straight).

SEX REASSIGNMENT SURGERY: See **Transition-Related Surgeries (TRS).**

SHE-MALE: A derogatory term to describe some pre-operative **transfeminine** individuals who have not undergone **transition-related surgery (TRS).**

SOCIAL TRANSITION: The various non-medical components of one's transition that help one affirm and realize one's **gender identity.** For example, this may include: changing one's legal identification with changes to sex markers and name; changing the clothes one wears, and changing one's voice, posture, and gait .

"T": Slang for Testosterone.

TOP SURGERY: For **transmasculine individuals** involves the construction of a **chest.** For **transfeminine** individuals, it may involve breast augmentation if desired results have not been achieved with **hormone treatment** (or if they cannot, or choose to not to, take estrogen)

TRANS: Umbrella term for people who are not **cis**, includes persons who are (or identify as) **non-binary** as well as **transmasculine individuals** and **transfeminine** individuals**.**

TRANSFEMININE: An umbrella term to describe all persons assigned male at birth who **transition** to live as girls/women (i.e. trans women) or somewhere on the feminine spectrum.

TRANSITION: The sum total of changes involved in moving from living as one gender identity to another. Typically a stage in a **trans** person's life. Includes **medical transition, legal transition** and **social transition.**

TRANSITION-RELATED SURGERIES (TRS): Previously known and sometimes still referred to as **sex reassignment surgery or gender reassignment surgery.** This refers to any number of surgeries that a **trans** person may undertake in order to better align their **sex** with their **gender identity.** Often assists trans persons in acquiring greater **conditional cis privilege** and in being **assumed cis.** May include both **bottom surgery(ies)** and **top surgery.** Important for some trans persons, but others may not be interested in TRS as part of their transition.

TRANSMASCULINE: An umbrella term to describe all persons assigned female at birth who **transition** to live as boys/men (i.e. trans men) or somewhere on the masculine spectrum.

TRANSPHOBIA: The fear and hatred of **trans** persons. Its expression usually involves some form of verbal, physical, and/or sexual violence. Also describes the ongoing microaggressions

experienced by those who are assumed to be trans by others in their everyday lives.

TRANSSEXUAL: Describes persons who undergo **medical transition, legal transition** and **social transition** to align the gender they live and present as with their internal **gender identity.**

TUCKING: Tucking refers to the process of concealing the penis and scrotum so that they are not conspicuous through clothing. One common method involves 'tucking' the genitalia back between the legs and binding along the perineum and/or between the buttocks.

TWO-SPIRIT: An umbrella term describing the diversity of gender expressions and sexual orientations present in traditional belief systems held by North American First Nations persons.

1. Byne W, Karasic DH, Coleman E, Eyler AE, Kidd JD, Meyer-Bahlburg HFL, et al. Gender dysphoria in adults: An overview and primer for psychiatrists. Transgender Health. 2018; 3(1):57–70.

APPENDIX I:
trans health resources for primary care providers

GENERAL

- World Professional Association for Transgender Health (WPATH), www.wpath.org
  - Download a free copy of the most recent version of the Standards of Care
  - Biennial conferences on Transgender Health
  - Become a member to sign up for listserv discussions and receive the quarterly *International Journal of Transgenderism*
- Canadian Professional Association for Transgender Health (CPATH), www.cpath.ca
  - Membership, Biennial conferences
- Rainbow Health Ontario's Trans Health Knowledge Base, http://transfaqs.rainbowhealthontario.ca/
- Project ECHO: University of Toronto and the Centre for Addiction and Mental Health
  - ECHO Ontario Trans and Gender Diverse Healthcare – Supporting clients with medical and surgical transition, https://camh.echoontario.ca/trans-health/
- University of Toronto, Department of Obstetrics and Gynecology, *'The Hub' online study guide, Transgender Health,* http://thehub.utoronto.ca/obgyn/transgender-health/
- UCSF Centre of Excellence for Transgender Health, www.transhealth.ucsf.edu
  - *Guidelines for the Primary and Gender-Affirming Care of Transgender and Gender Nonbinary People: 2nd Edition*, *http://transhealth.ucsf.edu/trans?page=guidelines-home*
  - Learning Centre (online learning, guides, reports, and fact sheets)
- Trans Care BC, http://www.phsa.ca/transcarebc
  - Resources on Trans Basics, Care & Support, Hormones, Surgery, and Children and Youth
  - *Gender-affirming Care for Trans, Two-Spirit, and Gender Diverse Patients in BC: A Primary Care Toolkit*, http://www.phsa.ca/transgender/Documents/Primary%20Care%20Toolkit.pdf

HORMONE THERAPY

- Rainbow Health Ontario Training Session: Trans and Gender Diverse Primary Care, https://www.rainbowhealthontario.ca/training/#available
- Endocrine Society Gender Dysphoria/Gender Incongruence Guideline Resources
  - *Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline,* https://academic.oup.com/jcem/article/102/11/3869/4157558
  - Clinical education resources, point of care tools and patient resources.

TRANSITION-RELATED SURGERY

- Rainbow Health Ontario Training Session: Transition-Related Surgeries - planning, referral, and care, https://www.rainbowhealthontario.ca/training/#available
- Sherbourne Health/Rainbow Health Ontario *TRS Summary Sheets*, https://www.rainbowhealthontario.ca/resources/transition-related-surgery-surgical- summary-sheets/
- Women's College Hospital TRS Program, http://www.womenscollegehospital.ca/programs-and-services/Transition-Related- Surgeries/
- Gender Reassignment Surgery (GRS) Montreal, https://www.grsmontreal.com/en/home.html
- Sherbourne Health Centre Acute Respite Care (ARC) Post-Operative TRS Program, http://sherbourne.on.ca/acute-respite-care/
- Trans Care BC - Gender Affirming Surgeries, http://www.phsa.ca/transcarebc/surgery
- Client resources:
  - *TRS FAQ*, https://www.rainbowhealthontario.ca/resources/transition-related-surgery-trs-frequently-asked-questions/
  - Sherbourne Health Centre Surgical Support Groups for Community Members, http://sherbourne.on.ca/get-involved/community-groups/

CONSULTATION AND MENTORSHIP

- Rainbow Health Ontario - Trans Health Mentorship call (https://www.rainbowhealthontario.ca/trans-health/#mentorship)
- E-consult services:
  - Ontario Telemedicine Network (OTN) https://otnhub.ca
  - Champlain LHIN eConsult Services https://www.champlainbaseeconsult.com
- TransLine: Transgender Medical Consultation Service, http://project-health.org/transline/

APPENDIX J:
reference ranges (Lifelabs)

Accurate as of Aug 7, 2019

Note: Reference ranges may vary between laboratories.
It is highly recommended to compare results to
reference ranges from the specific laboratory used.

17-Beta-Estradiol

	Age (yrs)		Serum level (pmol/L)
Female	14-18		<937
	>18	follicular phase	77-921
		mid-cycle	139-2382
		luteal	77-1145
		post-menopause	<103
Male	15-18		<142
	>18		<162

Luteinizing Hormone

	Age (yrs)		Serum level (IU/L)
Female	17-18		<8.5
	>18	follicular phase	2.0-12.0
		mid-cyclie	8.0-90.0
		luteal	1.0-14.0
		post-menopausal	5.0-62.0
Male	17-18		0.9-7.1
	>18		1.0-7.0

Total Testosterone

	Age (yrs)	Serum level (nmol/L)
Female	13-50	<1.8
	>50	<1.5
Male		8.4-28.8

Free Testosterone

	Age (yrs)	Serum level (pmol/L)
Female	≤10-29	<56
	≥30	<30
Male	≤10-49	196-636
	≥50	179-475

Note: The ordering of free testosterone is not routinely recommended (see *Guidelines for gender-affirming primary care with trans and non-binary patients, Part II: Monitoring and dose adjustments*). The reference ranges for free testosterone listed here are calculated via the Vermulean equation according to the current practice at Lifelabs.

APPENDIX K:
Checklist for Patient Review – Initiation of Feminizing Hormone Therapy

The decision to start hormone therapy is an individual one, based on the balance of risks and benefits for each person. In order to provide informed consent, it is important that you understand the expected feminizing changes as well the possible risks and side effects.

The use of feminizing hormone therapy (consisting of an anti-androgen and estrogen) is based on many years of experience treating trans people. A growing body of research is providing us with more information, however there are aspects of the medical effects and safety of feminizing hormone therapy that may not be fully understood.

It is possible that hormone therapy may not result in all of the changes that are hoped for.

Expected changes that can be permanent, even if you stop hormone therapy, include:

- Breast growth and development, the amount of breast tissue is variable and depends on a number of individual factors, usually breasts will become an A cup or smaller
- Genital changes - the testicles and prostate will get smaller and softer
- Infertility – the testicles will decrease (or even stop) making sperm (this may recover to a variable degree if hormones are stopped)

Expected changes that are not permanent and are likely to reverse if hormones are stopped include:

- Loss of muscle mass and strength
- Weight gain and/or redistribution of fat to the hips, buttocks, and thighs (some degree may be reversible)
- Softening of skin/decreased oiliness/change in body odour and amount of perspiration
- Decreased sex drive, decreased strength of and/or ability to get erections, decreased volume and thinning of ejaculate
- Thinning/slowing of body and facial hair growth
- Scalp hair loss may slow or stop, but hair does not generally grow back

Potential adverse effects of feminizing hormone treatment may include, but are not limited to:

- Increased risk of:
  - Blood clots (deep vein thrombosis, pulmonary embolism, and stroke)
  - Increase in liver enzymes (often temporary)
  - Decrease in, or loss of, fertility (the ability to make healthy sperm is reduced, and may be permanently affected by feminizing hormones, however you still need to use birth control if you are having penetrative sex with a partner who could become pregnant)
  - Increased triglycerides, a type of fat in the blood
  - Mood swings or depression (higher risk with cyproterone or progesterone)
  - Elevated levels of prolactin (a pituitary hormone), particularly in combination with cyproterone
- Possible increased risk of:
  - Heart disease and stroke
  - High blood pressure
  - Diabetes
  - Changes in cholesterol, which may increase risk for heart attack or stroke
  - Worsening of liver damage from other causes
  - Gallbladder disease, gallstones, and need for gallbladder removal
  - Pituitary tumours (tumor of small gland in the brain which makes prolactin)
  - Worsening of headaches or migraines

    - Breast tumours/cancer (risk is lower than in cis women, but may be higher than in cis men)
- Other common side effects include:
    - Decreased sex drive and sexual functioning
    - Fatigue

Specifically with spironolactone, adverse effects may include:

- Impaired kidney function
- Increased levels of potassium in the blood (which may cause abnormal heart rhythms)
- Low blood pressure/dizziness
- Frequent urination (especially in the beginning)
- Gastro-intestinal upset (nausea, vomiting, diarrhea)
- Rash

Specifically with cyproterone, adverse effects may include:

- Liver inflammation or acute liver failure (rare)
- Changes in blood components (low red blood cells, high platelets, or a lowering of all cell types)

Some adverse effects from hormone therapy are irreversible and can cause death.

The risks for some adverse effects may be significantly increased by:

- Pre-existing medical conditions
- Pre-existing mental health conditions
- Cigarette smoking
- Alcohol use
- Taking medication in doses that are higher than recommended

APPENDIX L:

Checklist for Patient Review – Initiation of Progestin Therapy

Evidence suggests that the addition of a progestin to feminizing hormone regimens may increase some of the risks associated with treatment, **over and above the risks of an anti-androgen and estrogen alone**. Since there has been no demonstrated benefit to adding progestins to feminizing hormone therapy, it is not recommended in Sherbourne Health's Guidelines.

Some patients may choose to trial progestin therapy in the hopes of attaining one or more of the following anecdotal (unproven) benefits:

- Increase in libido
- Increase in breast growth
- Increase in feminizing effects through further suppression of testosterone when not adequately suppressed
- Out of desire to more closely mimic the hormones that cis women have

Potential adverse effects of adding progestin to a feminizing hormone treatment may include, but are not limited to an increased risk of:

- Blood clots (deep vein thrombosis, pulmonary embolism)
- Heart disease and stroke
- Invasive breast cancers
- Psychiatric symptoms (depression and suicidal feelings)
- Changes in cholesterol and blood pressure which may increase the risk for heart disease and stroke
- Liver inflammation
- Abdominal pain, nausea, vomiting, diarrhea or constipation
- Migraines or other headaches
- Dizziness and fatigue
- Acne
- Body hair growth
- Weight gain and bloating/fluid retention
- Joint and muscle pain

Some adverse effects from hormone therapy are irreversible and can cause death. The risks for some adverse effects may be significantly increased by:

- Pre-existing medical conditions
- Pre-existing mental health conditions
- Cigarette smoking
- Alcohol use
- Taking hormones in doses that are higher than recommended

APPENDIX M:
Checklist for Patient Review – Initiation of Masculinizing Hormone Therapy

The decision to start hormone therapy is an individual one, based on the balance of risks and benefits for each person. In order to provide informed consent, it is important that you understand the expected masculinizing changes as well the possible risks and side effects.

The use of masculinizing hormone therapy is based on many years of experience treating trans people. A growing body of research is providing us with more information, however there are aspects of the medical effects and safety of masculinizing hormone therapy that may not be fully understood.

It is possible that testosterone therapy may not result in all of the changes that are hoped for.

Expected changes that can be permanent, even if you decide to stop testosterone therapy, include:

- Deepening of the pitch of your voice
- Growth of facial hair
- Increased growth, thickening, and darkening of body hair
- Possible scalp hair loss in androgenic pattern (at the temples and crown), with possible complete loss of scalp hair (baldness)
- Increase in the size of the clitoris/phallus

Expected changes that are not permanent and are likely to reverse if testosterone is stopped include:

- Menstrual periods will stop, usually within a few months of starting testosterone
- Increased muscle mass and strength
- An increase in oiliness of the skin (and sometimes acne), change in body odour
- Increased sex drive
- Weight gain and/or redistribution of fat from the hips/thighs/buttocks to the abdomen/mid-section (some degree may be irreversible)

Potential adverse effects of masculinizing hormone treatment may include, but are not limited to:

- Increased risk of:
    - Permanent reduction or loss of fertility
        - reduction of fertility is variable, and many transmasculine people have been able to conceive after stopping testosterone
        - testosterone is not reliable birth control even if your periods stop—birth control should always be used if having receptive sex with a partner who produces sperm
    - If pregnancy does occur while taking testosterone, it may cause birth defects or pregnancy loss
    - Increased number of red blood cells, which may cause headache, dizziness, confusion, visual disturbances, blood clots, heart attack, or stroke
    - Increase in liver enzymes (often temporary)
    - Severe acne
    - Changes in blood pressure and cholesterol levels which may increase the risk of heart attack and stroke (likely minimal)
    - Pelvic pain/cramping (cause not currently known)
    - Dryness and irritation of genital tissues, which may increase susceptibility to STIs including HIV

- Sleep apnea

- Possible increased risk of:
  - Endometrial hyperplasia (overgrowth of the uterine lining, which can be a precursor to cancer)
    - It is important to let your provider know if you have a return of bleeding once bleeding has been consistently stopped by testosterone
  - Diabetes
  - Worsening of liver damage from other causes
  - Mood changes such as increase in irritability or anger, increased aggression, possible worsening of bipolar disorder, schizophrenia and psychotic disorders
  - Tendon injury

Some adverse effects from hormone therapy are irreversible and can cause death.

The risks for some adverse effects may be significantly increased by:

- Pre-existing medical conditions
- Pre-existing mental health conditions
- Cigarette smoking
- Alcohol use
- Taking testosterone in doses that are higher than recommended

APPENDIX N:
Sample Request for an Unlisted Drug Product, Testosterone Enanthate (Delatestryl)

Ontario

Ministry of Health and Long-Term Care

Exceptional Access Program Branch
5700 Yonge Street 3rd floor
Toronto ON M2M 4K5

Request for an Unlisted Drug Product
Exceptional Access Program (EAP)

Please fax completed form and/or any additional relevant information to 416 327–7526 or toll–free 1 866 811–9908; or send to Exceptional Access Program Branch (EAPB), 3rd floor, 5700 Yonge Street, Toronto ON M2M 4K5. For copies of this and other EAP forms, please visit http://www.health.gov.on.ca/english/public/forms/form_menus/odb_fm.html

The Ministry of Health and Long-Term Care (the "ministry") considers requests for coverage of drug products not listed in the Ontario Drug Benefit Formulary under Section 16 of the *Ontario Drug Benefit Act*. This form is intended to facilitate requests for drugs under the Exceptional Access Program. The ministry may request additional documentation to support the request.
Please ensure that all appropriate information for each section is provided to avoid delays.

Section 1 – Prescriber Information

First name	Initial	Last name
sample		

Mailing Address
Street no. | Street name

City | Postal code

Fax no. ( )
Telephone no. ( )

Section 2 – Patient Information

First name	Initial	Last name
sample		

Health Number

Date of birth *(yyyy/mm/dd)*

☐ **New request** ☐ **Renewal of existing EAP approval** *(specify EAP#)* ____–____

Section 3 – Drug Requested

Requested drug product: Testosterone Enanthate (Delatestryl)
DIN: 00029246

Strength / Dosage form: 200 mg/mL
Frequency of administration: weekly, may require adjustment

Expected start date:
Duration of therapy: indefinite

Section 4 – Diagnosis and Reason for Use

Diagnosis for which the drug is requested:
Gender Dysphoria

Reason for use over formulary alternatives:
No alternative on formulary, needs EAP for both Testosterone Enanthate and Testosterone Cypionate, due to risk of backorder

If the patient is currently taking the requested product, please provide start date & objective evidence of its efficacy:
If applicable: improved mental health and psychosocial function.

Section 5 – Current and / or Previous Medications

a) Please provide details of alternatives *(listed drugs and/or non-drug therapy)* tried for this condition:

Name of drug *(indicate if currently or previously taken)*		Dosage	Approximate timeframe of therapy	Reason(s) why formulary alternatives are not appropriate
N/A	☐ current ☐ previous			
	☐ current ☐ previous			
	☐ current ☐ previous			
	☐ current ☐ previous			

b) Provide patient's concomitant drug therapies for other conditions:

Section 6 – Clinical Information

Please provide relevant medical data *(e.g. culture and sensitivity reports, serum drug levels, laboratory results):*
Patient is transgender and meets criteria for hormone therapy

The information on this form is collected under the authority of the *Personal Health Information Protection Act*, 2004, S.O. 2004, c.3, Sched. A (PHIPA) and Section 13 of the *Ontario Drug Benefit Act*, R.S.O. 1990c.O.10 and will be used in accordance with PHIPA, as set out in the Ministry of Health and Long–Term Care "Statement of Information Practices", which may be accessed at www.health.gov.on.ca. If you have any questions about the collection or use of this information, call the Ontario Drug Benefit (ODB) Help Desk at 1 800 668–6641 or contact the Director, Exceptional Access Program Branch (EAPB), Ministry of Health and Long-Term Care, 3rd floor, 5700 Yonge St., Toronto ON M2M 4K5.

Prescriber signature *(mandatory)*	CPSO number	Date

4406-87 (2009/04)

APPENDIX O:
Sample Request for an Unlisted Drug Product, Testosterone Cypionate (Depo-Testosterone)

Ontario **Ministry of Health and Long-Term Care**

Exceptional Access Program Branch
5700 Yonge Street 3rd floor
Toronto ON M2M 4K5

Request for an Unlisted Drug Product
Exceptional Access Program (EAP)

Please fax completed form and/or any additional relevant information to 416 327–7526 or toll–free 1 866 811–9908; or send to Exceptional Access Program Branch (EAPB), 3rd floor, 5700 Yonge Street, Toronto ON M2M 4K5. For copies of this and other EAP forms, please visit http://www.health.gov.on.ca/english/public/forms/form_menus/odb_fm.html

The Ministry of Health and Long-Term Care (the "ministry") considers requests for coverage of drug products not listed in the Ontario Drug Benefit Formulary under Section 16 of the *Ontario Drug Benefit Act*. This form is intended to facilitate requests for drugs under the Exceptional Access Program. The ministry may request additional documentation to support the request.
Please ensure that all appropriate information for each section is provided to avoid delays.

Section 1 – Prescriber Information

First name	Initial	Last name
sample		

Mailing Address
Street no. | Street name

City | Postal code

Fax no. ( )
Telephone no. ( )

Section 2 – Patient Information

First name	Initial	Last name
sample		

Health Number

Date of birth *(yyyy/mm/dd)*

☐ **New request** ☐ **Renewal of existing EAP approval** *(specify EAP#)* _____–_____

Section 3 – Drug Requested

Requested drug product: Testosterone Cypionate (Depo-Testosterone)
DIN: 00030783

Strength / Dosage form: 100 mg/mL
Frequency of administration: weekly, may require adjustment

Expected start date:
Duration of therapy: indefinite

Section 4 – Diagnosis and Reason for Use

Diagnosis for which the drug is requested:
Gender Dysphoria

Reason for use over formulary alternatives:
No alternative on formulary, needs EAP for both Testosterone Enanthate and Testosterone Cypionate, due to risk of backorder

If the patient is currently taking the requested product, please provide start date & objective evidence of its efficacy:
If applicable: improved mental health and psychosocial function.

Section 5 – Current and / or Previous Medications

a) Please provide details of alternatives *(listed drugs and/or non-drug therapy)* tried for this condition:

Name of drug *(indicate if currently or previously taken)*	Dosage	Approximate timeframe of therapy	Reason(s) why formulary alternatives are not appropriate
N/A ☐ current ☐ previous			
☐ current ☐ previous			
☐ current ☐ previous			
☐ current ☐ previous			

b) Provide patient's concomitant drug therapies for other conditions:

Section 6 – Clinical Information

Please provide relevant medical data *(e.g. culture and sensitivity reports, serum drug levels, laboratory results):*
Patient is transgender and meets criteria for hormone therapy

The information on this form is collected under the authority of the *Personal Health Information Protection Act*, 2004, S.O. 2004, c.3, Sched. A (PHIPA) and Section 13 of the *Ontario Drug Benefit Act*, R.S.O. 1990c.O.10 and will be used in accordance with PHIPA, as set out in the Ministry of Health and Long–Term Care "Statement of Information Practices", which may be accessed at www.health.gov.on.ca. If you have any questions about the collection or use of this information, call the Ontario Drug Benefit (ODB) Help Desk at 1 800 668–6641 or contact the Director, Exceptional Access Program Branch (EAPB), Ministry of Health and Long-Term Care, 3rd floor, 5700 Yonge St., Toronto ON M2M 4K5.

Prescriber signature *(mandatory)*	CPSO number	Date

4406-87 (2009/04)

APPENDIX P:
Template Letter in Support of an Application For Change of Sex Designation on an Ontario Birth Registration

Note: • The letter must be from a **physician**, **psychologist**, or **psychological associate** authorized to practice in Canada and must be on the medical professional or clinic's letterhead providing an address and phone number
• Patient must submit an original (not photocopy) signed in blue ink by the provider.

Date: _____

To: SERVICE ONTARIO, THE OFFICE OF THE REGISTRAR GENERAL

Re: Application by (_____) for a change in gender designation on their birth registration.
name of patient

I am a practicing member in good standing with the _____ .
specify the appropriate regulatory body

License No: _____ .

I have provided medical/psychological support and treatment to the applicant, (_____),
name of patient as shown on the birth registration

who is requesting a change in gender designation from _____ to _____ .

I confirm that the applicant's gender identity does not accord with the gender designation on the applicant's birth registration and I am of the opinion that the change of gender designation on the birth registration is appropriate.

Yours truly,

_____
signature and name of provider

APPENDIX Q:
Template Letter in Support of an Application For Change of Sex Designation on an Ontario Driver's License

Note: • The letter must be from a **physician**, **psychologist**, or **psychological associate** authorized to practice in Canada and must be on the medical professional or clinic's letterhead providing an address and phone number.
• Patient must submit an original (not photocopy) signed in blue ink by the provider.

Date: _____

To: THE ONTARIO MINISTRY OF TRANSPORTATION

Re: Application by (_____) for a change in gender designation on their driver's license.
name of patient

I am a practicing member in good standing with the _____.
specify the appropriate regulatory body

License No: _____.

I have evaluated the applicant, (_____), who is requesting
name of patient as shown on the driver's license

a change in gender designation from _____ to _____.

I confirm that the applicant's gender identity does not accord with the gender designation on the Applicant's driver's license and I am of the opinion that the change of gender designation on the driver's license is appropriate.

Yours truly,

_____
signature and name of provider

APPENDIX R:

Sample Support Letter for Trans Clients Applying for EI through the Just Cause Mechanism

---

Date: _____

To: Human Resources & Skill Development

Re: Application by (_____) for Employment Insurance benefits.
name of patient

My *(patient/client)* is a *(transgender woman, transgender man, gender fluid person, etc.)* As a transgender person, *(he/she/they)* report experiencing severe and prolonged mistreatment in *(his/her/their)* workplace, including:
Edit details to accurately reflect patient's case, providing as much specific detail as possible; the types of incidents commonly reported include:

- Breach of privacy and threat to safety through the non-consensual disclosure of transgender status by a co-worker/supervisor to others in the workplace
- Verbal harassment, including derogatory jokes and transphobic comments by other co-workers
- Deliberate and repeated use of the wrong gender pronoun by co-workers and supervisor – a practice which is considered harassment by anti-discrimination legislation in some jurisdictions
- Threats to the safety of self or loved ones by co-workers and customers
- Significant change to work duties and reduction of hours of work following disclosure or discovery of transgender status
- Sexual harassment following disclosure or discovery of transgender status
- Persistent hostility by the supervisor following disclosure or discovery of transgender status
- Pressure on the claimant to leave employment and pursue other work

I believe this meets the criteria for 'just cause' outlined in paragraph 29(c) of the Employment Insurance Act, as my patient had no reasonable alternative to leaving to ensure *(his/her/their)* safety and dignity.

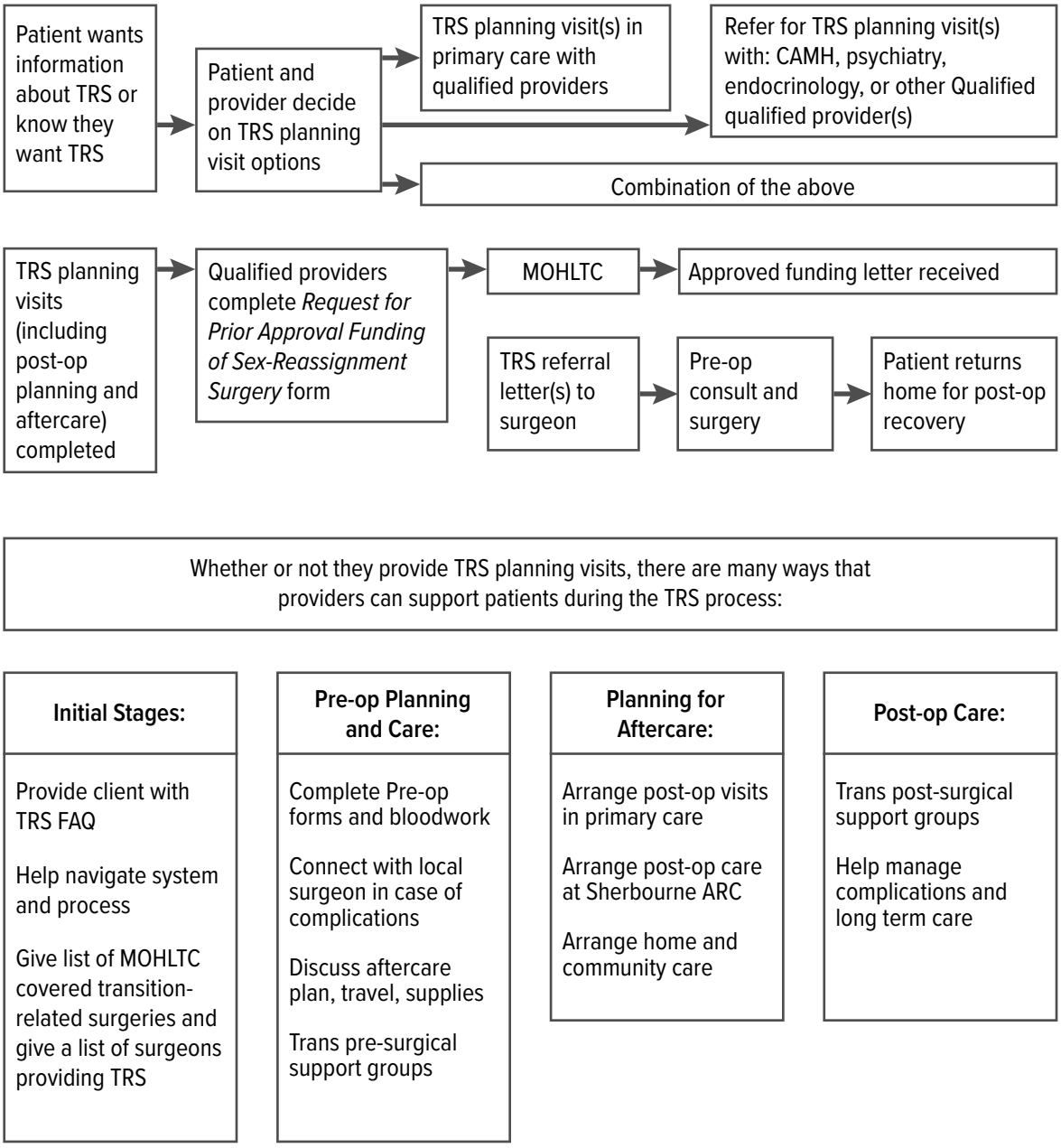
Please feel free to contact me if you require any additional information.

Yours truly,

_____
signature and name of provider

APPENDIX S:
Transition Related Surgery: System Flowsheet

Providers can gain TRS knowledge through: WPATH SOC; RHO Surgery Workshops; RHO Trans Mentorship call; Sherbourne Health Surgical Summary sheets; UofT/CAMH Trans ECHO; Trans E-consult with the Champlain LHIN; and/or mentorship with an experienced provider.



TRS – Transition-related surgery(ies)
CAMH – Centre for Addiction and Mental Health
MOHLTC – Ministry of Health and Long-term Care
WPATH SOC – World Professional Association for Transgender Health – Standards of Care
RHO – Rainbow Health Ontario, a program of Sherbourne Health
U of T – University of Toronto
LHIN – Local Health Integration Network