ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

The Ontario Drug Policy Research Network Drug Class Review on Testosterone Replacement Therapies

Final Report on Qualitative Study Findings

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Executive Summary

Background: The Ontario Drug Policy Research Network (ODPRN) conducted a drug class review of testosterone replacement therapy for the treatment of hypogonadism in adult men, which was selected as part of a formulary modernization initiative by the Ontario Public Drug Programs. This report highlights the findings of the qualitative study performed within the drug class review to determine the experiences of managing or treating hypogonadism with testosterone replacement therapy (TRT).

Methods: We used qualitative methods in a framework approach. One-on-one telephone interviews were conducted with nine patients, six primary care clinicians (i.e., physicians, nurses, and pharmacists), and seven specialists (i.e., urologists and endocrinologists). Interviews were recorded and analyzed using a framework for pharmaceutical policy analysis (i.e., the "Triple-A" framework: affordability, appropriateness, and accessibility of medications). Emergent findings were integrated into our framework, and the framework was adapted to convey specific experiences and perceptions relevant to funding policies on testosterone replacement therapies.

Key Findings: Findings in this report are summarized to represent common experiences and perceptions described across patient, primary care clinician, and specialist groups.

The diagnosis of hypogonadism can be complex: Although participants perceived that TRT is an acceptable treatment for individuals with exceptionally low testosterone levels, there was no consensus on the appropriateness of TRT for men who do not present with exceptionally low testosterone. This is because hypogonadism is not well understood; the administration and interpretation of testosterone tests varies across physicians; physicians and patients have a range of perceptions of the purpose of TRT and how it should be used; and there is a debate about the balance of risks versus benefits of TRT.

There are multiple factors that influence formulation choices: Decision making about formulation choices revolves around the affordability of products based on patient drug coverage, patient and physician preferences regarding the various TRT formulations (e.g., ease of use, perceived efficacy, and consistency of testosterone levels), and market availability of TRT.

Access to TRT is influenced by a number of factors: Information about the risks and side effects of TRT is less available to patients than is information about benefits; overall, patients desire better access to quality information about hormone therapies. Furthermore, patients may facilitate access to TRT by being persistent in obtaining these medications. In addition, physicians' philosophy toward TRT can affect access. It appears that physicians have little knowledge of the limited use (LU) code criteria for accessing TRT through the OPDP.

Conclusion: The findings from the qualitative study of the TRT drug class review informed the methods of other ODPRN research units conducting studies as part of the review. They also helped to contextualize the review's results. Overall, our findings shed light on the experiences of prescribing, dispensing, and using TRT for treatment of hypogonadism and unveil important information that can affect how patients access these drugs across Ontario.

Part 1: Introduction and Background

The Ontario Drug Policy Research Network (ODPRN) is conducting a series of drug class reviews as part of an initiative to update the public drug formulary (i.e., formulary modernization). Testosterone replacement therapies (TRT) were selected as the topic for the ODPRN's fourth drug class review.

TRT are a group of drugs used to treat male hypogonadism. Male hypogonadism is defined as the failure to produce either physiological concentrations of testosterone or normal amounts of sperm (Basaria, 2013). The 2010 Endocrine Society Guidelines recommend TRT for men with a confirmed diagnosis of hypogonadism that includes biochemical evidence of low circulating testosterone levels (Bhasin et al., 2010). The goal of TRT is to restore testosterone levels to the physiological range, which can improve quality of life, sexual function, muscle strength, and bone mineral density (Bassil et al., 2009). Seven TRT products are available in Canada, including two injectable products (i.e., testosterone enanthate [Delatestryl®] and testosterone cypionate [Depo-testosterone®]), four topical products (i.e., Androderm®, Testim®, Androgel®, and Axiron®), and one oral product (i.e., testosterone undecanoate [Andriol®]).

Currently, there is limited information on how physicians diagnose male hypogonadism and decide to prescribe TRT. Most TRT products are listed on the Ontario Drug Benefit (ODB) under a limited use code (i.e., restricted access) for male patients with confirmed low morning serum testosterone levels associated with classical causes of hypogonadism, such as symptomatic hypothalamic, pituitary, or testicular disease, and for those living with HIV. The listing does not include older men who may be suffering from late-onset hypogonadism with nonspecific symptoms, such as fatigue, malaise, or depression, and who have low-normal random testosterone levels. Since there has been a recent rise in the number of TRT prescriptions for older men in Ontario (Piszczek et al., 2014), more information is needed to understand how patients are accessing this group of drugs.

The purpose of the qualitative study that is being conducted as part of the ODPRN drug class review on TRT is to explore the various factors that may be related to TRT prescription, dispensing, and use for treating male hypogonadism. This information is warranted to understand and contextualize prescribing and usage patterns in Ontario and to highlight health equity issues that may be prevalent but currently unknown. The findings from the qualitative study were also used to inform the research plans of the other drug class review research units to ensure that stakeholder issues and priorities were being considered in their analyses.

Part 2: Methods

Design

We used a framework approach to qualitative research (Ritchie & Spencer, 1994). This approach allows researchers to focus on specific areas of interest when exploring a topic using qualitative methods, which can make the findings more applicable than alternative qualitative procedures. However, the approach also maintains the flexibility of qualitative methods to incorporate new ideas, emergent issues, or unanticipated results. The framework selected for this study was the "Triple-A" framework for pharmaceutical policy analysis developed by Morgan et al. (2009; see **Appendix A**). This framework highlights the need to explore affordability, accessibility, and appropriateness of a drug class when determining policy-relevant issues.

Sampling

Stakeholders identified for the TRT drug class review included primary care clinicians (i.e., primary care physicians, pharmacists, and nurses), specialists (i.e., urologists and endocrinologists), and patients who have current or prior experience using TRT to treat hypogonadism. We aimed to recruit 6 to 8 primary care clinicians, 6 to 8 specialists, and 20 to 25 patients based on the assumption that these sample sizes would be sufficient to reach saturation of findings among relatively homogenous groups of participants (Kuzel, 1999). A purposive sampling approach using a convenience sample was used to recruit participants who will be involved in or affected by drug policy decisions related to TRT. Recruitment methods included a) cold calling, b) e-mailing and faxing, c) recruiting at primary care and specialist clinics, d) sending recruitment letters through e-mail distribution lists of professional organizations and advocacy groups, e) posting recruitment notices on the ODPRN website and social media accounts (i.e., Twitter and Facebook), g) posting recruitment notices on public advertisement websites (i.e., Craigslist and Kijiji); and h) snowball sampling (i.e., asking participants to connect with individuals they know for the purpose of recruitment to the study). Participants were recruited from across Ontario.

Data Collection and Analysis

Qualitative data were collected through one-on-one telephone interviews that were 30 to 45 minutes long and conducted between April 2014 and August 2014. All interviews were conducted with a semi-structured interview guide that was developed using the "Triple-A" framework for pharmaceutical policy analysis (Morgan et. al., 2009) and input from clinicians and the drug class review team. Each interview was audio recorded and transcribed. The interview transcripts comprised the primary source of data. The interviewer and/or a note taker took field notes during the interview to serve as a secondary source of data.

The framework approach was used to guide data analysis. Two independent analysts engaged in familiarization of the data by reading all primary and secondary data sources and generating initial codes that could be incorporated into the "Triple-A" framework (Morgan et. al., 2009). These codes comprised the coding framework, which was reviewed by the qualitative research

team and applied to the data by two analysts during in-depth analysis. Inter-rater reliability between the two analysts was > 80%. The analysts and the qualitative research team mapped and interpreted the coded data to generate the final themes.

Research Ethics

This study was approved by the St. Michael's Hospital Research Ethics Board in Toronto, Ontario, Canada in April 2014.

Part 3: Findings

Participant Demographics

Patients

Nine patients participated in the study. Among these patients, 45% (*n* = 4) were over the age of 65 years, 11% (*n* = 1) were 55–64 years, 22% (*n* = 2) were 45–54 years, 11% (*n* = 1) were 35–44 years, and 11 % (*n* = 1) were 25–34 years. These patients represented a variety of experiences with hypogonadism and TRT.

Primary Care Clinicians

Six primary care clinicians participated in the study. Among these participants, 33% (*n* = 2) were nurses, 50% (*n* = 3) were family physicians, and 17% (*n* = 1) were pharmacists. Out of the three family physicians, two had a special interest in men's health. All clinicians were from urban settings and worked in full-time practices.

Specialist Clinicians

There were seven specialists interviewed for this study: two (29%) endocrinologists and five (71%) urologists. Among these participants, 29% (*n* = 2) had practiced for less than 5 years, 29% (*n* = 2) had practiced for 5–15 years, and 42% (*n* = 3) had practiced for over 15 years. The specialist clinicians were all from urban settings and worked in full-time practices.

Detailed participant demographics can be found in **Appendix B**.

Key Themes Related to the Use of TRT in Adult Men

The following findings are based on the perceptions of interview participants. The experiences and perceptions of patients, primary care clinicians, and specialists have been summarized into three themes.

1. **The Appropriateness of TRT**
    a. Diagnosis of Male Hypogonadism
    b. Perceptions of the Purpose of TRT

c. Perceptions of the Risks of TRT

2. **Factors that Influence Formulation Use**
    a. Affordability
    b. Patient Preferences
    c. Perception of Oral Formulation
    d. Availability of Injectable Products

3. **Factors that Determine the Accessibility of Testosterone Replacement Therapies**
    a. Patient Access to Information
    b. Patient Health-Seeking Behaviours
    c. Physician Prescribing Philosophy
    d. Physician Perception of Limited Use Code
    e. Pharmacist Restrictions

Detailed findings on each of these themes are described below.

The Appropriateness of TRT

Clinician and patient participants had a range of perceptions regarding the appropriateness of TRT for hypogonadism in adult men. While there are five guidelines related to TRT use for hypogonadism, the diagnosis of hypogonadism can be complex and there is debate about how to define it. There is also some dispute about the purpose and safety of TRT, which has led physicians and patients to develop a variety of conclusions about hypogonadism treatment. This theme is predominantly discussed from the clinician group perspective.

A. The Diagnosis of Male Hypogonadism

> "*I think the deeper, more sophisticated question that should be asked, but we don't have the answer for is..., is your current testosterone too low for you or is it too low for what you are used to? You know, because it's a range*"—Primary Care Physician

Data from clinician interviews revealed that there are a number of factors that can make it challenging to diagnose hypogonadism. The first step in determining whether TRT is appropriate for a male patient is to obtain an accurate diagnosis of hypogonadism. Male hypogonadism can be the consequence of many different processes, such as pituitary failures, genetic abnormalities, aggressive cancer treatments, and aging. Patients who do not have a congenital condition (e.g., Klinefelter's syndrome) that directly interferes with testosterone production were described as more difficult to diagnose. One reason why hypogonadism is difficult to diagnose in the absence

of a congenital condition is that the symptoms of hypogonadism are non-specific (e.g., low energy, loss of muscle mass, low libido, mood disturbances, and erectile dysfunction and could be due to another condition, such as depression or thyroid abnormalities. In addition, not all patients with low testosterone levels present with symptoms. This has led some physicians to wonder whether what is considered "normal" for one man may be "low" for another man.

The clinicians and patients we interviewed described six different diagnostic strategies for hypogonadism, which have been summarized in Table 1. Some clinicians expressed a desire to rule out other health conditions before starting a trial of TRT. Others preferred to start therapy, monitor its effects on the patient, and then decide if further testing is warranted. Most clinician participants described testing their patients' testosterone levels if patient complained about the above mentioned symptoms. Currently, however, there is no consensus regarding what test result is considered "abnormally low," the "low end of normal," or "normal." Physicians described using testing cut-offs for hypogonadism that ranged from 0 to 15 nanomols per litre of testosterone.

> *"It's actually nice when the value is either extremely low, so everything's obvious or very high so it's obvious the other way, but usually it's somewhere in the middle where someone with that level could have, certainly experience symptoms of testosterone deficiency but also people with no symptoms if you check their level for whatever reason may have that same number so it's not all that helpful, it's a big gray zone. And then you're stuck deciding along in cooperation with the patient whether a trial would be reasonable, of maybe three or four months to see if there is a significant improvement in symptoms and then to decide whether this warrants a long term therapy or not and if it didn't make any difference in symptoms, raising the level, then it's probably not worth any risks associated with the therapy."*—Primary Care Physician

Clinicians and patients also described different preferences for the types of tests used. Some patients prefer the serum testing because it is covered by OHIP. Some clinicians prefer the serum testing because they have doubts about the accuracy of bioavailable tests conducted in private laboratories. Other clinicians conduct both tests and compare results. Clinicians also described preferences about the timing of testing. All specialist participants prefer to have the tests performed in the morning and repeated at least twice, which is consistent with the 2010 Endocrine Society Guidelines. Most patients and primary care clinicians, in comparison, did not identify the timing of the test as an important factor.

Most patients we spoke to described having to do some form of testosterone testing before starting therapy. However, not all physicians who prescribe TRT require lab testing. One patient described having only an informal discussion about symptoms before starting treatment. Another described hearing from friends who had either emailed their doctor with a description of symptoms or had an informal discussion with their doctor, which was enough evidence for the doctor to write a prescription.

"*And I'm not saying it's right or wrong, it's just, but I know people get not just this drug but other drugs sometimes without going through the proper testing and, because that takes time and some people don't have the time or the inclination for it.*"—Patient

Table 1. Diagnostic strategies described by both patient and clinician participants.

Diagnostic Strategy*	Administration of a Symptom Questionnaire	Informal Discussion About Symptoms	Bioavailable/ Free Testosterone Test	Serum/Total Testosterone Test	Testing to Rule Out Other Conditions (e.g., Thyroid Abnormalities and Depression)
A	✔	✔		✔	✔
B		✔	✔	✔	✔
C		✔	✔	✔	
D		✔		✔	
E		✔	✔		
F		✔			

* The purpose of this table is to display the range of diagnostic strategies that are potentially being used in Ontario; it may not include all available strategies. Because we collected data using qualitative methods, we did not survey the number of participants who used each strategy. Instead, we noted the strategies mentioned by physicians during the interviews.

There was also variety in the TRT monitoring strategies used by clinicians. Some physicians require patients to come in every 6 or 12 months after they have started therapy. Others require patients who have recently started TRT to come in every three months for dosage adjustment. Some clinicians require patients to undergo regular prostate-specific antigen (PSA) tests, and others require no follow-up with the patient at all.

B. The Perception of the Purpose of Testosterone Replacement Therapies

Participants had a variety of perceptions about the purpose of TRT, which were influenced by their impressions of the appropriateness of TRT in different groups of men.

Patient Perspectives

"*I think there is a difference to be made there between aging men with libido problems and then their salvation is Androgel® for that matter – or any other testosterone thing – and then other people with low testosterone levels because of,*

well, I think maybe certain illnesses, like in my particular case that was the long-term effects of cancer treatment."—Patient

"*I'm thinking about in terms of public policy, and heath awareness, and general health and fitness, engagement with life and quality of life and all that stuff, that if some awareness can be done from a public health perspective to say men you don't have to grow old, you can stay active and healthy and engaged in life more than just the sexual aspect, that may encourage more people to have good conversations with their physicians about this therapy.*" —Patient

Patients had dichotomous views on the purpose of TRT. Those with congenital abnormalities and chronic diseases described TRT as a vital treatment that is crucial to ensure the presence of libido and overall health and well-being. These patients perceived a difference between their needs and the needs of other men who either a) have hypogonadism as a consequence of aging or b) may not have hypogonadism and use TRT to build muscle mass. They expressed a view that the use of TRT in these groups may not be necessary, and some have even observed harmful effects of inappropriate use in their friends and acquaintances (e.g., loss of fertility). They also described how this perception of inappropriate use has influenced the attitudes of some pharmacists and created a stigma about TRT that has resulted in more restricted access to prescriptions in some communities.

Patients who did not suffer from congenital or chronic diseases perceived TRT as an acceptable treatment for all aging men who have experienced a sudden loss of self-efficacy accompanied by a recent decline in the ability to build muscle mass or perform sexually. Patients who held this view also described a desire to "act their age," remain youthful, and continue doing the activities they enjoyed in their younger years. They described developing this perception through conversations with co-workers, friends, fitness experts, and doctors and by viewing online or print media.

Clinician Perspectives

"If they have decreased testosterone and they have the clinical manifestations, I feel very strongly that they should be treated. I don't buy the argument that it's part of aging because if we buy the argument, we shouldn't treat the people who develop cataracts or we shouldn't treat the people who develop arthritis in the hips because these are consequences of aging, they won't kill you but they'll make your life miserable."—Urologist

"I can't remember the guy's name, but basically that all the guy does. He prescribes testosterone and unfortunately it sounds like he prescribes it to every human being, every man that walks through that door. Because in some way, shape or form he finds that they need it. They filled out the questionnaire or whether they go through blood tests or both. That is misuse, that is over-use, that is offering a potentially dangerous substance on a chronic basis to patients for

quote, lifestyle management and that's not appropriate use of the medication."—Primary Care Physician

Data from clinician interviews revealed three different perspectives on the appropriateness of TRT. First, some clinicians described TRT as a treatment that should be reserved for only "profoundly low" cases where men have lost the ability to produce testosterone naturally due to disability, aggressive cancer treatment, or congenital disease. In general, specialists who had a special interest in specific clinical areas, such as pituitary disorders or oncology, tended to hold this view. The second perspective was held by from physicians (both primary care and specialists) who have a special interest in men's health. This group tended to believe that the appropriateness of TRT can vary depending on a patient's symptoms, test results, and overall health profile. Physicians in this group were more likely to entertain the idea of prescribing TRT to patients who are on the low end of normal testosterone levels. The third perspective was held by general practitioners and general urologists, who described TRT as appropriate for any patient with symptoms and a low test result regardless of the underlying cause. Some of these practitioners also described having posters in their clinic with information on TRT and its use.

C. Perceptions of the Risks of TRT

"*To the endocrinologist who casually treats testosterone, every so often, and maybe isn't up on the literature; I can see how someone might see the latest studies and say "Oh my God this is proof that they are dangerous drugs". I think that someone like myself who follows the literature closer understands that there are potential risks and there are potential benefits but I don't think there are any studies that have definitely proven things one way or another. I think what we need is more evidence and I'm not taking my patients off testosterone because of two observational studies.*"—Endocrinologist

"While we are potentially trying to increase access for patients who truly need it, we gotta think, if we flood the market with this product, what are the long term consequences? We really have no idea, there is no study that is over 3 years of testosterone supplement."—Urologist

Clinician participants discussed their perceptions of the safety of TRT and how this may affect provision of these therapies. One key safety consideration was the potential side effects of TRT. According to most physicians, side effects are monitored regularly to ensure safe use; these include skin irritations and screening for polycythemia and rising PSA. Side effects of particular formulations of TRT (specifically topicals, which can cause transference of gel to others) can influence the types of TRT clinicians prescribe and the decision to switch products. Factors influencing the selection of TRT products are described in greater detail below.

An additional safety consideration reported by clinician participants was patient history and comorbidities. For example, one clinician reported that he may not start patients with a cardiac history or pre-existing polycythemia on TRT products. Similarly, a clinician who works with

HIV-positive patients perceived that TRT might cause harm to patients, although this participant did not report any patients experiencing adverse events due to TRT.

Clinicians' viewpoints greatly focused on the current state of evidence regarding TRT and the need to balance the risks of TRT use with the benefits. One clinician noted that studies demonstrating negative consequences of TRT are limited in number and believed that this lack of evidence on risks should not preclude provision of these therapies to men who require them. Another clinician perceived that "myths" about the safety of TRT exist, specifically those regarding the potential harms of TRT use in men with prostate cancer. This participant also noted, however, that the balance of evidence largely favours TRT use.

Other clinicians noted that no studies examine the long-term consequences of TRT, which they believed should be considered before enabling wider access to these drugs. The case of hormone replacement therapy in women was cited as an example of an aggressively promoted treatment that ultimately resulted in notable harms. Most clinician participants agreed that TRT may not be suitable for men with prostate cancer; it should be noted that this aligns with the 2010 Canadian Endocrine Society Guidelines.

Theme Summary: Overall, participants perceived TRT as an accepted treatment for individuals with exceptionally low testosterone test results in whom there is a clear underlying condition (e.g., Klinefelter's Syndrome and testicular cancer). However, for the following reasons, there was no consensus on the appropriateness of TRT for men who do not present with exceptionally low test results:

a) Hypogonadism is not well understood and can be the consequence of a variety of health conditions.
b) While there are two types of tests for testosterone, the administration and interpretation of the tests varies across physicians.
c) Physicians and patients have a range of perceptions of the purpose of TRT and how it should be used.
d) There is a debate about the balance of risks versus benefits of TRT.

The Factors that Influence Formulation Use

Patients and physicians were asked to describe their perceptions of the pros and cons of different TRT formulations and how these affect their decision making on either starting or switching products. Participants described four factors that influence their formulation choices.

A. Affordability

"*One of the important issues is cost. Some of them are very expensive particularly if the patient is very hypogonadal and he requires large amounts of testosterone,*

others are less expensive. Most of them are covered by plans but sometimes you have patients who are not covered by any plan"—Urologist

In general, participants across all groups described that patients who do not have drug coverage prefer to use injectable products, particularly Delatestryl®, because they are cheaper. Physician participants who are able to provide samples may provide Androgel® sachets to a patient as a trial to determine if the patient will benefit from TRT. However, because TRT contains a controlled substance, not all physicians may be comfortable storing samples in their clinics. In some cases, they provide patients with a drug card from the manufacturer, which can be presented at a pharmacy to receive samples. One patient described having to stop using the gel product because he could not afford the cost.

B. Patient preferences

Participants described that patients have different preferences for formulations. The table below displays the full list of pros and cons described by both patients and physicians. Physician participants described that they discussed these preferences with their patients when selecting an appropriate product. However, some patient participants explained that they were not presented with the option to choose between different formulations. In these cases, physicians made the choice based on their assumption of patient preferences and affordability. The most preferred products among participants in this study were the gel products (e.g., Androgel®) and the injectables (e.g., Delatestryl®).

	Topicals	Injectables	Pills
Pros	• Ease of use • Keeps testosterone levels consistent (i.e., no peaks and dips) • Perceived to be more "natural" than other formulations	• More affordable • Can perceive an immediate effect of the injection • Regular interaction with physician or nurse	• Ease of use
Cons	• Skin irritation • Potential for contact with partner or children • Perception that having a consistent testosterone level is unsafe or unnatural • Effect is not immediate	• Uncomfortable administration • Need to schedule regular appointments • Self-administration is difficult and often not possible • Prior to subsequent injection, effects of fatigue and other symptoms are common (due to dips in testosterone levels)	• Need to be consumed with fats • Hard to remember to take if patient is taking multiple mediations—"pill burden" • Perceived as less effective than other formulations

C. Physician Preferences

Many clinician participants perceived that the oral formulation of testosterone is not as effective as the topical or injectable products. Only one urologist described regularly prescribing the oral formulation. All other clinicians had doubts about the effectiveness of the oral formulations. Physicians also noted that the need for patients to consume oral formulations with fats was a deterring factor for prescribing them. In general, most participants perceived the topical and injectable products as most effective and therefore were more likely to prescribe these to patients.

D. Manufacturer Shortages

Participants across both patient and physician groups described periods of time during which the injectable product Delatestryl® was unavailable due to a shortage from the manufacturer. In these cases, patients were given an alternative product, Depo-testosterone®, which was less preferred. Patients prefer Depo-testosterone® less than Delatestryl® because the concentration of testosterone in Depo-testosterone® differs from that in Delatestryl®. In addition, Depo-testosterone® injections need to be twice the volume of Delatestryl® injections or administered twice each time.

Theme Summary: Data from interviews revealed four main findings relating to decision making about formulation choices:

a) Some patients with partial or no drug coverage prefer the injectable products over others because they are the most affordable.
b) Patients have a variety of perceptions about each formulation, mostly relating to ease of use, perception of efficacy, and consistency of testosterone levels.
c) Some physicians and patients prefer the oral formulation less than the other products on the market.
d) Delatestryl® is sometimes unavailable for patients and must be temporarily replaced with the Depo-testosterone® product, which patients prefer less.

Factors that Determine the Accessibility of TRTs

Participants identified five factors that influence the accessibility of TRT:

A. Patient Access to Information

> *"People in public, whatever, you know, 40 plus, that are talking positively about it and that filters down to other people that you know most of the time believe what they say, and then it goes by word of mouth"*—Patient

> *"A little better ... awareness and knowledge, that would be important to me, the other would be about the whole replacement thing, what happens to you know when you stop taking it, what's recovery, what is, if you start at 44, or you know whatever and go until what, 50, or 70, and then stop, what happens to a 70 year old that has been taking, taking this medicine for 20 years or whatever, I'd like to know a little bit more about that and I don't know if that is even knowledgeable about that yet."*--Patient

Participants described that patient access to information on TRT can facilitate their eventual access to TRT. Some patients described learning about TRT and its uses through posters at their pharmacy or family doctor's clinic. Others heard about TRT through friends or coworkers or did their own research on the internet. While most patient participants found it easy access to information on the positive effects of TRT and how to acquire it, they seemed to have little knowledge about its side effects or risks. Some expressed a desire to receive more information from their doctor on the availability of different formulations, the pros and cons of each formulation, and the risks of long-term use of TRT.

B. Patient Health-Seeking Behaviours

> "*They do not want to prescribe it, even if it'll help you. Because it is a controlled substance, and it's just it's so sad that there's people suffering because of a few baseball players. You know they won't prescribe, it's just stupid. But anyway, I was very persistent and they agreed to try it and sure enough for me it's made a huge difference.*"—Patient

> "*Maybe a few years before the actual diagnosis I started doing some research.*" —Patient

> *"I know when I was talking to another friend of mine, when he wanted it I think he got it without the test, but that's because he put up a big stink about it."*— Patient

Both physicians and patients described that some patients are very persistent in their quest to acquire TRT and ensure that it has the effect they desire. Physicians have noticed an increase in the number of patients requesting to be put on a trial for TRT. Some patients have spent hours reading online magazines, sifting through academic journals, and requesting referrals to specialists. One participant described that because he did not feel satisfied with the advice he

received from his doctor, he adjusted the dose of his TRT himself and subsequently asked to switch products when he did not perceive any immediate effects of the medication. Another participant described his experience of buying a topical TRT from a supplier at his gym. Patients who are particularly persistent have described going to multiple doctors until they were able to find one who agreed to prescribe TRT them.

C. Physician Prescribing Habits

> *"Well doctors, and it's really funny because well the first doctor wasn't so bad, he says ok you know what, we can try it. We'll give you a low dose, see what happens. And that's how we started with that. Then the second doctor was very very reluctant, because I fell just inside the normal range"*—Patient

> "*I know some physicians who will prescribe it for anything at all and I know some who will not prescribe it unless someone's testosterone levels are near-undetectable. I'm somewhere in between. I think that there are people who genuinely benefit from testosterone but I think there are a lot of people who have been put on it for the wrong reasons and end-up being sent to me to kind of fix.*"—Endocrinologist

Patient and physician participants described that access to TRT is highly dependent on the personal prescribing philosophy of a physician. Some clinicians are extremely conservative prescribers of TRT, some are moderate, and others are very liberal. Patients who are able to find a doctor who is a liberal prescriber are more likely to get access to TRT.

D. Physician Perception of Limited Use Code

Nearly all clinicians we spoke to admitted that they were not familiar with the criteria for the limited use (LU) code. They were also not completely sure about which products were covered through ODB and which were not. When probed further about the LU code, some specialists explained that there is a need to develop more definitive criteria for eligibility. Currently, the criteria state that "*older males with nonspecific symptoms of fatigue, malaise, depression who have a low normal random testosterone level do not satisfy these criteria*". However, since there is no consensus about the interpretation of test results, it is not clear what the definition of "low normal random" is. Additionally, it was suggested that older males with naturally diminishing testosterone may also have pituitary or hypothalamic abnormalities.

> *"It's difficult because I think most physicians don't even know the LU criteria to be honest; I think everyone writes down something without knowing."*—Specialist

> *"So it really, I know it's easy for articles and things to say oh these doctors don't prescribe, or companies to say, or even the government for LU codes to say clear evidence of lab values. What does that mean? …well a lot of doctors would take it*

as, you don't qualify. I ask my colleagues about this, to deal with it, and a lot of them say I don't go with the lab values even if that question is asked to me my clinical opinion, this number is low, I don't care what the lab value says I think it's low based on this. I will say this is, this patient should qualify for this. I don't know what the, what ODB means with that LU code of evidence of early morning low levels, does that mean by the lab, which lab, who's lab, what does it mean? It's very gray and I think it's very confusing for everybody. But I think using those numbers it's not, it really disservices a lot of men that do benefit from therapy, but just don't qualify in that technical, it's a very administrative thing, it really has nothing to do with medicine so."—Primary Care Physician

E. Pharmacist Restrictions

"It's not so bad now. I'm at a pharmacy that I think understands it a little bit better. I find there is a general misunderstanding in the pharmacy community about what testosterone actually treats and why someone in their thirties would be getting this drug. When I got prescribed it, I was living in a smaller regional centre where maybe they didn't understand what it might be used for, quite as well. I had a pharmacist…you know the usual process for people getting their drugs filled is taking it to a pharmacy clerk and they review the prescription, fill it and off they go but for the first 3 pharmacies I went to, the pharmacist insisted on talking to me one-on-one and finding out more about why I was taking it. I told them "well the doctor prescribed it so what more do you need?" So I found that very frustrating." – Patient

Although most patients did not describe any difficulties with obtaining TRT at their pharmacies, one patient participant discussed pharmacy-related challenges in detail. Consistent with the fact that TRT is a controlled substance, this patient reported that pharmacists have scrutinized his prescriptions in detail. The participant believed that negative perceptions about TRT use are prevalent in rural areas, which may lead to suspicion about why TRT is being used and increase questioning by pharmacists. This experience is notable because it may be shared by other patients in Ontario.

Theme Summary: According to study participants, access to TRT is affected by a number of important factors at the patient and provider levels:

a) Patients readily access information about the benefits of TRT, but information about the risks and side effects are less available. Overall, patients desire better access to quality information about hormone therapies.
b) Patient health-seeking behaviours can be a significant determinant of access to TRT as many patients are persistent and push to obtain these medications.
c) Physicians' prescribing habits can facilitate or hinder access to TRT depending on the physician's philosophy of the drugs.
d) Physicians have little knowledge of the LU code for access to TRT through the OPDP. Lack of knowledge of criteria and lack of clarity of the criteria themselves can affect how physicians prescribe TRT.
e) Some patients may face restrictions to TRT access at their local pharmacy. However, most patients in our sample did not describe any challenges.

Discussion

Key Findings

Our study findings highlight many key experiences and perceptions that shed light on the prescription and use of TRT. One key finding was that people differ in their beliefs about who should access TRT. It is apparent that at the patient and provider levels, there are varying opinions on why TRT should be made available and little consensus on perceptions of the balance between the risks and benefits of these drugs. This study also highlights perceptions on appropriate diagnosis of hypogonadism and what constitutes an appropriate clinical test to determine the need for TRT. Furthermore, we found that patients, physicians, and pharmacists require access to better information on TRT and the LU criteria to access TRT, which can be addressed through appropriate education and knowledge translation.

Health Equity Considerations

The findings from this study highlight the disparity in access that exists across most drug classes; those who are under 65 years of age and are not eligible for the Trillium Drug Program but still require TRT may have difficulty paying for these drugs.

Limitations

Participant recruitment was the primary limitation of our study. In other qualitative research on TRT, researchers have reported difficulty with recruiting men to interviews (Sader et al. 2003); potential reasons for this difficulty may be the sensitive nature of the health topics surrounding TRT. The telephone interviews had the potential to touch on the symptoms of hypogonadism,

including libido and sexual performance, and this may have been a deterrent for men who considered participating in this and other TRT studies. Another recruitment challenge was that TRT is used across multiple conditions and does not have a centralized patient network that we could engage with.

It should be noted that qualitative findings are not representative of the general population of individuals from which our study sample was drawn. The information presented in this report is a summary of the personal impressions and opinions of participants, which have been shaped largely by their experiences rather than by empirical clinical evidence. The purpose of presenting this information is to provide context for patient and prescriber decision making as it relates to TRT usage trends in Ontario. We aimed to include as many diverse viewpoints as possible through our sampling efforts.

Conclusions

The findings from the qualitative study of the TRT drug class review informed the methods of other ODPRN research units that are conducting studies as part of the review. Moreover, our qualitative study helped to contextualize the results of the systematic review, pharmacoepidemiological analysis, and environmental scan performed within the separate research units of the TRT drug class review. On a broader scale, our study findings fill a gap in knowledge on access to TRT and related clinical issues. Overall, our findings shed light on the experiences of prescribing, dispensing, and using TRT. They also unveil important information that can affect how patients access these drugs across Ontario.

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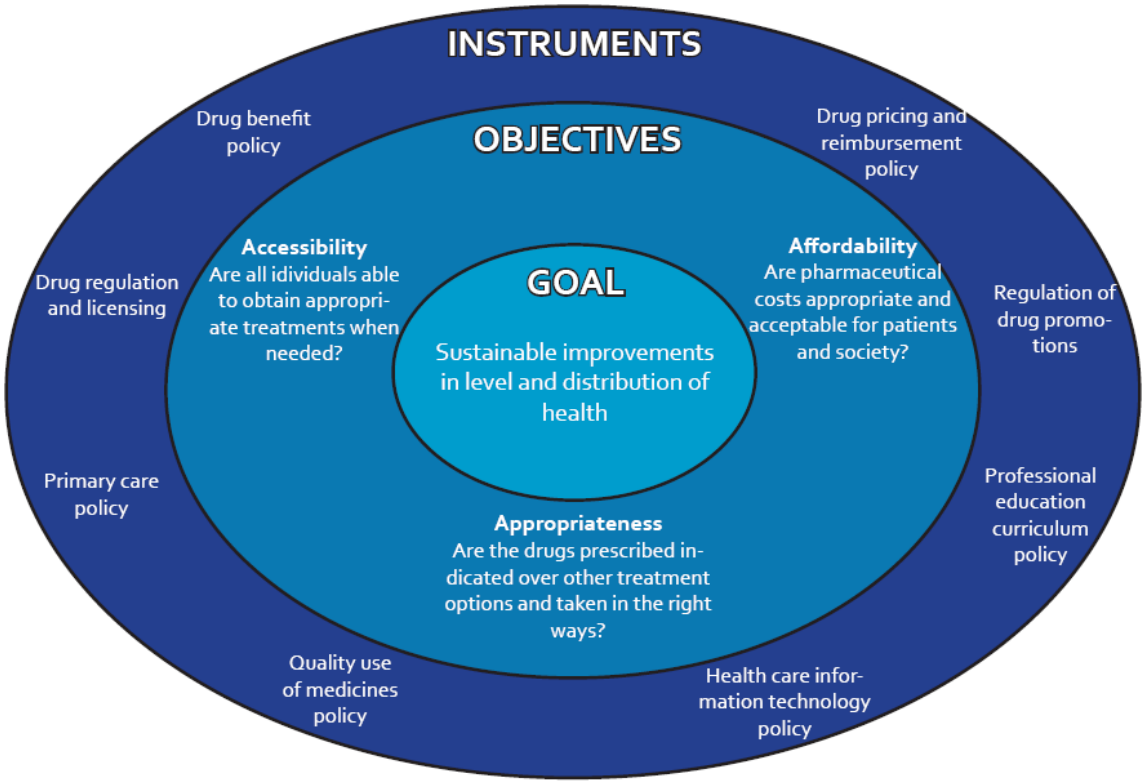
Appendix A: "Triple-A" Framework for Pharmaceutical Policy Analysis



Adapted from: Morgan S, Kennedy J, Boothe K, McMahon M, Watson D and Roughead E. (2009) Toward an Understanding of High Performance Pharmaceutical Policy Systems: A "Triple-A" Framework and Example Analysis. *Open Health Services and Policy Journal:2;* 1-9

Appendix B: Participant Characteristics and Demographics

Patients

Demographic Characteristic (n=9)	n	%
Gender		
Male	9	100 %
Age		
25 -34	1	11 %
35-44	1	11 %
45-54	2	22 %
55-64	1	11 %
65+	4	45 %
Employment Status		
Full-time	5	55 %
Part-time	0	0 %
Unemployed (retired, disability)	4	45 %
Diagnosed with a Clinical Condition		
Klinefelter's Syndrome	1	11 %
HIV	1	11 %
Hodgkin's Lymphoma	1	11 %
Years on TRT		
<5	6	67 %
5-15	2	22 %
>15	1	11 %
TRT Prescribed By		
Family Doctor	5	55 %
Urologist	2	22 %
Endocrinologist	1	11 %
Independent Supplier	1	11 %
TRT Currently Using		
Delatestryl®	3	33 %
Androgel®	4	45 %
Andriol®	2	22 %

Primary Care Clinicians (Primary Care Physicians (n=3), Nurses* (n=2), Pharmacists* (n=1))

Demographic Characteristic (n=6)	n	%
Years of practice		
<5	0	0 %
5-15	3	50 %
>15	3	50 %
Type of Practice		
Full-time	5	83 %
Part-time	1	17 %
Geographic Location		
Urban	6	100 %

*Note that this participant acts as a consultant and does not directly prescribe TRT.

Specialist Physicians (Urologists (n=5) and Endocrinologists (n=2))

Demographic Characteristic (n=7)	n	%
Years of practice		
<5	2	29 %
5-15	2	29 %
>15	3	42 %
Type of Practice		
Full-time	7	100%
Geographic Location		
Urban	7	100%