

# ODPRN Comprehensive Research Plan: Testosterone Replacement Therapy

Pharmacoepidemiology Unit

April 29, 2014

## ODPRN Drug Class Review Proposal Pharmacoepidemiology Unit

**Study Title: Epidemiologic analyses of testosterone use in Canada**

- Objectives:**
1. To examine national and provincial trends of testosterone use and costs among public drug plan beneficiaries over the past 5 years
  2. To perform cross-provincial comparisons of the characteristics of testosterone use among a population of public drug plan beneficiaries
  3. To characterize users of testosterone products in Ontario
  4. To describe current patterns of testosterone adherence in Ontario

### Objective 1a: National and provincial trends in testosterone use

**Study Design:** Design: Time series analysis with quarterly time intervals  
Study period: January 2009 to February 2014  
Population: All provinces and territories  
Data Source: *IMS Compuscript*: aggregated data for all prescriptions dispensed at retail pharmacies across Canada

- Study Population:** Inclusion Criteria:
- All privately and publically-funded testosterone prescriptions dispensed in Canada
    - Oral formulations
    - Topical formulations
    - Patch formulations
    - Injectable formulations
  - Men
  - All ages

- Outcome(s) of Interest:** Measured over entire study period (quarterly):
- Number and rate of testosterone prescriptions dispensed
  - Total cost of testosterone prescriptions
- Stratify all analyses by:
- Province
  - Payer (public, private)
  - Testosterone formulation (oral, topical, patch, injectable)

- Limitations:**
- There is no patient-level data available through IMS Compuscript; information is only available at the prescription and unit level.

## Objective 1b: Cross-provincial changes in prescribing of testosterone in public drug programs

<b>Study Design:</b>	<p><u>Design:</u> Time series analysis with quarterly time intervals</p> <p><u>Study period:</u> January 2000 to December 2012</p> <p><u>Data Sources:</u></p> <ul style="list-style-type: none"> <li>• <i>National Prescription Drug Utilization Information System Database (NPDUIS)</i>: aggregated data for all publically funded prescriptions dispensed in Alberta, Saskatchewan, Manitoba, New Brunswick, Nova Scotia, PEI and BC</li> <li>• <i>Ontario Drug Benefit Database (ODB)</i>: individual level data for all publically funded prescriptions dispensed in Ontario. This dataset contains additional variables (long-term care residence, public drug plan coverage) that is not available through NPDUIS</li> </ul>
<b>Study Population:</b>	<ul style="list-style-type: none"> <li>• Inclusion Criteria: <ul style="list-style-type: none"> <li>○ All publically-funded testosterone prescriptions dispensed in Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, PEI and BC <ul style="list-style-type: none"> <li>○ Oral formulations</li> <li>○ Topical formulations</li> <li>○ Patch formulations</li> <li>○ Injectable formulations</li> </ul> </li> <li>○ Men</li> <li>○ All ages</li> </ul> </li> </ul>
<b>Outcome(s) of Interest:</b>	<p>Measured over entire study period (quarterly):</p> <ul style="list-style-type: none"> <li>• Number and rate of testosterone users</li> <li>• Total costs</li> <li>• Average cost per user</li> </ul> <p>Stratify all analyses by:</p> <ul style="list-style-type: none"> <li>• Province</li> <li>• Testosterone formulation (oral, topical, patch, injectable)</li> <li>• Age (&lt;65, 65+)</li> </ul>
<b>Limitations:</b>	<ul style="list-style-type: none"> <li>• Publically-funded, patient-level prescription data is only available as of 2005 for PEI and as of 2006 for BC. We are therefore unable to determine testosterone use prior to that date.</li> <li>• There is no patient-level data available for publically paid prescriptions in Quebec, Newfoundland &amp; Labrador or the Territories. Therefore, we will be unable to make comparisons between Ontario rates and rates of use in these provinces.</li> </ul>

## Objective 2: Cross-provincial comparisons of characteristics of testosterone use in public drug programs

**Study Design:** Design: Cross-sectional analysis  
Study period: January 2012 to December 2012  
Data Sources:

- *National Prescription Drug Utilization Information System Database (NPDUIS)*: aggregated data for all publically funded prescriptions dispensed in Alberta, Saskatchewan, Manitoba, New Brunswick, Nova Scotia, PEI and BC
- *Ontario Drug Benefit Database (ODB)*: individual level data for all publically funded prescriptions dispensed in Ontario. This dataset contains additional variables (long-term care residence, public drug plan coverage) that is not available through NPDUIS

**Study Population:**

- Inclusion Criteria:
  - All publically-funded beneficiaries of Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, PEI and BC
  - Men
  - All Ages

**Outcome(s) of Interest:**

For each province, report:

- Number of patients eligible for public drug coverage
- Number and rate of testosterone users (overall and by testosterone formulation)
- Number and rate of testosterone prescriptions dispensed (overall and by testosterone formulation)
- Age at time of first prescription over the study period (Mean, SD)

Stratify the above analysis by age (<65, 65+) and formulation at drug initiation (oral, topical, patch, injectable)

**Limitations:**

- There is no patient-level data available for publically paid prescriptions in Quebec, Newfoundland & Labrador or the Territories. Therefore, we will be unable to make comparisons between Ontario rates and rates of prescribing in these provinces.

## Objective 3: Characteristics of testosterone users in the Ontario Public Drug Program

**Study Design:** Design: Cross-sectional analysis  
Study period: January 2012 to December 2012  
Data Source:

- *Ontario Drug Benefit Database (ODB)*: individual level data for all publically funded prescriptions dispensed in Ontario.

**Study Population:**

- Inclusion Criteria:
  - All publically-funded beneficiaries in Ontario
  - Men
  - All Ages

**Outcome(s) of Interest:**

## Patient level

- Total number of testosterone users
- Age (mean, SD and categories (<45, 45-55, 55-65, 65-75, ...))
- Total number of testosterone users living in urban vs. rural areas
- Total number of users by socioeconomic status (Income Quintile)
- Total number of users living in a LTC home
- Number of hospitalizations within the last 3 years
- Number of emergency room visits within the last 3 years
- Number of physician office visits within the last 1 year
- Specialist visit within the last year (yes/no):
  - Cardiologist
  - Endocrinologist
  - Urologist
- Charlson comorbidity score (based on last 3 years of hospitalization data)
- Comorbidity measures:
  - Hypogonadism
    - Physician visit with hypogonadism indicated within the past 3 years
    - Testosterone lab tests within the last 1 year
  - HIV any time in the past
  - Diabetes any time in the past
  - Cardiovascular diseases and procedures (past 3 years)
    - atrial fibrillation and flutter
    - angina
    - ventricular dysrhythmia
    - peripheral vascular disease
    - percutaneous coronary intervention
    - coronary artery bypass surgery
    - Stroke/TIA
    - Heart failure
    - AMI
    - Hypertension
- Any cardiovascular disease or procedure within the past 3 years (yes/no)

Stratify the above analysis by age (<65, 65+) and formulation at drug initiation (oral, topical, patch, injectable)

**Limitations:**

- Some comorbidities (e.g. hypogonadism) are not well captured in administrative data – therefore their sensitivity and specificity are unknown.

## Objective 4: Patterns of Testosterone Adherence in Ontario

### Study Design:

Design: Cross-sectional analysis

Study period: accrual January 2009 to December 2012;

maximum follow-up: December 2013

Data Sources:

- *Ontario Drug Benefit Database (ODB)*: individual level data for all publically funded prescriptions dispensed in Ontario.

### Study Population:

- Inclusion Criteria:
  - All publically-funded beneficiaries of Ontario who initiate testosterone therapy over the study period (defined as no prescription for testosterone in the past 365 days)
  - Men aged 66+ at time of testosterone first dispensing

### Outcome(s) of interest:

- Duration of Testosterone Therapy:
  - Define ongoing use of testosterone therapy according to receipt of a subsequent prescription within 120 days of the prior prescription.
  - Date of discontinuation: date of last prescription + days supply of final prescription
- Report the following:
  - Total number of new testosterone users
  - Number of individuals who received only 1 prescription for testosterone before discontinuing.
  - Among those with more than 1 prescription dispensed over period of continuous use:
    - Median duration of therapy
    - Number of different testosterone drugs (based on drug name) and formulations prescribed over the period of testosterone use
  - Stratify by formulation
    - oral, topical, patch, injectable
    - oral, topical ointment, topical gel, patch, injectable
  - Analysis: Kaplan Meier curves constructed and log-rank test used to test for differences by formulation.

### Limitations:

- Due to issues with incomplete data and unavailability of eligibility information, this analysis is restricted to patients aged 66 and older. Therefore, these findings may not be generalizable to the younger population.