ODPRN ONTARIO DRUG POLICY RESEARCH NETWORK

Agents for Overactive Bladder:

Pharmacoepidemiology Unit

FINAL COMPREHENSIVE RESEARCH PLAN

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Objectives

1. To examine national and provincial trends in use of agents for overactive bladder (OAB) across Canada
2. To perform cross provincial comparisons of the trends in utilization of OAB agents in public drug programs
3. To describe characteristics of individuals prescribed publically-funded OAB agents in Ontario
4. To investigate the average duration of OAB agent use among new users of these products in Ontario
5. Review of observational studies that explore the comparative safety and/or adherence of OAB agents

Objective 1: National and Provincial Trends in Overactive Bladder Agents Utilization

Study Design: Cross-sectional analysis with quarterly time intervals

Study Period: National and provincial trends (IMS Compuscript): October 2009 to March 2015

Population: All provinces

Data Sources: IMS Compuscript: aggregated data for all prescriptions dispensed at retail pharmacies across Canada

Inclusion Criteria: All privately and publically-funded OAB agent prescriptions dispensed in Canada:

- Darifenacin
- Fesoterodine
- Flavoxate
- Mirabegron
- Oxybutynin (all dosage forms)
- Solifenacin
- Tolterodine (all dosage forms)
- Trospium

Outcomes (measured quarterly):

- Number and rate of prescriptions dispensed
- Total cost of prescriptions

Stratifications:

- Province
- Payer (Public, Private, Cash, NIHB)
- OAB agent

Limitations: The IMS data is only available at the prescription and unit level. Therefore, national and provincial trends in prescribing cannot determine the number of *users* of these products

Objective 2:
Cross Provincial Comparisons of the Trends Overactive bladder agent Utilization in Public Drug Programs

Study Design: Cross-sectional analysis with quarterly time intervals

Study Period: January 2000 to June 2015

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.

Inclusion Criteria: All publically-funded OAB agent prescriptions dispensed in Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, PEI and BC

Outcomes (measured quarterly):
- Number and rate of users

Outcomes (measured in 2014 only):
- Number and rate of users
- Number of prescriptions dispensed
- Total costs of OAB agents
- Average cost of OAB agents per user

Stratifications:
- Province
- In 2014 only:
    - Age groups (<65, 65+)
    - OAB agents

Limitations:
- Publically-funded, patient-level prescription data is only available as of 2005 for PEI and 2006 for BC. We are therefore unable to determine OAB agent use prior to that date in these provinces.
- 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 use in these provinces.

Objective 3:
Characteristics of Individuals Prescribed Publically-Funded Overactive bladder agents in Ontario

Study Design: Cross-sectional analysis

Study period: April 2012 to March 2014

Data Sources:

- Ontario Drug Benefit Database (ODB)
- Canadian Institute for Health Information-Discharge Abstract Database (CIHI-DAD)
- Canadian Institute for Health Information- National Ambulatory Care Reporting System (CIHI-NACRS)
- Ontario Health Insurance Plan Claims Database (OHIP)
- ICES Physician Database (IPDB)

Inclusion Criteria: All publically-funded beneficiaries in Ontario who are prescribed an OAB agent

Cohort Entry Date: Date of first prescription for an OAB agent over the study period.

Index Drug: Defined as the OAB agent that was prescribed on cohort entry date. Those on combination will be reported separately

Note: *We will report the prevalence of various combinations but all combinations will be reported as one group.*

For the Established Cohort, Measure:

- Number of patients
- Age at cohort entry date (mean, SD, and by category (<65, 65-74, 75+))
- Proportion of patients who were male
- Proportion of patients residing in LTC at cohort entry
- Proportion of urban residents at cohort entry
- Socioeconomic status (measured using income quintiles at cohort entry)
- Prescriber of initial prescription:
    - Specialist
        - Urologist
        - Gynecology
    - General Practitioner
- Number of physician office visits within the last 1 year (median, IQR)
- Number of Emergency Department visits in the past 1 year (median, IQR)
- Number of hospitalizations in in the past 1 year (mean, SD)
- Proportion of patients in each daily dose range (Low or medium/high)
- Proportion with an OAB diagnosis in past 5 years (n, %)
- Proportion on dual OAB agents at index (n, %)
- Proportion with a previous prescription for onabotulinumtoxinA treatment for incontinence in previous 5 years (Limited Use code: 440) (n, %)
- Hospitalization in the last year for:
    - Falls/fracture (N, %)
    - UTI/ vulvovaginitis (N, %)
- Visit within the last 6 months to specialist (n, %)
        - Urologist
        - Gynecology
- Measures of Comorbidity
    - Charlson comorbidity score (based on last 3 years of hospitalization data)
    - Number of medications used in past 1 year
- Past medication use (120 days):
    - Psychotropics
    - Alpha-blockers
    - 5-alpha reductase inhibitors

Stratification:
- OAB agents

Objective 4:
Duration of OAB Agent Utilization Among New Users of These Products in Ontario

Study Design: Cohort Study

Study Period: January 2011-December 2014

Accrual Period: January 2011-December 2013

Maximum Follow-Up Date: December 2014

Data Sources:
- Ontario Drug Benefit Database (ODB)
- Canadian Institute for Health Information-Discharge Abstract Database (CIHI-DAD)
- Ontario Health Insurance Plan Claims Database (OHIP)
- ICES Physician Database (IPDB)

Inclusion Criteria: All publically-funded beneficiaries in over the age of 66 years of age Ontario who newly initiate an OAB agent over the study period.

- New users defined as those with no prescription for an OAB in the past 365 days

Cohort Entry Date: Date of first prescription for an OAB agent over the study period.

Index Drug: Defined as the OAB agent that was prescribed on cohort entry date

Duration of use:
Define ongoing use of OAB agent according to receipt of a subsequent prescription within 1.5 times the days supply of the prior prescription. If no subsequent prescription, then person discontinued use.

Date of Discontinuation: Date of last prescription + Days supply

Follow-up until First Of:
- Discontinuation of therapy
- Death
- End of study period (December 31, 2014)

Variables of Interest:

Outcomes:
- Median time to discontinuation of OAB agent (using Kaplan-Meier estimates) among those with more than 1 prescription
- Use of only one prescription (N, %)
- Number of different OAB agents within 1 year (mean, SD)
    - Agents switched to from Index drug
- Use of any OAB agent for over 6 months (N, %)
    - Proportion at one year using same agent as index agent (N, %)

- Use of any OAB agent for over 1 year (N, %)
    - Proportion at one year using same agent as index agent (N, %)

Note: The rate of mortality will be assessed to determine whether a competing risks analysis will be needed. Baseline characteristics between agents will be compared to determine the need to analyze difference in discontinuation rates using a Cox proportional hazards model.

Stratification:

- OAB agents

Limitations:

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

Objective 5:
Summary of Observational Literature Related to the Comparative Safety and Adherence of Overactive Bladder Agents

Objective:

Review of population-based studies investigating the comparative safety and/or adherence of OAB agents

Study Population:

Adults using OAB Agents

Study Design:

Rapid review of observational studies

- Comparative safety studies
- Comparative adherence/persistence studies

Study inclusion Criteria:

1. Observational study design
2. English Language
3. Published in last 10 years

Interventions:

OAB agents

Comparators:

OAB agents

Outcomes:

Any reported safety or adherence related outcomes