diltiazem and verapamil with respect to heart rate. Knowledge of rs2238018 status might be clinically relevant as heart-rate reduction can be either the objective of treatment or an adverse effect and might add to the future ambitions of tailored pharmacotherapy with diltiazem and verapamil; however, further studies on clinical relevant endpoints are needed.

360. Appropriateness and Persistence of Testosterone Replacement Therapy in the Public Payer System

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Background: Rates of prescribing for testosterone replacement therapy (TRT) products have been increasing in Ontario, Canada, despite criteria in the public drug formulary, which limit TRT to males with confirmed low serum testosterone levels associated with documented and symptomatic hypothalamic/pituitary/testicular disease or in HIV-infected patients.

Objectives: The objectives of this study were to evaluate the degree to which prescribing of TRT through the Ontario Drug Benefit program aligns with current prescribing criteria and to compare persistence between available formulations.

Methods: We conducted a retrospective cohort study of publicly funded testosterone utilization among males aged 66 years or older in Ontario between January 2009 and December 2013 using linked health administrative data. All males newly prescribed a testosterone product during the study period were included, and comparisons between TRT formulations were made among continuous users (individuals with a subsequent prescription within 180 days). We estimated the prevalence of hypogonadism and HIV and lab tests for serum testosterone in the year prior to therapy initiation. We also conducted a Kaplan–Meier analysis to test for differences in the median duration of therapy.

Results: Among the 6728 males initiating TRT over the study period, 47.5% of injectable users, 30.9% of transdermal patch users, 23.4% of topical users, and 22.8% of oral users received only one prescription. Among the 4797 continuous users, between 5.4% and 15.4% of users had a diagnosis of hypogonadism, and less than 1% had a diagnosis of HIV. Furthermore, the number of users with no prior testosterone lab test ranged from 29.0% for topical users to 39.5% for injectable users. The median duration of TRT differed significantly across formulations and was highest among oral users (383 days) compared with topical (319 days), injectable (283 days), and transdermal patch (160 days; $p < 0.001$) users.

Conclusions: A large proportion of older men in Ontario are initiating and remaining on TRT without meeting the listing criteria. Given the cardiovascular safety concerns of TRT, changes in listing of testosterone products should be considered to reduce inappropriate prescribing.

361. Patterns of Angiotensin Converting Enzyme Inhibitor Prescriptions for Different Indications: A Population-based Study

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Background: Angiotensin converting enzyme inhibitors (ACEIs) are widely prescribed. While ACEIs are usually initiated for lifelong treatment, many patients stop or switch treatment. Exploration of such patterns is important because the discontinuation of these drugs is associated with poor clinical outcomes.

Objectives: The aim of this study was to study usage patterns for different indications of ACEIs.

Methods: We defined a cohort of patients older than 45 years who started ACEI treatment between 2007 and 2013 in the Clinical Practice Research Datalink (CPRD). Indications for ACEI treatment (hypertension

(HTN), heart failure (HF), myocardial infarction (MI), renal failure (RF), or combinations of them (COT)) were retrieved from the medical records, and duration of ACEI treatment was calculated. We distinguished between continuous use, discontinued use, switch to an alternative drug, and restart, considering 6 months time interval between two prescription periods. Five-year persistence among the different indications was calculated using the Kaplan–Meier method, and times to discontinuation were compared using the log-rank test.

Results: In total, 222 058 patients initiating ACEIs were identified with the following indications: HTN (68.2%), MI (5.1%), RF (4.4%), HF (1.9%), and COT (20.4%). Five-year persistence rates were 62.4% for HF, 58% for HTN, 70.1% for MI, 45.5% for RF, and 55% for COT. Time to discontinuation was significantly different between indications (log-rank p-value < 0.0001). RF patients used ACEIs for the shortest period of time (average 23 months and median 13 months). Within the discontinuation group for different indications, the percentage of total switchers ranged from 37.6% for RF to 56.2% for HTN patients. For the patients who restarted, the percentages ranged from 12.6% for HF to 16.7% for RF patients. Of the 42 327 switchers, 58.6% switched to an angiotensin receptor blocker (ARB), which varied for different indications from 56.2% for HTN to 78.6% for MI patients.

Conclusions: Dependent on indication, there are different rates of discontinuation of ACEIs and switching to ARBs. Patients with RF are most vulnerable to discontinue treatment.

362. Methodological Issues in Harmonizing Data from Electronic Health Record Systems for International Pharmacosurveillance

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Background: Electronic health records (EHRs) are creating unprecedented opportunities to develop near real-time international pharmacosurveillance systems. To harness this potential, a variety of methodological issues need to be addressed, including data harmonization and the comparability of populations and health systems.

Objectives: The aim of this study was to estimate the impact of using (1) prescribed relative to dispensed prescription data to measure drug exposure, (2) diagnostic code-based versus clinical enriched data to assess co-morbidities, and (3) national differences in prescribing practices on the risk of cardiovascular events (CVE) with different hypoglycemic therapies in a population of newly treated diabetics.

Methods: EHRs from Britain, Canada, and the United States were used to assemble a cohort of 45 129 newly treated diabetics between 2011 and 2013. Time-varying measures of hypoglycemic use were created from prescription data and compared with dispensing data, as were national differences in drug use within therapeutic class. Obesity, renal impairment, and hyperlipidemia were measured using diagnostic codes and compared with enriched measures using clinical data. Cox proportional hazards models were used to assess the impact of different methodological approaches to risk assessment.

Results: Twenty-five percent of prescriptions were never filled, resulting in biased estimates of the effect of non-drug use on the risk of cardiovascular events. There were fourfold increases in the prevalence of obesity using BMI (13% to 60%), renal impairment using creatinine (12% to 47%), and lipid disorders (16% to 47%), but had no impact on confounding related to drug exposure. There was a twofold increase in the risk of CVE with sulfonylureas in the United States (HR: 3.3 95%CI: 2.0–5.5) compared with Britain (HR:1.4 95%CI: 1.1–1.7), which may be explained by substantial differences in the sulfonylureas used in Britain.

Conclusions: EHRs can improve measurement of drug exposure and morbidity and elucidate potentially important differences in the risk of drug use in different countries.

363. Pharmacy Drug Dispensing after Physician Discontinuation Orders

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