The Canadian Association for Population Therapeutics / Association Canadienne pour la Thérapeutique des Populations presents:

"20 Years of CAPT: How Far We Have Come"

ABSTRACTS:

October 17th – 18th, 2016
Toronto, Ontario
MaRS Discovery District
101 College Street

J Popul Ther Clin Pharmacol Vol 23(Supplement 1):e1-e27; November X, 2016

ORAL PRESENTATIONS

1: Factors Associated with Usage of Castration-Resistant Prostate Cancer Treatments: Population-Based Study

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Background: Castration-resistant prostate cancer (CRPC) management currently comprises several different treatments. However, evidence is currently lacking in terms of their uptake in the real-world setting. This study aims to assess factors associated with utilization of CRPC treatments in Quebec.
Methods: The cohort selected patients dying of prostate cancer from January 2001 to June 2013 from the Quebec public healthcare insurance program databases based on reception of CRPC treatments. Multivariable logistic regression was used to identify patient and geographic factors associated with the use of specific CRPC treatments (chemotherapy, bone-targeted therapy, and palliative radiotherapy).
Results: The study cohort consists of 2898 patients overall, of which 19% of patients received chemotherapy, 26% received bone-targeted therapy and 21% received palliative radiotherapy. Following multivariable adjustments, use of chemotherapy was associated with age (odds ratio (OR): 0.94; 95% confidence interval (CI): 0.92-0.95), previous local primary treatment (OR: 1.36; 95%CI: 1.11-1.66), and residing close to a university-affiliated hospital (OR: 2.02, 95%CI: 1.55-2.63). Concerning bone-targeted therapy use, older age (OR: 0.97; 95%CI: 0.96-0.99) was associated with decreased use. Use of palliative radiotherapy was associated with age (OR: 0.96; 95%CI: 0.95-0.97), and previous local primary treatment (OR: 1.52; 95%CI: 1.26-1.84). Additionally, patients receiving one type of CRPC treatment also likely received the other types of CRPC treatments (ORs ranging from 1.50 to 3.35, all $p<0.05$).
Conclusions: In our cohort, the type of initial primary treatment was associated with certain treatment patterns in CRPC. Older age is also associated with decreased use of chemotherapy, bone-targeted therapy and palliative radiation.

2: Are the Benefits of Statin Cholesterol Reduction Over Estimated by the Cholesterol Treatment Trialists? A Meta-Regression Study of Bias in Statin Trials

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Background: The Cholesterol Treatment Trialists' (CTT) Collaboration has published a series of meta-analyses of the effects of statins in which the authors link relative reductions in the rate of cardiovascular morbidity and mortality to levels of absolute lowering of low-density lipoprotein (LDL) cholesterol. We aimed to investigate whether bias in RCTs of statins included in previous CTT meta-analyses resulted in over-estimation of reductions in major coronary events, nonfatal myocardial infarction (MI) and mortality.
Methods: We conducted meta-regression analyses relating absolute reduction in LDL cholesterol to major coronary events, nonfatal MI and all-cause mortality, comparing crude estimates to estimates adjusted for baseline LDL cholesterol and risk of bias. The meta-regression included 27 RCTs analyzed by the CTT in a 2012 meta-analysis and used data published by the CTT and from the original trial publications. The influence of a 1 mmol/L absolute reduction in LDL was estimated using random effects meta-regression.
Results: When adjusted for risk of bias and baseline LDL cholesterol, model effect estimates for absolute reduction in LDL cholesterol moved closer to the null for major coronary events (from risk ratio 0.80, 95%

CI 0.72-0.90, to RR 0.89, CI 0.76-1.05); nonfatal MI (from RR 0.79, CI 0.69-0.90, to RR 0.83, CI 0.68-1.02); and all-cause mortality (from RR 0.91, CI 0.81-1.03, to RR 0.95, CI 0.87-1.04).
Conclusions: Our findings suggest that bias in the trials included in CTT meta-analyses led to over-estimation of reductions in major coronary events, nonfatal MI and all-cause mortality related to reductions in LDL cholesterol.

3: Incidence of Mood and Anxiety Disorders and Psychotropic Use in Spouses of Dementia Individuals: A Population-Based Study

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Background: Spouses of dementia patients face tremendous physical, emotional and financial stress. This study aimed to quantify the incidence of mood and anxiety (MAD) disorders, as well as the incident use of psychotropic drugs in spouses of dementia individuals in the community setting.
Methods: In this population-based, matched cohort study using the Manitoba administrative databases between April 1998 and March 2015, each spouse of dementia individuals were matched to three comparison spouses based on age, sex and geographic region. Applying a 3-year washout period, risk of clinical depression, anxiety and other stress-related disorders and new users of psychotropic medications were estimated using cox-proportional hazards models, adjusting for matching variables, socioeconomic status and comorbidities.
Results: Over a median follow-up period of 3.5 years (IQR 1.3 to 7.0 years), we observed 2,768 cases of MAD among 13,463 spouses of dementia individuals, and 5,432 cases among 42,264 comparison spouses. The adjusted HR for mood and anxiety disorder was 1.63 (95% CI 1.56 0 1.71; p<0.0001) compared to spouses without a dementia partner. Incident use of psychotropic drugs was 84.5 (95% CI 82.9 – 86.1) per 1000 person-years and 57.3 (95% CI 56.7 – 57.9) per 1000 person-years for dementia spouses and non-dementia spouses, respectively, with an adjusted HR of 1.48 (95% CI 1.42 – 1.53; p<0.0001). Incident uses of antidepressants, benzodiazepines, other sedatives and antipsychotics were all significantly higher for dementia spouses.
Conclusion: A higher risk of psychiatric morbidity and psychotropic drug use can be attributed to having a spouse with dementia.

4: Preliminary Evaluation of the Use of Integrated Comprehensive Care (ICC) Bundle Care Program When Treating Patients with Chronic Obstructive Pulmonary Disease

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Background: The St. Joseph's Health System has recently implemented an integrated comprehensive care bundle care (ICC) program with the hopes that it would improve patients' care while reducing overall costs. The aim of this analysis was to evaluate the performance of the ICC program within patients admitted with chronic pulmonary obstructive disease (COPD) and provide recommendations for future studies of complex healthcare interventions.
Methods: We conducted a retrospective observational cohort study comparing ICC patients to Non-ICC patients admitted to St. Joseph's Healthcare Hamilton for COPD being discharged with support services between June 2012 and March 2015, using administrative data. Confounding adjustment for patients' age, gender, prior number of hospitalizations and seasonality of the initial hospitalization was achieved through the

use of propensity score matching. Medical resource utilizations during the initial hospitalization and within the 60 days following discharge were compared using regression models.
Results: Seventy-six out of the 268 eligible Non-ICC patients (28.4%) were matched 1:1 to all 76 patients who entered the ICC program. Matching achieved balance on all four baseline characteristics. Length of stay (6.47 [7.29] vs. 9.55 [10.21] days, p-value < 0.01) and resource intensity weights (1.16 [0.80] vs. 1.64 [1.69], p-value < 0.01) were lower in the ICC group within the initial hospitalization but healthcare resource use did not statistically differ following discharge although numerical differences were observed in favour of ICC.
Interpretation: The ICC program was able to reduce initial medical resource utilization without increasing subsequent medical resource use.

5: The Efficacy of Fall-Risk-Increasing Drug (FRID) Withdrawal on Falls Prevention: A Systematic Review and Meta-Analysis

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Funding: None

Background: Falls are the leading cause of injury and injury-related hospitalizations for seniors in Canada with annual healthcare costs exceeding $2 billion. Despite limited evidence of effectiveness, the withdrawal (discontinuation or dose reduction) of fall-risk-increasing drugs (FRIDs) is typically part of falls prevention strategies and Accreditation Canada ROP initiatives.
Objectives: To determine the preventive efficacy of FRID withdrawal on falls and fall-related complications.
Methods: Electronic search conducted in MEDLINE, EMBASE, CENTRAL and CINAHL. Grey literature search included trial registries and conference abstracts. All randomized controlled trials in adults aged 65 evaluating FRID withdrawal compared to usual care on falls rate or incidence, fall-related injuries, fractures or hospitalizations and/or adverse effects related to the intervention were included. Two reviewers independently screened eligible studies, abstracted data and assessed risk of bias. The GRADE criteria were used to rate overall confidence in effect estimates for each outcome.
Results: Five trials involving 1309 participants met eligibility criteria for inclusion. A FRID withdrawal strategy did not significantly change the rate of falls (RaR 0.98, 95% CI 0.63 to 1.51), number of fallers (RR 1.06, 95% CI 0.84 to 1.34) or rate of fall-related injuries (RaR 0.89, 95% CI 0.57 to 1.39) over a 6- to 12-month follow-up period.
Conclusions: There is insufficient evidence that a FRID withdrawal strategy is effective for preventing falls. Based on very low quality evidence, it is uncertain whether FRID withdrawal leads to any appreciable clinically important benefit. Data evaluating the potential harms of FRID withdrawal is lacking.

6: Impact of Early In-Hospital Medication Review by Clinical Pharmacists on Health Services Utilization

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Background: Adverse drug events (ADEs), a leading cause of emergency department visits and prolonged hospital stays, are commonly missed by physicians, contributing to poor health outcomes. We assessed the effect of pharmacist-led medication review on the health outcomes of high-risk emergency department patients.
Methods: Using a quasi-randomized design, we evaluated a quality improvement project in three British Columbian hospitals. A clinical decision rule incorporated into triage pathways allowed identification of patients at high-risk for ADEs. After randomly selecting the first eligible patient, we systematically allocated subsequent patients to medication review (comprising a best-possible medication history and reviewing medications for appropriateness and ADEs) or usual care. The primary outcome, the number of days spent in-

hospital over 30 days, was ascertained using administrative data. We used median and inverse propensity score weighted logistic regression to determine the effect of medication review on downstream health services use.
Results: Of 10,807 patients, 6,416 received the intervention and 4,391 usual care. The median number of hospital days was reduced by 8% [0.48 days (95%CI: 0.00-0.96; p=0.058)] in the medication review group compared to usual care, and by 11% [0.60 days (95%CI: 0.06-1.17; p=0.03)] among patients aged under 80. There was no significant effect on emergency department revisits, admissions, re-admissions, or mortality.
Conclusion: Early pharmacist-led medication review was associated with reduced hospital-bed utilization compared to usual care among high-risk patients under 80 years old. These results suggest that pharmacist-led medication review in emergency departments may impact the subsequent length of stay in select patient populations.

7: Primary Non-adherence to Inhaled Corticosteroids According to Indication for Use

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Objective: To describe adherence to incident prescriptions for ICS therapy according to indication for use.
Methods: Electronic prescribing data from the Medical Office of the XXI Century (MOXXI) research platform was utilized which is used by over 150 family physicians in Quebec City and Montreal. MOXXI features an electronic prescribing interface that requires physicians to document at least one treatment indication per prescription. Study patients were those who received an incident ICS prescription between January 1 2003 & December 31 2013. Indications for ICS therapy were categorized according to acute respiratory conditions (eg. cough) and chronic respiratory conditions (eg., asthma). Drug dispensing data from the Quebec pharmanet system were also utilized to determine patient adherence to incident ICS prescriptions.
Results: 2,328 patients were prescribed incident ICS therapy where mean (SD) age was 62 (18) and 65% were female. The most common indication for ICS treatment was asthma (62%), followed by chronic bronchitis (18%) and COPD (13%). Overall, 423 (18%) patient did not fill their incident ICS prescription within 12 months where patients with an acute respiratory condition were less likely to fill their prescription (36% primary non-adherence) compared to those with a chronic respiratory condition (18% primary non-adherence). Specifically, primary non-adherence in patients with COPD/emphysema, chronic bronchitis and asthma as the indication for treatment were 9%, 7%, and 23% respectively.
Conclusion: Primary non-adherence differed according to indication for ICS use. Further research is required to determine the impact of adherence to ICS therapy and respiratory related adverse events according to indication.

8: Tramadol and the Risk of Seizure: A Retrospective Cohort Analysis

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Background: Tramadol is a widely prescribed analgesic that influences both opioid and monoamine neurotransmission. Seizures emerged as a concern within a year of its US market entry in 1995, but the risk has not been adequately studied in post-market analyses. We examined the risk of seizures with tramadol relative to codeine, another pharmacologically similar opioid.
Methods: A nested case-control study among

patients in US MarketScan databases. In the primary analysis, we defined cases using a broad definition of seizure, based on either an outpatient physician claim for seizure disorder or a seizure-related emergency department visit or hospitalization. In a secondary analysis, we used a more specific definition of seizure restricted to principal diagnosis of seizure in an emergency room visit or hospitalization. We selected controls matched on age, sex, state of residence and cohort entry within 365 days. Conditional logistic regression was used to estimate rate ratios associated with tramadol versus codeine (>=15 mg) within 30 days of index date.

Results: We identified 96,753 cases and 888,540 controls. In the primary analysis, we found no increased risk of seizure among patients treated with tramadol compared to codeine (rate ratio 1.03; 95% CI 0.93 – 1.15). However, in the secondary analysis, we observed a higher relative risk of emergency department visit or hospitalization for seizures (rate ratio 1.41; 95% CI 1.11 – 1.79).

Conclusions: Tramadol use is associated with an increased risk of emergency room visits or hospitalization for seizures. However, this finding was sensitive to the outcome definition used.

9: Characterizing the Utilization of the Trillium Drug Program by an Oncology Patient Population

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Objectives: The Trillium Drug Program (TDP) was developed for Ontarians who require financial assistance for prescription drug costs. The aim of this study was to analyze TDP utilization overall and specific to cancer.

Methods: Individuals with a cancer diagnosis from 2000-2009 were ascertained from the Ontario Cancer Registry. The Ontario Drug Benefit database was used to identify TDP claims with plancode “T” “F”. Patients were then grouped as: (1) no TDP claims and age < 65; (2) no TDP claims and age < 65; (3) first TDP claim before diagnosis; (4) first TDP claim on or after diagnosis. A 3-year lookback window was used to determine claim history. Baseline characteristics of the patient population in each TDP usage group were examined.

Results: There were 525,820 individuals in the cancer cohort, 238,554 (45.4%) of which were <65 years at diagnosis. The majority (98.5%) of the cancer patients were never on TDP. Of the 5,407 TDP individuals with a claim after cancer diagnosis, 4,654 were <65 years. This TDP cohort’s average age was 61.4 years, 53.5% were male and 23.2% had prostate cancer. Their first TDP claim came on average 1,604 days (4.4 years) after cancer diagnosis.

Conclusions: This is the first attempt to characterize TDP in oncology so it is difficult to assess whether or not our results confirm that the TDP is being underutilized. The authors plan to conduct further analysis to determine further characteristics of TDP utilization over time and across cancer disease sites.

10. Risk of Mortality Associated with Starting DPP-4 Inhibitors in a Cohort of New-Users of Metformin with Chronic Kidney Disease

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Background: To assess risk of mortality associated with starting dipeptidyl peptidase-4 inhibitors (DPP4i) in new-users of metformin monotherapy with chronic kidney disease (CKD). We hypothesized that DPP4i will be associated with a lower mortality risk compared to other antidiabetic agents.

Methods: This was a cohort study conducted using the UK Clinical Practice Research Datalink database. Among new-users of metformin monotherapy, we identified patients >30 years of age with CKD [<2 eGFR values <60mL/min/1.73 m^2 >90-days apart] who initiated a DPP4i, sulfonylurea (SU), insulin, or thiazolidinedione (TZD). Multivariable Cox's hazard regression was used to assess the association between starting DPP4i, SU, insulin, and TZDs as second-line agents.
Results: We identified 7,773 patients with CKD prior to initiating their second-line agent [1,023 DPP-4i, 5,688 SU, 161 insulin, and 754 TZD]. There were 6413 patients with Stage 3A (eGFR 45-<60); 1235 with Stage 3B (30-<45); 113 with Stage 4 (15-<30); and 12 with Stage 5 (<15) CKD. Mean age was 70 years, 46% were male, and mean follow-up was 1.5 years. There were a total of 705 deaths [DPP-4i=22.1 deaths/1000 person-years; SU=39.9 deaths/1000 person-years; insulin=141.6 deaths/1000 person-years; TZD=14.9 deaths/1000 person-years]. The adjusted hazard ratio for mortality among second-line DPP4i initiators was 0.74 [95%CI 0.52-1.04, p=0.08] vs. SU initiators; 0.96 [95%CI 0.59-1.56, p=0.9] vs. TZD initiators; and 0.28 [95%CI 0.18-0.45, p<0.001] vs. insulin initiators.
Conclusion: Second-line DPP4i therapy was not associated with a significant reduction in mortality compared to SUs or TZDs but showed a protective effect compared to insulin in patients with CKD.

POSTER PRESENTATIONS

11: Utilization of Psychotropic Drugs in Spouses of Dementia Individuals: A Population-Based Study

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Background: Limited studies suggested increased prevalence of depressive symptoms amongst dementia spouses, but little is known about utilization of psychotropic medications in this population. This study aimed to evaluate the prevalent use of psychotropic medications amongst spouses of dementia individuals in the community setting.
Methods: In this population-based, matched cohort study using the Manitoba administrative databases between April 1998 and March 2015, spouses of dementia individuals were matched to three comparison spouses based on age, sex and geographic region. Use of psychotropic drugs was evaluated based on corresponding ATC codes for antidepressants, sedatives and antipsychotics. Prevalent use of psychotropic medications was calculated as defined-daily dose (DDD) per person years, and intensity of use was estimated as DDD per user per year from the index date.
Results: Over a median follow-up period of 4.4 years (IQR 1.8 to 8.5 years), we observed 10,038 users of psychotropic drugs amongst 13,463 spouses of dementia individuals, and 22,992 users among 42,264 comparison spouses. DDD rate was 142.6 (95% CI 142.5 – 142.6) per person-year and 84.5 (95% CI 84.4 – 84.5) per person-year for dementia spouses and non-dementia spouses, respectively. DDD rates were significantly higher for dementia spouses for all subclasses of psychotropic drugs. Intensity of use over time amongst psychotropic users was not significantly different between the dementia and non-dementia spouses.
Conclusion: Psychotropic drug use was more prevalent in spouses of dementia individuals compared to non-dementia spouses. However, there was no difference in intensity of use amongst users of the two groups.

12: Prospective Validation of Clinical Decision Rules to Identify Emergency Department Patients at High Risk of Adverse Drug Events

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Introduction: Adverse drug events (ADEs), a leading cause of emergency department visits and unplanned admissions, are commonly missed by

physicians. Our objective was to validate previously-derived clinical decision rules, which identify emergency department patients at high risk for ADEs, in a new patient sample.
Methods: This multi-centre (three hospitals in two provinces), prospective study enrolled adult emergency department patients over 12 months. Nurses evaluated patients for standardized clinical findings, and applied the rules prior to assessments by clinical pharmacists and treating physicians. The primary outcome was a moderate or severe ADE, an unintended and harmful medication-related event requiring a change in therapy, diagnostic testing, consultation, or admission. An independent committee adjudicated uncertain and discordant cases. We calculated the diagnostic accuracy of each rule.
Results: Among 1529 patients, 191 (12.9%) were diagnosed with an ADE. The rule containing the variables (i) having a pre-existing medical condition or having taken antibiotics within one week, and (ii) age > 80 or having a medication change within 28 days, had a sensitivity of 91.1% (95%CI: 86.1–94.7%) and a specificity of 38.1% (95%CI: 35.5–40.8%) for ADEs when applied by pharmacists. In this cohort, 39.9% of patients would have proceeded to medication review having screened high-risk.
Conclusions: This rule was sensitive in identifying ADEs. Its implementation would limit the number of clinical pharmacist-led medication reviews required to identify the majority of ADEs in acute care patients. These are the first validated criteria allowing hospitals to meet Accreditation Canada's requirement to risk-stratify incoming patients for medication review.

13: Hypoglycemia Reporting and the Design of Randomized Clinical Trials (RCTs): A Systematic Review on RCTs Conducted for SGLT-2 Inhibitors

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Background: Hypoglycemia is a significant side effect of diabetes pharmacotherapy. The workgroups from the American Diabetes Association and the Endocrine Society tried to address defining and reporting hypoglycemia with clinical practice guidelines and scientific statements. Objective: To explore the association between reporting hypoglycemia occurrences during RCTs and the design of RCTs.
Methods: A systematic review utilizing PubMed for obtaining data on RCTs conducted for SGLT-2 inhibitors limited to the English language.
Results: The RCTs, which had at least 2 phases including a core period and an extension period, were included in this analysis. In total, 8 published studies were found. The length of the core period from the RCTs was on average 36(14) weeks [mean(SD)] and the length of extension period on average was 67(14) weeks. On average, the reported rate of hypoglycemia for core period was 9.8%(13%) and for the extension period was 2.5%(1.8%). The absolute risk difference between the rate of hypoglycemia reported for the core period and the extension period was 7.3%, which clinically is important, however, is statistically not significant (p=0.07).
Conclusion: This study illustrates that there are critical differences for reporting hypoglycemic events between the core period and the extension period of RCTs conducted on SGLT-2 inhibitors. This may indicate differences between protocols for the 2 periods or susceptibility of patients to hypoglycemia during up-titration or dropping out of susceptible patients during the core period of RCTs. This is important for the safety evaluation of diabetic medication and the length of exposure.

14: Suicide After Intentional Drug Overdose in Canadian Youth: A Population-Based Cohort Study

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Background: Suicide is the second most common cause of death among Canadian youth (10-35yrs), and poisoning is the leading method of attempted suicide. Unlike violent methods, survival following overdose is common, providing an opportunity for secondary prevention.
Methods: We conducted a population-based cohort study using multiple linked healthcare databases in Ontario, Canada from January 2001 to December 2012. We identified all adolescents aged 10-20 years presenting to hospital after a first intentional overdose. Each was matched with 50 population-based reference subjects with no such history, matching on age, sex and calendar year. We determined the risk, time course and predictors of completed suicide after adolescent intentional drug overdose.
Results: We identified 20,471 adolescents discharged following overdose and 1,023 487 matched controls. Over a median follow-up of 7 2 years (cumulative 7,215 751 person-years) 248 (1–2%) adolescents died, most (n=126; 51%) by suicide. The risk of suicide following overdose was markedly increased relative to controls (HR 32–1; 95%CI 23 6 to 43 6). Median time from hospital discharge to suicide was 3–0 (IQR 1.1 to 5–3) years. Predictors of suicide included recurrent overdose (HR 3.5; 95%CI 2.4 to 5.0), male sex (HR 2–5; 95%CI 1–8 to 3–6) and recent psychiatric care (HR 1 7; 95%CI 1 1 to 2 5). Adolescents hospitalized for overdose were also more likely to die from all causes (HR 3.9; 95% CI 2.8 to 5.4) during follow-up.
Conclusions: Intentional overdose is a strong predictor of suicide and premature death in the ensuing decade, and identifies a high-risk group for targeted, sustained prevention efforts.

15: Treatment Patterns for Advanced Prostate Cancer in Contemporary Era in Quebec

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Objective: This study aims to identify factors that are associated with metastatic castration-resistant prostate cancer (mCRPC) management in a real-life setting and to describe the impact of abiraterone (abi) introduction in Quebec in 2012.
Methods: The study cohort consists of patients treated for mCRPC at the Jewish General Hospital and the Montreal General Hospital from 2010 to 2014. Patient information was collected retrospectively. Then, the cohort was divided into two groups regarding their mCRPC diagnosis year (pre/post-2012). Kaplan-Meier and Cox regression were used.
Results: Analysis of 320 patients indicated that the median age at CRPC was 74.0 yo. First line treatments for mCRPC in the pre-2012 group were doce (51%) and doce (30%) and abi (26%) in the post-2012 group. Overall, 84% of patients received doce and 48% received abi in the pre-2012 group vs 55% and 77% in the post-2012 group. Metastases at CRPC diagnosis were predictors of receiving doce and abi: bone and lymph nodes ([HR: 2.4; 95%CI 1.4 – 4.1], [HR: 1.9; 95%CI 1.1 – 3.2]), visceral ([HR: 3.3; 95%CI 1.8 – 6.2], [HR: 2.4; 95%CI 1.3 – 4.7]), respectively. Being younger than 80 y/o at CRPC diagnosis was a predictor of having doce (HR: 1.9; 95%CI 1.3 – 2.8).
Conclusion: Current study showed that metastases extent and moment of diagnosis with mCRPC are predictive factors for receiving doce or abi, younger patients were more likely to receive doce. It also showed that the introduction of abi led to a decline in the use of docetaxel.

16: Cost and Management of Targeted Treatments for Metastatic Renal Cell Carcinoma Patients in Canada

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Funding: MUHC

Background: The objective of our study was to evaluate the economic impact of targeted therapies for the treatment of clear cell metastatic RCC in Canada using real-world data through The Canadian Kidney Cancer information system (CKCis).
Methods: CKCis was used to select the cohort of advanced RCC patients. The use of targeted treatment was needed in order to include the

patients, as well as starting and ending dates. The database was used to describe the health care utilization of targeted therapies over the advanced phase of the disease and to estimate the associated cost. Unit costs of targeted therapies were pulled from the RAMQ list of medications.
Results: The cost of targeted therapy per patient for a median follow-up of 23 months was $55,986. Using 2 lines of therapies cost in average $83,314 per patient for a median follow-up of 25 months. Few patients received 3 lines of treatment; this leads to an additional cost of $16,764, totalling an average of $100,078 per patient. 366 patients had one treatment line, 132 had two and 33 patients had 3 lines. Among patients receiving targeted therapies, 85% of patients received sunitinib, 23.3% received everolimus, 21.6% received pazopanib and 11.5% were treated with axitinib. Patients receiving therapy were on treatment for a median of 10.5 months, 7.1 months and 4.6 months for each line of therapy, which is consistent with the PFS results found in the literature.
Conclusion: The findings of this study might inform decision-makers concerning budget planning and funding.

17: Utilization of Benzodiazepine and Antipsychotic Medications in Urban versus Rural Dwelling Seniors in Newfoundland and Labrador

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Objective: To compare prescription rates of benzodiazepines and antipsychotics in seniors living in urban and rural areas within Newfoundland and Labrador (NL).
Methods: Individuals aged 65 and older who received NL drug coverage between 1April2011 and 31March2014 were identified using the NL Prescription Drug Plan database and linked with the provincial registry and Meditech long-term-care module. Direct age-sex standardized rates of prescription for the drugs of interest per 1,000 total prescriptions were used to compare drug use across area for those living in long-term-care facilities (LTCFs) and the community. General linear modelling with auto-regressive correlation was used to assess differences in prescription rates by area.
Results: Of the 4,966,944 prescription records examined 338,402 (6.8%) were for seniors in LTCFs. Among seniors in LTCFs, mean age was 84 years, 29.4% were male, and received an average of 24 prescriptions per quarter. Among those in the community, mean age was 75 years, 42.6% were male, and received an average of eight prescriptions per quarter. Prescription rates for benzodiazepines were higher in urban (41/1,000) versus rural (39/1,000) LTCFs. For those prescribed benzodiazepines in the community, prescription rates were higher in urban (56/1,000) than rural (45/1,000) areas. A similar pattern was observed for antipsychotic use in community dwelling seniors in urban (17/1,000) versus rural (11/1,000) residents. However, antipsychotic prescription rates were lower in urban (54/1,000) compared to rural (57/1,000) residents living in LTCFs.
Conclusion: Given the differences observed in prescription rates by geographic locale, further investigation into factors explaining these differences is warranted.

18: Determining the Cost of Equipment and Supplies of Radiation Therapy Departments Using Management Information Systems Data

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Objectives: The cost of radiation therapy (RT) is variable and few studies have accounted for the cost of RT equipment and supplies. The objective of this study was to determine the cost of equipment and supplies of RT departments at Ontario institutions

using management information systems (MIS) data.
Methods: Costs were obtained from the 2012 MIS financial data using the primary account code for Radiation Oncology (71466), and secondary MIS codes for equipment (71000-79000, 94000) and supplies and miscellaneous (4****, 6****). RT visits were obtained from the 2012 National Ambulatory Care Reporting System (NACRS) using Canadian Classification of Health Interventions (CCI) codes 1.**.27. Individuals without a valid Ontario Health Card number were excluded from the study. An RT visit was defined as a single patient-institution-day encounter. Total MIS costs were divided by the total number of RT visits, for an equipment and supplies cost per RT visit.
Results: All costs are in 2012 Canadian dollars. Fourteen institutions had both MIS costs ($51,783,346) and RT visit (563,776) information. There was wide variation in equipment and supplies cost per visit, from $6.88 to $196.68. The mean equipment and supplies cost per RT visit was $100.43 – $54.69, and the median was $102.46 (interquartile range: $69.10 – $133.44).
Conclusions: This is the first attempt to calculate an average cost per RT visit for equipment and supplies using current MIS data. The authors are working on developing a costing algorithm for RT cost per visit.

19: Shifting Trends: An Analysis of IV and Take-Home Cancer Drug Use and Public Spending in Ontario

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Background: The development and use of oral chemotherapy and other take-home cancer drugs (THCD) have significantly increased over the past decade. Ontario Public Drug Programs provides public funding for outpatient use of both THCD and intravenous cancer drugs (IVCD). To inform system planning and support sustainable reimbursement policies, we examined trends in costs and utilization of THCD and IVCD over the last 6 fiscal years (2010-2015).
Approach: Ontario Drug Benefit claims data, sourced from the Institute of Clinical Evaluative Sciences, were reviewed to identify 74 THCD for inclusion. Claims data were obtained for all 39 IVCD funded through Cancer Care Ontario's New Drug Funding Program. Annual government costs and number of utilizing recipients were collected to estimate average annual growth rates (AAGRs).
Results: At the time of analysis, government spending on THCD rose from $199 to $371 million over a six-year span at an AAGR of 13.4%. Spending on IVCD increased from $219 to $344 million at an AAGR of 9.7%. In 4 of the 6 years, THCD spending was higher than IVCD. Over the 6 years, the number of utilizing recipients grew by 25.4% for THCD compared to 15.3% for IVCD. In 15/16, 98,548 and 28,315 recipients had claims for THCD and IVCD respectively.
Interpretation: While both utilization and costs of IVCD and THCD continue to grow, use, spending and growth for THCD have outpaced IVCD. This expansion from the cancer clinic to home-based care may have implications for patient care and for cancer drug reimbursement policy.

20: Patient-Centred Outcomes and Health-Related Quality of Life Measures in RCTs Conducted on SGLT-2 Inhibitors (A Systematic Review)

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Funding: None

Background: SGLT-2 inhibitors utilization has been associated with weight loss and low rate of hypoglycemia in comparison to SU utilization. These factors can improve health-related quality of life for patients with diabetes. Evidence illustrates that weight loss and avoidance of hypoglycemia will increase the feeling of well-being amongst patients with diabetes.
Objective: To systematically explore RCTs on SGLT-2 inhibitors for measuring and reporting health-related quality of life changes and patient-centred outcomes during conducting RCTs.
Method: Systematic review of SGLT2 receptor inhibitors limited to RCTs and English language was conducted utilizing PubMed databases.
Results: Totally, 118 RCTs were reviewed and 62 RCTs were included in the study, which met the inclusion criteria. PK/PD studies and RCTs or non-outcome RCTs or short-term (under 12 weeks)

RCTs or duplicate published RCTs were excluded from the review. All studies/RCTs (62) reported BMI changes and HgbA1c reduction; however, only 55 studies (88%) reported hypoglycemia events. Furthermore, measures of Health-Related Quality-of-Life (HRQofL) were reported only in 2 RCTs (1.5%); one study on dapagliflozin and one study on canagliflozin. Furthermore, establishing the difference between un-measured and non-reported versus measured and non-reported HRQofL variables with reviewing the protocols of RCTs was not possible.
Conclusion: Despite evidence of improving HRQoL with weight loss and hypoglycemia avoidance, only a small portion of RCTs on SGLT-2 inhibitors reported HRQofL. Future studies should consider measuring and reporting patient-centred outcomes such as HRQofL variables during RCTs.

21: Truvada for Pre-exposure Prophylaxis

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Daily use of Truvada (emtricitabine/tenofovir disoproxil fumarate) in HIV-negative individuals is known as PrEP (pre-exposure prophylaxis) and is indicated in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 in adults at high risk.A simplified economic evaluation determined the cost-effectiveness of Truvada for PrEP versus placebo, from a health care system perspective. The outcome was the cost per HIV infection prevented over 100 person-years of treatment. Clinical inputs for the model were informed by trials of efficacy (in men who have sex with men [MSMs], serodiscordant heterosexual couples, and single heterosexuals) plus two pragmatic trials of effectiveness (both in Western MSMs). The rate of reduction in HIV incidence seen in Western pragmatic trials (86%) was applied. The baseline incidence of infection varied from 2.0 to 9.0 per 100 person-years of treatment, depending on the population studied. Cost of Truvada included drug therapy ($29.08 per day, markup, dispensing fee) and management (physician visits, lab tests). The lifetime cost per HIV infection ($320,571) was determined from the literature. Costs were in 2016 Canadian dollars. At higher rates of infection (as seen in Western MSM populations), Truvada for PrEP was dominant – more effective and less expensive than placebo. Truvada for PrEP became cost saving at a baseline HIV infection rate of 4.3 per 100 person-years. Below this rate, the cost of Truvada for PrEP could still be cost-effective. The main limitation of this simplified analysis was that it excluded projections beyond the observed person-years of treatment.

22: A Population-Based Study of Health Care Costs and Survival for Dialysis Patients in Ontario

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Background: Policy initiatives to expand home dialysis in Ontario require comprehensive evidence concerning potential benefits. This study estimated healthcare costs and survival for all dialysis modalities.
Methods: Ontario patients aged >18 years who initiated chronic dialysis from April 2006 to March 2012 were selected from registry data (N=9,302), and grouped by initial modality: facility hemodialysis (HD), home HD, facility short daily or slow nocturnal HD (SD/SN), peritoneal dialysis (PD). We estimated

cumulative and monthly costs ($2012 Canadian) from the public payer perspective for all healthcare, including non-dialysis-related, from dialysis initiation to kidney transplantation, death, or March 2013, with covariate adjustment (age, co-morbidity, sex). We used Cox's proportional hazards model to estimate effects of modality and covariates on survival.
Results: Most patients (75.2%) initiated facility HD, 23.5% PD, <1% home HD or facility SD/SN. Mean adjusted cumulative costs for initiators of home HD and PD were similar (one-year $94,106 and $81,677; five-year $324,434 and $308,251), and much lower than for facility HD initiators (one-year $134,775; five-year $380,799). Adjusted monthly costs for time on home HD and PD (initial and subsequent) were approximately $8,500 and $7,500, respectively, at month 1 and <$7,000 at month 60, compared with $15,500 (month 1) to $11,000 (month 60) for facility HD. Five-year adjusted survival was highest for home HD (82%), followed by PD (55%), SD/SN (48%), facility HD (44%). **Conclusions:** Our study suggests that home dialysis is associated with economic and survival advantages, but some of these may be attributable to unmeasured patient and clinical factors.

23: A Quantitative Evaluation of The Growth in Non-physician Prescribing in Canada and the Resultant Impact to Key Provinces and Therapeutic Areas

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Background: To improve patient access, reduce ambulatory physician visits and increase healthcare system efficiency provinces have differentially introduced legislative changes that expand prescribing practice to select non-physician healthcare providers. As a result, non-physician prescriptions (NPPs) by pharmacists, nurses and optometrists have shown marked growth. The purpose of this study was to quantify national NPP growth and understand the key geographies and therapeutic areas affected.
Methods: IMS Brogan GPM retail pharmacy prescription database (Apr-2014 to Apr-2016) was used for this analysis. This is a projected database covering all retail pharmacy prescriptions in Canada and includes information on prescribers, therapeutic class, products and provinces.
Results: Over 19,000,000 NPPs were dispensed in Canada since Apr-2015, a marked 27% increase from the previous year. Quebec has seen the largest NPP growth driven primarily by pharmacist NPP prescribing. In contrast, Ontario nurses are the current drivers of NPP growth and volume. As anticipated, prescriptions pertaining to chronic illnesses such as cardiovascular disease, diabetes and respiratory therapy represent the majority of NPPs prescribed. Other therapeutic areas include psychotherapeutics, analgesics, vaccines and contraceptives. Interestingly, nearly 1.2 million narcotic analgesic NPPs have been dispensed in the last three years.
Conclusion: Canadian NPP growth has continued to expand at a marked rate in recent years. Differential provincial legislation is resulting in varied regional non-physician prescriber foci. The impact of NPPs to patient access, outcomes, and healthcare system efficiency will need evaluation to understand its full impact in Canada.

24: Potentially Inappropriate Medications in Elderly Patients: Prevalence and Changes During Hospital Stay

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Objective: To estimate the prevalence of potentially inappropriate medications (PIMs) upon admission and describe changes made during hospitalization.
Methods: We conducted a study of patients seen at the McGill University Health Centre in Montreal, Quebec, Canada from May 2014-October 2015 who were over the age of 65. Medications patients were taking upon admission to hospital were obtained from drugs dispensed in the past 3 months retrieved from the provincial pharmanet system as was their reconciliation action. The STOPP criteria were utilized to identify PIMs effecting the central nervous system (CNS) and included use of 1st generation antihistamines & prolonged use (>4weeks) of benzodiazepines, tricyclic antidepressants (TCAs) & antipsychotics since they are commonly prescribed in this patient population.

Results: Among the 2,042 included patients, mean age (SD) was 77 (8), and 44% were female. Patients were admitted to hospital with a total of 19,282 drugs (9 on average per patient). A total of 718 CNS drugs were considered to be potentially inappropriate; 28% of patients were admitted with at least one PIM. Of the 718 inappropriate medications at admission, 417 (58%) were benzodiazepines, 221 (31%) were antipsychotics, 30 (4%) were antihistamines and 50 (7%) were TCAs. 29% of PIMs present at admission were stopped upon discharge from hospital; antihistamines were the least likely to be discontinued (36%) while antipsychotics were the most likely (22%). Additionally, 31% of benzodiazepines were discontinued.
Conclusion: The majority of PIMs were not discontinued at discharge, therefore future research should evaluate interventions to increase their discontinuation during the hospital stay.

25: Drug Costs in Castration-Resistant Prostate Cancer (CRPC): A Real-Life Study in Quebec

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Background: The management of CRPC is complex and costly. This study aims to estimate the cost of drug treatments over the CRPC period, in a real-life setting.
Methods: The study cohort consists of patients treated for CRPC at the Jewish General Hospital and the Montreal General Hospital from 2010 to 2014. Patients' information were collected retrospectively. The database was used to estimate the associated drug costs over the CRPC phase. Unit costs of medications were pulled from the RAMQ list of medications. Drug exposure was measured over the CRPC period. All costs were assigned in 2015 Canadian dollars ($). Primary and supportive drug costs were estimated.
Results: The management of non-metastatic patients was associated with a mean total cost of $836.0 per patient (95%CI: $423-$1,248) over an average period of 15.3 months while the burden of metastatic disease was significantly higher with a mean cost of $40,354 per patient (95% CI: $35,638-$45,070) over an average period of 27.6 months. The mean cost increased to $45,234 (95% CI: $39,791-$50,677) per patient over an average period of 30.9 months for patients who had at least two lines of treatment. Bone-targeted therapies accounted for 15.8% of costs.
Conclusion: Our study estimates the direct drug costs associated with mCRPC treatments in the Quebec healthcare system over a period when abiraterone was publicly reimbursed only in post-docetaxel setting. Obviously, drug costs over this phase after 2014 should be raised with the public reimbursement of abiraterone and other therapies for chemotherapy-naive patients.

26: Pregnancy Outcomes after TNF-Alpha Inhibitors Exposure in Inflammatory Bowel Diseases (IBD) Pregnancy: A Systematic Review and Meta-Analysis

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Background: TNF-alpha inhibitors are increasingly used in patients with inflammatory bowel diseases (IBD) during pregnancy to control disease activity and to prevent pregnancy complications. Despite of their efficacy in controlling IBD in pregnancy, the safety of using TNF-alpha inhibitors in pregnancy has not been confirmed.
Methods: We conducted a systematic literature search in MEDLINE, EMBASE, Web of Science from conception to Feb 2nd, 2016 to look for studies reporting birth outcomes after pregnancy exposure to TNF-alpha inhibitors in IBD population. We included case reports, case series, cohorts, case controls, and clinical trials in the systematic review. Only data from cohorts, case controls, and clinical trials will be included for meta-analysis. The primary outcomes are live birth (LB), spontaneous abortion (SA), stillbirths (SB), preterm births (PTB), low birth weight (LBW), and congenital abnormalities (CA). The risk of each outcome will be expressed in an overall relative risk (RR) with 95% confidence intervals. Two reviewers independently performed

abstract review, full text review and data extraction.
Results: There were 1715 references generated from database search, including 289 duplicates. The rest 1426 references went through title screening. Based on the preliminary results from the first reviewer, we included 48 eligible articles for full text review, including 13 case reports, 24 case series and 11 cohort studies.
Conclusion: Based on the preliminary results, majority of the studies did not report any adverse pregnancy outcomes. (Full text review and meta-analysis are expected to finish in August 2016 to generate a solid conclusion.)

27: Use of Health Technology Assessment for Drugs in the Private Payer Environment in Canada: A Literature Review

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Background: Private insurers (PIs) in Canada have used different criteria when deciding to list a new drug on their formulary. Traditionally, PIs have not formally used Health Technology Assessment (HTA) processes which are used for public reimbursement decision-making. The objective of this review was to examine the literature for public HTA or cost-effectiveness methodologies used by the PI market.
Methods: A targeted literature review was conducted in MEDLINE as well as in the grey literature using MeSH terms and other keywords. Publications written in English presenting HTA associated with PIs were included.
Results: The literature search identified 39 citations which provided guidance on what PIs should consider when evaluating a drug's value; ways to reduce inefficiencies in current spending, limitations of cost-effectiveness analyses in addressing certain payer questions, and emerging private-sector models for producing timely HTAs in the US. No study spoke to the use of HTA or its appropriateness for PIs. Conclusions: Few publications address HTA in the PI market. Cost-effectiveness appears to be used in a limited manner by PIs. The paucity of literature demonstrates there is no best practice for evaluating drugs for PIs in Canada. Considerations for the types of evidence PIs may be interested in are presented, however, an appropriate use or methodology for HTA within the PI market is not described.
Discussion: There are significant differences in perspectives and therefore methodological approaches needed for public versus PI markets; these differences need to be clearly understood.

28: No Substitution: Not Just for Physicians Anymore

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Funding: IMS Brogan supplied the time and materials needed to complete this analysis.

In recent years, considerable effort has been expended to maximize the use of generic rather than branded pharmaceuticals by both private and public payers. This study examined pharmacy transactions to better understand the source and magnitude of branded pharmaceutical product requests using a do not substitute (DNS) instruction by physicians, patients, and pharmacists in Ontario. Ontario prescription records in IMS Brogan's LRx pharmacy prescription database were analyzed, with the top 16 DNS products between June-2014 and May-2016 included in this study. Free text prescription signa was used to identify the source of the DNS, supplemented by the reimbursement source. As a predefined lexicon was used to identify DNS, only clearly identified notes were analyzed. Therefore, absolute transaction volume is believed to be understated, while proportional market share and growth is representative. This study analyzed 209,740 transaction records. Despite a 26.5% decrease in selected brand volume between May-2016 and May-2015, DNS instructions rose by 3.3%. The combined effect translates into an approximate doubling of the DNS market share from 15.8% in June-2014 to 30.1% in May-2016. During May-2016, patient directed DNS requests dominated total prescriptions at 14.9%, while physician directed DNS composed 10.9%. While, patients have consistently eclipsed physicians in directing DNSs in public reimbursed transactions for the past two years, private reimbursed patient directed DNS only eclipsed physician directed DNS in March-2015.This research can be useful in understanding the drivers

of branded prescriptions post loss of exclusivity, and peer into the reasons on why a DNS is directed.

29: An Evaluation of the Breast Cancer Well Follow-up Care Initiative using Administrative Databases: A New Model of Analysis

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Objective: The purpose of this work is to evaluate differences in health system resource utilization and costs in breast cancer survivors enrolled in well follow-up care.
Methods: Cancer Care Ontario partnered with the Regional Cancer Programs (RCPs) to implement new models of well follow-up care for breast cancer survivors. RCPs received one-time funding (2012) to develop and implement new models to transition follow-up care for cancer survivors with no ongoing treatment issues from oncologists to primary care providers, either through direct transition to the community or through a transition clinic based at the cancer centre. Cases were matched to a control group (also with a diagnosis of breast cancer), based on diagnosis, gender, age, cancer stage, comorbidity, income, and health system resource utilization. Differences in resource utilization and costs between the two groups were examined. Probability of survival between the two groups was also examined.
Results: Preliminary results of 2,325 well follow-up cases and the same number of controls (mean age 64.4 and 65 respectively) showed fewer inpatient hospitalizations, cancer clinic visits, reduced use of long-term care, home care, and complex continuing care in the well follow-up group, and at least equivalent outcomes in terms of survival (93.4% vs. 87.2% 5-yr survival probability in the well follow-up and control group, respectively). There was no difference between the two groups in terms of prescription drug use or laboratory tests.
Conclusions: Next steps will be to examine the mean costs per patient in the well follow-up and control cohort.

30: Variability in the Cost Per Event for Hypoglycemia Treatment Amongst Different Health Care Systems

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Funding: None

Background: Hypoglycemia is a significant side effect of diabetes pharmacotherapy. Hypoglycemia leads to reduction in health-related quality of life and its treatment is costly.
Objective: To explore variability in the cost per event for hypoglycemia treatment amongst different health care systems.
Methods: Systematic review utilizing PubMed Databases to obtain the data on the cost per event for hypoglycemia.
Results: All costs reported have been adjusted for inflation to 2016 U.S. dollars. The cost per event at outpatient settings on average reported, was $575 ($436) [mean (SD)] with a minimum cost of $15, maximum of $1452, median of $444. The cost per event at emergency settings on average reported, was $508 ($442) [mean (SD)] with a minimum cost of $97, maximum of $1548, median of $396. The cost per event at inpatient settings on average reported, was $4904 ($5338) [mean (SD)] with a minimum cost of $551, maximum of $19598, median of $2851. There was no significant difference between outpatient and emergency room settings (p-value more than 0.05). There was a significant difference for inpatient settings versus other settings (p-value = 0.001). The inpatient settings in the U.S. reported higher costs per event for inpatient setting [$15558 ($6810)] compared to European countries [$3179 ($1666)] (p-value = 0.08).
Conclusion: There is a large variability for reported cost per event of hypoglycemia for all settings including inpatient, outpatient and emergency room. The costs in settings reported from the U.S. are much higher than the costs reported from European countries specifically for inpatient settings.

31: Multi-Level Public-Private Negotiations for Government Drug Plan Reimbursement: An Analysis of the Pan-Canadian Pharmaceutical Alliance

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Funding: None

In its sixth year of operation, the pan-Canadian Pharmaceutical Alliance (pCPA) reached two significant milestones in 2016: over 100 medicines or drug indications have been successfully negotiated by public drug program bargaining units; and all federal and provincial public drug programs are active members. Thousands of multi-source drugs are subject to the pCPA's tiered pricing scale, ranging from 85% of the innovator price down to 18% for selected products. This presentation, reflecting on and updating a number of our analyses written between 2011 and 2016 and published in trade journals, magazines and CAPT's own peer-reviewed journal assesses the successes and challenges of the pan-Canadian Pharmaceutical Alliance. Notably, since the last quarter of 2015, an increasing number of new products have been the subject of a backlog, as the volume of new products or indications increases and as the pCPA takes more time to evaluate negotiation pathways and value before rejecting new medicines for negotiation or assigning a public drug plan to lead the discussions. We review the political, health policy, economic and legal aspects of the pCPA and provide a number of considerations or recommendations for the next phase of pCPA evolution, especially in the context of the current federal-provincial-territorial health accord discussions and the ongoing call from stakeholders for the establishment of a national pharmacare program.

32: Development and evaluation of a Comprehensive Diabetes Management Program in Long Term Care

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Description: Diabetes is an increasingly prevalent disease in long term care (LTC) among frail elderly, with a rise of 74% from 2003 to 2013 and is associated with several comorbidities and functional impairment. LTC practice guidelines are lacking due to a paucity of studies in this population and a care gap remains. A comprehensive diabetes program was developed by an inter-professional health care team and introduced in 16 LTC facilities in Ontario, Canada. The following is a subgroup analysis among 827 residents in 8 LTC facilities conducted after two years (June 2013-June 2015) of this continuous quality improvement initiative.
Aim: Reduce hypoglycemic events by 30% through a comprehensive diabetes management program by June 2015.
Actions Taken: An operational toolkit was developed to ensure consistency in the implementation of the program across all homes. Change concepts included a 3-month diabetes management audit (pre-intervention period) with feedback and education to LTC staff, identification of a Diabetes Champion at each facility and implementation of an evidence based protocol.
Summary of Results: There was a reduction in hypoglycemic events (53%), sliding scale insulin regimen (50%) and sulfonylurea use (23%) after 2 years. An upward shift in glycemic control was noted and reflects an appropriate, individualized, less stringent approach to diabetes management. The program is now being spread to other LTC facilities.

33: Net Impact Analysis for BLINCYTO(TM) (blinatumomab) to Support Listing on the Liste de médicaments-établissements for the Treatment of Adults with Philadelphia Chromosome-Negative Relapsed or Refractory B Precursor Acute Lymphoblastic Leukemia

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The Net Impact Analysis (NIA) describes the economic impact of reimbursing a new drug to the health care system. The NIA is based on real world clinical setting and clinical evidence.
Objective: To compare the net impact of

BLINCYTO(TM) (blinatumomab) versus current treatments for adults with Philadelphia chromosome-negative relapsed or refractory B precursor acute lymphoblastic leukemia (R/R Ph(-) ALL).
Method: Hemato-oncologists and pharmacists specialized in the management of ALL were consulted to determine treatment patterns and required monitoring for patients. The drug preparation and administration costs as well as monitoring costs were considered in the analysis. The cost of adverse events was excluded.
Results: The net impact cost of BLINCYTO was higher compared to current treatments mainly due to higher drug costs since many of the current chemotherapies are less expensive generics. However, costs attributed to the preparation, administration and monitoring costs were lower for BLINCYTO compared to current treatments with a difference of $31,006 compared with Hyper CVAD, $16,642 compared with ARA-C, and $5,163 compared with FLAG-IDA. Fewer health care resources are utilized with BLINCYTO treatment. Treating patients with BLINCYTO would improve hospital efficiency by freeing up health care professionals time and resources, in addition to reducing the patients? time spent in the hospital.
Conclusion: While the drug cost of BLINCYTO is greater than the currently used treatments, it offers savings in health resource utilization such as health care professional time and hospitalization cost.

34: Broadening the Value of the Drug Safety and Effectiveness Network (DSEN) for the Federal Regulator

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Issue: The Drug Safety and Effectiveness Network (DSEN) has the mandate to increase and generate new evidence for decision-making by policy-makers, regulators and drug insurance plan managers. Health Canada wishes to evolve the partnership and increase the types and scope of decision-making that would benefit from targeted research designed with the regulator in mind.
Description: Health Canada identified five areas where improved dialogue with DSEN's research teams and coordinating office is needed to increase utility and value: (1) regulatory policy questions, (2) pediatric issues and needs, (3) characterization of safety risk and context, (4) effectiveness and impact of risk mitigation actions, and (5) program effectiveness.
Results: Over 45 queries have been submitted to DSEN since 2009. Health Canada continues to engage DSEN researchers to better understand Health Canada's decision-making context and to provide timely and relevant scientific evidence. Health Canada needs real-time signal detection, design and expansion of Canadian data sources for federal pharmacovigilance, informed regulatory policy and operational questions such as those related to prevention of adverse reactions, risk communication, monitoring in clinical trials, drug abuse and misuse, and surveillance in vulnerable populations (children, seniors, First Nations).
Impact and Implications: The timely generation of important drug safety evidence relevant to federal regulatory decision-making will serve to further strengthen Health Canada's role in identifying new risk issues associated with health products sold on the Canadian market, ultimately leading to the improved health of Canadians.

35: Monitoring Private Payer Drug Reimbursement - A Conceptual Framework

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Background: Whereas drug plan sustainability has become a growing concern over the past few years, the rate of changes in the Canadian private payer drug reimbursement landscape has reached an unprecedented level, for which more has happened in the last 3 to 4 years than in the last 30 years. However, little is known about how these changes in policies are affecting patient access to innovative medicines over time.
Objective: To develop a framework for evaluating and monitoring private payer drug reimbursement coverage in Canada through a set of key indicators.
Results: This project, based on Mapol Inc.'s drug reimbursement monitor database, proposes a conceptual framework for the implementation of a systematic way to visualize and compare drug

reimbursement coverage uptake over time. It would be designed to measure the differences observed in drug coverage uptake based on different time series and according to the following key indicators: (1) the percentage of private payer lives, and (2) the coverage type.
Conclusion: The implementation of the proposed conceptual framework could be a useful approach to evaluate how drug reimbursement policies adopted by private payer affect access to medicines over time.

36: A Systematic Review on Hypoglycemia Rate Attributed to SU Utilization in Randomized Controlled Trials (RCTCs) On DPP4 Inhibitors

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Objective: To explore the rate of hypoglycemia attributed to SU utilization in RCT settings on DPP4 inhibitors.
Methods: A systematic search was conducted for RCTs on DPP4 inhibitors. PubMed database was utilized for this search. The search was limited to RCT reports in English language.
Results: Totally, 478 RCTs were found. Amongst all trials, totally, 22 trials have an arm with SU alone or with placebo or add on to metformin. The characteristics of patients at baseline were as follows: age 57 (1.6) years-old [mean (SD)], duration of disease 6.5 (1.8) years, baseline HgbA1c 8.0% (0.5%). Average duration of trials was 47 (34) weeks, with an average 443 (437) number of patients, and mean bioequivalent glimepiride was 4.0 (1.4) mg/day. During trials on average 16% (13%) hypoglycemia was reported; The range was varied between 0.6% and 37%; there was a significant gap between reported and confirmed hypoglycemia (p-value less than 0.0001): most trials did not reported severe versus non-severe hypoglycemia rate; however, the average rate of severe hypoglycemia from reported trials was between 1.5% and 4.7% according to different sensitivity analysis; there was no correlation between duration of the studies or bioequivalent doses of SU and the rate of hypoglycemia attributed to SU utilization (p-value more than 0.05).
Conclusion: This study illustrates that reported hypoglycemia rate amongst patients exposed to SU in RCT settings on DPP4 inhibitors widely varies, despite similarity in characteristics of patients at baseline. This calls for more homogenous definition and reporting of hypoglycemia in RCT settings.

37: Biosimilar policies and practices to promote uptake in Canada - International comparisons

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Background: By 2020 many of the top-selling innovative biologic drugs will lose patent protection thereby allowing the entry of lower priced biosimilars. However, the novelty, manufacturing complexity, and more rigorous clinical requirements for biosimilars compared to generics, raises unique questions for all stakeholders on how these products will be effectively integrated into health care systems. To date, Canada's experience with biosimilars is limited, and its approach to reimbursement varies widely across individual jurisdictions. Biosimilars have the potential to contribute to health system savings but have been unable to significantly impact the prescribing for biologics.
Methodology: Given the perceived uncertainty surrounding these drugs, and the relatively limited uptake of these products in Canada, PDCI Market Access Inc. initiated a qualitative study to better understand how health care systems in other countries have been able to impact biosimilar uptake. Interviews were conducted with key reimbursement authorities and regulators, as well as originator and biosimilar manufacturers in Oceanic and European nations to understand how biosimilars entered those markets.
Results: Results indicate that Canada lags behind other key jurisdictions in addressing questions regarding switching and in the education of stakeholders. Furthermore, challenges and opportunities vary widely among international authorities, but most believe their actions in the short term will have a significant impact on long-term sustainability of their healthcare systems and the emerging biosimilar sector.
Conclusion: These results provide insights and guidance for decision makers, both in Canada and internationally, to most effectively realize the uptake

and subsequent savings of biosimilars in their markets.

38: Clinical Trial versus Real-Life Data for Listing Recommendations

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Background: Actinic keratosis (AK) is the most common risk factor for developing squamous cell carcinoma. Various field-directed therapies are available in Canada (including 5-fluorouracil [Efudex], imiquimod 5% [Aldara], imiquimod 3.75% [Zyclara], and ingenol mebutate [PICATO]) with different reimbursement statuses. Ingenol mebutate has the shortest treatment duration. However, in the absence of head-to-head trials, conflicting information exists in the literature in regard to comparative efficacy.
Purpose: To determine if sometimes real-life, clinical practice data provide helpful information that should be used by decision makers for listing recommendations, instead of using published and/or unpublished indirect comparisons.
Methods: A survey was developed and administered to 7 Canadian clinical experts to gather real-life comparative efficacy and safety data of field-directed therapies in the management of AK
Results: Due to the shorter treatment duration of ingenol mebutate (days vs. weeks) and the shorter lived local skin reactions, in the absence of the clinical trial environment, adherence to treatment was reported to be higher with a reduced rate of discontinuation. This resulted, based on the clinical experts, in better clinical efficacy and safety scores for ingenol mebutate. In addition to improved quality of life, it was reported that fewer treatment cycles are needed with ingenol mebutate to achieve desired clinical outcomes. Real-life data provide valuable information that should be used by decision makers.

39: The Intergenerational Transmission of Adiposity across Countries

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There is a worldwide epidemic of obesity. We are just beginning to understand its consequences for child obesity. This paper addresses one important component of the crisis, namely the extent to which obesity, or more generally adiposity - is passed down from one generation to the next. Using the Body Mass Index (BMI) as a measure of adiposity, we find that the elasticity of intergenerational transmission is very similar across countries and relatively constant, at 0.2 per parent. Our substantive finding is that this elasticity is very comparable across time and countries - even if these countries are at very different stages of economic development. Quantile analysis suggests that this intergenerational transmission mechanism is substantively different across the distribution of children's BMI - more than double for the fattest children what it is for the thinnest children. These findings have important consequences for the health of the world's children.

40: Neurotoxicity, Mitochondrial and mtDNA Damage of Ketamine in Young Children Undergoing Procedural Sedation in the Emergency Department

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Background: Ketamine is routinely administered during procedural sedation in emergency departments. However, its safety in children has been questioned. In animal models, ketamine kills neurons via neuro-apoptosis. We explored potential adverse effects of ketamine on human brain cells and cellular mitochondria function and DNA (mtDNA) in children
Methods: We conducted a translational clinical trial with internal controls. We enrolled children (3-48 months) who were administered intravenous ketamine for procedural sedation (1-3.5mg/kg). Blood samples were drawn prior to- and 2-24h post-ketamine. We compared post- to pre-ketamine levels of serum biomarkers (Neuron Specific Enolase [NSE], glial fibrillary acidic protein [GFAP], S100B),

which correlate with death of 3 unique CNS cell types. We isolated lymphocytes from pre- and post-ketamine samples and analyzed for mitochondrial changes: cells were stained with mitochondrial membrane potential-specific dye and imaged to reveal morphologic changes. Mitochondrial content and mtDNA damage were probed using quantitative PCR

Results: 56 children (males=35; median age=20mo; median sampling time=150 minutes). Biomarkers: Total ketamine dose was associated with significant increase in serum NSE ($p=0.042$) and borderline significant increase in s100b ($p=0.050$) and GFAP ($p=0.051$) in children 2-4yrs compared with those <2yrs. Mitochondria: Exposed cells exhibited 24% reduction in mitochondrial biomass ($p<0.004$), 16% increase in mitochondrial polarization and a mean 0.4 oxidative DNA lesions in mtDNA per 10kb, indicative of oxidative stress

Conclusions: Ketamine administered to young children induced increase in serum biomarkers indicative of neuronal cell death and lysis and resulted in oxidative stress evidenced by measurable mitochondrial biomass changes and mtDNA damage.

41: Moving Towards An Enhanced Assessment of Value in Private Drug Plans Review

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Over the recent months there has been a focus from some private payers on public HTA reports and recommendations. However, it is important to understand there is a fundamentally different framework underlying public HTA evaluations compared to the priorities of private payers. Applying public HTA reports directly to the private drug plan environment can lead to decisions that underestimate the overall value of the product to the beneficiaries of private insurance and their families; and in turn undermine the intended role of a private drug plan in an employer's overall benefits and compensation package. When assessing a medicine's value from the perspective of a private drug plan there are "best practices" which can be applied so that the priorities of key stakeholders are appropriately reflected. Such "best practices" take into consideration many factors that are important for employers and their employees, and overcome the many limitations of applying public HTA assessments to the private payer market. Although the "best practices" proposed for private payer value assessments capture some areas that are similar to public drug plan assessments the perspective and focus of the assessments differ. To reflect the priorities and needs of their clients, private payer value assessments should go beyond traditional sources of information used within public assessments. They should take into consideration aspects such as convenience of administration, the impact on absenteeism, presenteeism (productivity when returning to work), impact on family or caregivers, short and long term disability- all factors not considered by public payers.

42: Risk Stratification for the Prevention of Venous Thromboembolism in Medical Patients

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Background: Approximately 75% of hospital associated venous thromboembolism (HA-VTE) occurs in medical patients. The benefit-to-risk ratio for thromboprophylaxis in this population is poorly defined. The Padua Prediction Score (PPS), Improve VTE Score (IVS), and Improve Bleeding Score (IBS), were developed to identify medical patients who may benefit from thromboprophylaxis. The thromboprophylaxis rate in medical patients at SHSC in 2015 was approximately 95%, possibly representing over-treatment.

Objective: Quantify the proportion of medical patients at high risk of HA-VTE using RAMs, and to evaluate their role to support decision making.

Methods: In this cross-sectional analysis, the

PPS, IVS, and IBS were applied to 71 consecutive medical admissions between March 28 and April 3, 2016. The Fisher?s exact test and chi-square test were used to compare results to inception cohorts of original studies.
Results: The PPS identified 15 (21%) patients as high risk of HA-VTE, significantly less than the inception cohort (p=0.0016). The IVS identified 7 (10%) patients as high risk of HA-VTE, similar to the inception cohort (p=0.82) The IBS identified 11 (15%) patients as high risk of any bleed, similar to the inception cohort (p=0.15); including 4 (27%) and 3 (43%) patients also identified as high risk of HA-VTE by PPS and IVS, respectively.
Conclusions: Available RAMs suggest the risk of bleeding may outweigh the benefits of thromboprophylaxis in medical patients. Prospective evaluation is required to establish the feasibility of RAMs and the safety of reducing the proportion of medical patients who receive thromboprophylaxis.

43: A Systematic Review and Network Meta-Analysis of Safety and Efficacy of Active and Passive Immunization in Mild-to-Moderate Alzheimer`s Disease

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Rational: Alzheimer`s disease (AD) is caused by accumulation of β-amyloid which triggers neuronal degeneration. In principle, Aβ can be targeted with injected antibodies and thus several clinical trials are published or are ongoing in evaluating the safety and efficacy of immunotherapies in AD.
Objectives: The primary objectives are to assess the clinical safety and efficacy of using passive and active immunotherapies in AD.
Methods: A systematic review of published RCTs was performed in MEDLINE, EMBASE, PubMed and Cochrane. Two reviewers independently selected the studies, extracted the data and assessed risk of bias. Clinical efficacy and safety outcomes were changes from baseline in ADAS-cog, CDR, MMSE, amyloid related abnormality with edema (ARIA-E), neoplasms and mortality. A meta-analysis using a random effects model and a network (direct and indirect) comparison was conducted to calculate mean differences in treatment effects, SUCRA and ranking probabilities.
Results: 12 RCTs on adults with mild-to-moderate AD were included in the analysis. After a sensitivity analysis, immunotherapies produced a significant improvement in ADAS-cog (MD=-0.387, 95% CI -0.42, -0.35, P<0.01) and MMSE from baseline. In terms of safety, rate of ARIA-E was significantly higher with antibodies than placebo. There was no significant difference between placebo and immunotherapies in terms of rate of neoplasms and mortality. Solanezumab and AN1792 (vaccine) were drugs of choice for efficacy and safety outcomes.
Conclusion: In terms of efficacy, the review results showed a significant improvement in two AD specific scales in favour of immunotherapies. vaccines are still under development for further clinical evaluations.

44: Comparative Effectiveness of Thiazide Diuretics and Other Monotherapies for Non-diabetic Individuals with Hypertension

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Background: Thiazide diuretics (TD) are cost-effective first-line anti-hypertensives, however they are less prescribed than other options. We compared use and outcomes of TD, converting enzyme inhibitor (ACEi), calcium-channel blockers (CCB), and angiotensin-2 antagonists (ARB) used as monotherapy.
Methods: Using MarketScan Databases 2011-2013, we constructed a retrospective cohort of non-diabetic hypertensive adults who were new users of a TD, CCB, ACEi, or ARB. Time zero (T0) was first prescription, and new use was defined as no prior filled prescription in the 12 months prior to T0. We performed Cox regression models to assess the risk for drug discontinuation, adding a drug or switching to a new drug. A separate model considered a composite outcome of clinical events including myocardial infarction, unstable angina, stroke, and

heart failure. Patients were censored at time of death, loss of health plan coverage, event date, or end of study period. The models were adjusted for baseline covariates.
Results: 17,083 patients started monotherapy with ACEi(38.3%), CCB(25.7%), TD(20.1%), and ARB(15.9%). The TD group were more likely to discontinue therapy versus ACEI (HR=0.79 95%CI 0.74-0.84), ARB (HR=0.66 95%CI 0.61-0.72) and CCB (HR=0.86 95%CI 0.80-0.92). Similar trends were found for adding a drug or switching to a new drug. There was a higher risk for the clinical events in ACEi (HR=1.46 95%CI 1.08-1.96) or CCB (HR=1.54 95%CI 1.13-2.11) groups versus TD, while the comparison with ARB were inconclusive.
Conclusions: Fewer patients on TD monotherapy had harmful clinical events versus ACEi and CCB although residual confounding may partially explain results.

45: Evaluation of the Canadian Drug Safety and Effectiveness Cross-Disciplinary Training (DSECT) Program between 2009-2015

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Background: The need for drug safety and effectiveness (DS&E) evidence is steadily increasing and, consequently, more DS&E researchers and trainees are needed. The Drug Safety and Effectiveness Cross-disciplinary Training (DSECT) Program was established as a CIHR Strategic Training Initiative in Health Research in 2009. The objective was to bridge scientific domains related to DS&E research through an interdisciplinary training program to improve research capacity. The objective of this study was to understand the program's impact between 2010-2015. The findings will enhance DSECT for future years.
Methods: This was a descriptive program evaluation that examined training program outputs and program feedback from participating trainees between 2010-2015. Data from trainees were collected from applications, annual reporting, and annual anonymous feedback surveys.
Results: There were 84 trainees from 7 provinces who completed the one-year training program. They varied by degree level (32 Masters, 27 Doctoral, 17 Post-doctoral Fellow, 8 Other), with 19 health professionals. 212 peer-reviewed articles and 225 presentations were produced by DSECT trainees and alumni. Feedback survey response rates were 65% across the 5 years. On a 5-point Likert scale, trainees rated the program highly (4.3), with the highest scores for administration (4.5) and the Objective Structured Knowledge Translation Event (OSKTE; 4.4). Two areas identified for improvement were the curriculum website (4.1) and secondary mentorship (3.8).
Conclusion: DSECT had a substantial impact on generating research capacity in DS&E. Trainees provided positive feedback about the program, but noted 2 areas for improvement, which will be addressed in future years and re-evaluated.

46: Characterizing the Senior High-Cost Health Care User in Ontario: A Preliminary Analysis

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Background: High cost users (HCUs) are a small proportion of the population that use disproportionate healthcare resources. In 2011, 5% of Ontarians accounted for 65% ($19.8 billion) of provincial health expenditures. Understanding HCU multi-morbidity and drug use is required to target interventions to

improve clinical outcomes and contain healthcare costs.
Objectives: To compare Ontario senior HCUs to non-HCUs based on demographics, co-morbidities, medication use, health service utilization, clinical outcomes and costs.
Methods: A retrospective population-based matched cohort analysis of incident senior HCUs defined as Ontarians age > 66 years in the top 5% of total health care costs in FY2013. Health care and prescription drug utilization data were obtained from Ontario health administrative databases. The primary outcomes were annual total health care expenditures per patient, total drug costs per patient and drug-to-total health care expenditure ratio. Secondary outcomes were one-year mortality and hospitalization rate.
Results: Senior HCUs (n=176,604) accounted for $4.9 billion in total health care expenditures and $433 million in medication costs in FY2013. Compared to non-HCUs (n=529,812) on a per patient basis, HCUs incurred higher total health care costs ($27,697 vs. $2233) and higher medication costs ($2453 vs. $842). HCUs were characterized by greater polypharmacy (>5 medications, 87.7% vs. 47.6%) and multi-morbidity (median John Hopkins Expanded Diagnosis Clusters [EDCs], 14 vs. 10). HCUs had higher annual mortality (10.39% vs. 0.72%) and hospitalization rates (3.20 vs. 0.06 hospitalizations per 1000 person-years).
Conclusions: Compared to non-HCUs, senior HCUs are a frail, multi-morbid and vulnerable cohort. The contribution of prescribing and medication utilization quality deserves further study.

47: Health Care Utilization and Costs among Senior High-Cost Users in Ontario: Preliminary Results

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Background: Senior high cost users (HCUs) present a growing fiscal challenge. Understanding the contribution of different care cost components can help inform health care planning and reforms.
Methods: We undertook a retrospective, population-based cohort study using Ontario health administrative databases. Senior HCUs defined as Ontarians age > 66 years in the top 5% of healthcare costs users in FY2013 were matched to non-HCUs by age, sex and geographical location. Incremental healthcare use and costs were determined using a Difference-in-Differences approach. Care component costs were then expressed as a proportion of total provincial government health care expenditures.
Results: The annual incremental resource utilization per senior HCU (n=176,604) was a mean of 0.76 hospitalizations, 1.31 emergency department visits, 29.7 physician visits, and 24.9 home care visits. Compared to non-HCUs (n=529,812), HCUs incurred an additional $23,757 per patient in total health care costs. Inpatient care ($12,143), physician services ($3,015), and home care ($1,387) had the highest incremental costs. Incremental prescription medication costs were $941 per patient. Among HCUs, inpatient care as a proportion of total expenditures increased from 2.8% in the year before becoming an HCU to 44.7% in the incident HCU year. The proportion of expenditures attributed to prescription drugs fell from 40% to 8.9%.
Conclusions: The relative healthcare resource use is substantial among senior HCUs, with the greatest incremental costs coming from inpatient care. Targeted research is needed to determine the optimal mix of services to help avoid inpatient care.

48: Assessing the Effect of Exposure Definition on an Observed Association in Population-Based Pharmacoepidemiology Studies of Metformin in Type 2 Diabetes Patients

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Background: A variety of methods are used to define exposure in pharmacoepidemiologic studies. Although each method has known biases, the relative effect of these biases on an observed association has not been fully examined. Our objective was to explore the influence of exposure definitions on estimates, using the association between metformin and all-cause mortality as a model.
Methods: New users of oral anti hyperglycemic agents (OHA) were identified using administrative databases from Alberta between 1998 and 2010. Metformin exposure was described using commonly used definitions. All analyses included the same covariates of age, gender, and a comorbidity score. The measure of association was calculated using a Cox Proportional Hazards model for cohort and conditional logistic regression for case-control studies. Patients not receiving metformin served as the reference group.
Results: We identified 64,293 new OHA users. Mean age was 68.9 years, 33,131 (52%) were male, 55,525 (86%) had at least 1 metformin prescription, and 24,745 (39%) of patients died during an average follow-up of 5.8 years. The association between metformin and mortality varied widely ranging from 75% reduced risk of mortality (aHR 0.25, 0.24-0.26) to 29% increased risk (HR 1.29, 1.25-1.33). Most exposure definitions provided estimates in the 0.6-0.8 range aligning with the previous observational studies.
Conclusions: We observed a wide range of associations between mortality risk and different exposure definitions. Since no exposure definition is completely free of bias pharmacoepidemiological studies should consider using at least 2 exposure definitions and sensitivity analysis to provide more robust and potentially valid estimates.

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