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CAPT ACTP

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Taking Action on Real World Evidence: from Analysis to Impact

ABSTRACTS

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ORAL PRESENTATIONS

1. Influence of opioid prescribing standards on drug utilization among patients with chronic opioid use: a retrospective cohort study

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Background: In mid-2016, the College of Physicians and Surgeons of British Columbia (CPSBC) issued prescribing standards and guidelines relating to opioid drugs, and a policy on prescribing of the opioid substitution therapy buprenorphine/naloxone. We evaluated whether the Colleges policies influenced prescription drug utilization.
Methods: We used a longitudinal cohort study design with monthly repeated outcome measures. Patients with chronic prescription opioid use during a 6-month identification period were followed for a 24-month pre-policy period and 12-month post-policy period, and were compared to equivalent historical controls who were followed one year earlier and were therefore not exposed the policies. We estimated changes in the utilization of opioids, high-dose opioids (>90 milligrams of morphine equivalents (MME)/day), opioids with sedatives/hypnotics, opioid discontinuation, and opioid substitution therapy (methadone or buprenorphine/naloxone).
Results: The study included 68,113 patients in the main cohort and 68,429 historical controls; 47,416 patients were in both cohorts. Following the opioid policies, we observed reductions in average monthly utilization levels of opioids (adjusted difference -63 MME; 95% CI -81 to -45), high-dose opioids (adjusted difference 0.2 days; 95% CI -0.3 to -0.2), and opioids with sedatives/hypnotics (adjusted difference -0.2 days; 95% CI -0.2 to -0.1). There were increases in opioid discontinuation and opioid substitution therapy. The study did not evaluate the impact of the opioid policies on health outcomes.
Conclusion: The CPSBC opioid policies modestly reduced utilization of opioids, high-dose opioids and opioids with sedatives/hypnotics among patients with chronic use of prescribed opioids while increasing use of opioid substitution therapy.

2. Estimating the Impact of Treatment Evolution in Non-Small Cell Lung Cancer (NSCLC): the iTEN model

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Objectives: Treatments options for patients with advanced NSCLC (aNSCLC) are rapidly expanding. The iTEN model was developed to support medical decision-making by predicting aNSCLC patient survival and associated costs, from a Canadian healthcare system perspective.
Methods: A discrete event simulation of aNSCLC treatment patterns was developed. Treatment sequencing and eligibility were derived from a modified Delphi process with Canadian clinical experts. Published Kaplan Meier progression free and overall survival data were fit with parametric functions to estimate treatment efficacy and guide the determination of progression and death events. Treatment history was assumed to have no impact on the efficacy of subsequent therapies. Costs included were: drug acquisition and administration, monitoring, imaging, physician visits, end-of-life, best supportive care and adverse events. Model survival predictions were validated against published real-world estimates from the Ontario Cancer and TYROL registries and a US medical records analysis (Nadler, 2018).
Results: The Ontario Cancer Registry, TYROL registry, and US medical records study reported overall survival for patients receiving two-lines of

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chemotherapy, up to five-lines of treatment with chemotherapy/targeted therapies or up to three-lines of treatment with immunotherapies/chemotherapy/targeted therapies, respectively. One-year survival rates in these studies were 67%, 38% and 49%; corresponding iTEN estimates, after restricting the treatment pattern to match each study, were 61%, 39% and 60%. Based on current Canadian practice patterns, the estimated one-year survival and life-time cost of treating aNSCLC were 46% and $89,899.

Conclusions: Further validation is planned; however, the model may reasonably estimate the clinical and cost consequences of treating aNSCLC.

3. Patient characteristics, treatment patterns and survival for unresectable stage III non-small cell lung cancer in Ontario, Canada

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Objectives: In anticipation of new treatment strategies for unresectable stage III NSCLC, we undertook a retrospective study to determine how these patients have been managed in Ontario, Canada and their survival by treatment approach.

Methods: Individuals diagnosed between April 1, 2010 and March 31, 2015 were identified in the Ontario Cancer Registry. Patients were unresectable if no surgery was undertaken within 3 months of diagnosis. Initial treatments included: radiation (RT), chemotherapy, concurrent and sequential chemo+RT (cCRT, sCRT). Survival was calculated from date of diagnosis to death.

Results: There were 24,729 individuals diagnosed with NSCLC; 5,243 (21.2%) were stage III and 4,542 (18.4%) were stage III unresectable. Mean age of the latter group was 69.7 Â± 10.3 years; 54.2% were male. 64.2% of patients were treated within 3 months of diagnosis. The frequency of treatment approach was: cCRT (21.6%), palliative RT (21.3%), curative RT (20.2%), no treatment (19.6%), chemotherapy (11.6%), sCRT (4.9%) and targeted therapy (0.7%). Median survival (IQR) was 2.9 yrs (1.7-4.8) for targeted therapy, 2.0 yrs (1.0-5.5) for cCRT, 1.4 yrs (0.7-3.4) for curative RT, 1.4 yrs (0.7-3.1) for chemotherapy, 1.2 yr (0.6-2.9) for sCRT, 0.6 yrs (0.3-1.2) for palliative RT and 0.5 yrs (0.2-1.2) for no treatment.

Conclusion: Although cCRT is generally considered standard of care for stage III unresectable NSCLC, patients in Ontario receive various treatment approaches. Survival outcomes vary widely.

4. Time trends among new users of osteoporosis drugs over 20 years: considerations for pharmacoepidemiologic study design

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Background: Oral bisphosphonates entered the market in 1996 and are the main osteoporosis drugs prescribed in Canada. Introduction of new therapeutic options, updates to practice guidelines, and healthcare policy changes may make studies examining new-users of bisphosphonates susceptible to time-varying biases. Objective: To compare characteristics of first-time bisphosphonate users in Ontario, Canada over time.

Methods: The Ontario Drug Benefit (ODB) program covers prescription drugs listed on the ODB formulary for residents aged 65 or more years. We identified first dispensation of an oral bisphosphonate among Ontario residents from 1996/04 to 2015/03. We excluded patients aged younger than 66 years, taking other osteoporosis drugs, with health conditions known to impact bone, and long-term care facility residents. Medical and pharmacy claims within the year prior to bisphosphonate dispensation were used to characterize patients. Descriptive statistics were used to summariz e and compare patient characteristics by fiscal year.

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Results: We identified 523,210 eligible seniors (mean age 75 years). A larger proportion of men (6.2% to 29.0%) and diabetics (8.7% to 17.8%) initiated therapy over time. History of benzodiazepines decreased (26.6% to 11.5%), while prior statin use (9.5% to 42.8%), oral corticosteroid use (10.6% to 14.7%), and prior bone mineral density testing (46.7% to 68.0%) increased. A shift in prescriptions from etidronate to alendronate and risedronate was documented.
Conclusions: Characteristics of new initiators of oral bisphosphonates among Ontario seniors changed over time, reflecting changes in healthcare delivery and osteoporosis management. Consideration must be given to time-trends when designing pharmacoepidemiologic studies in this population.

5. Interrupted time series analysis of long-acting injectable antipsychotic use

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Background: Long-acting injectable (LAI) antipsychotics are recommended to improve adherence to maintenance antipsychotic therapy; however, injectable antipsychotic therapy may be negatively perceived and subsequently underutilized. We hypothesized LAI use increased after market entry of the second-generation antipsychotic (SGA) risperidone in LAI formulation in 2004.
Methods: Administrative health databases at the Manitoba Centre for Health Policy (MCHP) were accessed to identify and describe LAI antipsychotic users. Interrupted time series analysis with Poisson regression was used to model LAI user counts between 1998 and 2016. Predictor variables included time in fiscal quarters, a dummy variable indicating quarters pre- or post-LAI risperidone market entry, and time since LAI risperidone market entry. The Manitoba population was included as an offset variable and the model was adjusted for autocorrelation. Analysis was conducted with SASÂ® software.
Results: A downward trend in LAI use was observed prior to LAI risperidone market entry (RR: 0.976, p<0.0001). Post-entry, the trend reversed (RR: 1.038, p<0.0001), resulting in a net increase of 1.4% per quarter after 2004 (RR: 1.014, p<0.0001). Median time to LAI initiation following schizophrenia diagnosis decreased from 3.3 years (IQR 0.7-6) in 2004 to 0.3 years (IQR 0.1-0.9) in 2015 (p=0.003).
Conclusions: The introduction of LAI risperidone in 2004 had a positive impact on LAI use. Furthermore, initiation of LAIs occurred earlier after schizophrenia diagnosis in 2015 compared with 2004. Acknowledgements Results and conclusions are those of the authors; no official endorsement by Manitoba Health, Seniors and Healthy Living or MCHP is intended or should be inferred.

6. Outcomes of metastasectomy in metastatic renal cell carcinoma patients: The Canadian Kidney Cancer information system experience

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Objective: Surgical resection of metastasis can be integrated in the management of metastatic renal cell carcinoma (mRCC) as it can contribute to delay disease progression and improve survival. This study assessed the impact of metastasectomy in mRCC patients using real-world pan-Canadian data.

Methods: The Canadian Kidney Cancer information system (CKCis) database was used to select patients who were diagnosed with mRCC between Jan 2011 and Dec 2017.All patients having had a complete or incomplete metastasectomy and no metastasectomy during follow-up where included in the study cohort. Each patient having received a complete or incomplete metastasectomy was matched with up to 10 patients with no metastasectomy by several potential confounding factors, such as: age, time from RCC diagnosis until metastasis, clear cell histology and use of targeted treatment before metastasectomy and having had a nephrectomy.
Results: A total of 329 patients had complete (221 patients) and incomplete (10 8 patients) metastasectomy, while 1,318 mRCC patients did not undergo a metastasectomy. At 12 months, 99.1%, 88% and 76.8% of patients were alive in the complete metastasectomy, incomplete metastasectomy and no metastasectomy group, respectively (p<0.001). A total of 298 patients receiving metastasectomy (101 incomplete metastasectomy and 197 receiving complete) have been matched to a control group of patients who did not have metastasectomy. Finally, patients receiving metastasectomy show an increased survival compared to patients not having had a metastasectomy HR: 0.48 (95%CI 0.37-0.63), p<0.001.
Conclusion: Our study revealed the positive effect of metastasectomy performed in mRCC with an improved OS compared to patients with no metastasectomy.

7. A non-opioid alternative to intravenous (IV) opioids in emergency departments (ED) would significantly reduce the economic burden on the healthcare system. A societal perspective cost-consequence analysis.

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Background: IV opioids are commonly used for the management of pain in ED. This drug utilization results in significant costs to the healthcare system. The objective was to evaluate the cost-effectiveness of methoxyflurane (MXF) in the treatment of adult patients requiring analgesia for moderate to severe acute pain associated with minor trauma.
Methods: A retrospective analysis of medical records, as well as primary and secondary researches were conducted. A cost-consequence analysis (CCA) was chosen to compare MFX to IV opioids (morphine, fentanyl, hydromorphone). The cost per consequence avoided and total cost of treatment per patient were evaluated in the CCA. The consequences included IV opioid's side effects/complications and the use of healthcare resources.
Results: The total cost of treatment per patient were $165.85 for MFX, $316.54 for morphine, $320.41 for fentanyl and $315.33 for hydromorphone. MFX in ED can generate savings of $151.58 per patient by reducing nursing/physician time for IV administration and patient monitoring. MFX has an improved safety profile with less nausea (2.0% for MFX versus 12.1% morphine, 21.1% fentanyl and 19.0% hydromorphone), vomiting (2.0% versus 5.8%, 9.5% and 10.7% respectively), hypotension (1.0% versus 2.1%, 1.6% and 1.1% respectively), respiratory depression (0.0% versus 1.1%, 1.1% and 1.1% respectively) and no complication (phlebitis, extravasation and harmful IV errors) associated with IV opioids. Which translates into additional savings of $90.66 per patient for avoided consequences.
Conclusion: MFX is a cost-effective alternative to IV opioids with an improved safety profile and a reduced economic burden on the healthcare system.

8. Real-world safety of second-generation direct-acting antivirals in Hepatitis C

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Objective: To compare the safety of direct-acting antivirals (DAA) hepatitis C virus (HCV).

Methods: We performed a retrospective cohort study of adults with HCV using MarketScan databases. Cohort entry was the date of first prescription of simeprevir/sofosbuvir (SIM/SOF), ledipasvir/sofosbuvir (LDV/SOF), ombitasvir/paritaprevir/ritonavir+dasabuvir (OPrD), sofosbuvir/velpatasvir (SOF/VEL), or elbasvir/grazoprevir (EBR/GZR) between Jan/2014-Nov/2016. Adverse events were defined as rashes, anaemia, and hepatic decompensation recorded in hospital or outpatient claims between cohort entry and therapy completion or discontinuation. Patients with any of these diagnoses before cohort entry were excluded. Cox regression was performed to estimate hazard ratios (HR) and 95% confidence intervals (CI) for a composite outcome (at least one event) adjusted for demographics, co-morbidities, past HCV drugs, concomitant ribavirin, and baseline health care use.
Results: We identified 15,480 HCV patients treated with DAAs (72.9% LDV/SOF, 13.3% OPrD, 9.4% SIM/SOF, 2.9% SOF/VEL, and 1.5% EBR/GZR); 11.8% used ribavirin concomitantly. Median age was 58 years (interquartile range 53-62) and 61.6% were male. The frequency of skin events ranged from 0.2% (95%CI 0.0-0.7.) in SOF/VEL to 2.2% (95%CI 0.3-4.1) in EBR/GZR. The frequency of anaemia ranged from 0.7% (95%CI 0.5-0.9) in LDV/SOF to 2.7% (95%CI 2.0-3.4) in OPrD. Hepatic decompensation was rare (<0.6% overall). Multivariate analyses were unable to establish differences between drugs. Ribavirin use (HR 1.89, 1.36-2.62), baseline cirrhosis (HR 2.05, 1.65-2.54) and previous hospitalization (HR 1.21, 1.01-1.45) were associated with shorter time to an adverse event.
Conclusion: We found similar safety profiles for different DAAs agents. Reasons for altered risk should be further explored.

POSTER PRESENTATIONS

9. Assessing the cost-effectiveness of the build better bones with exercise pilot trial

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Objectives: The Build Better Bones with Exercise (B3E) pilot trial evaluated the effects of home exercise on community-dwelling older women with vertebral fractures. The objective of this exploratory economic analysis was to examine the health resource utilization and cost-effectiveness of the B3E study.
Methods: The B3E study participants were randomized in a 1:1 ratio to a 12-month home exercise program or equal attention control group. Clinical and health system resources such as adverse events (AEs), allied health visits, caregiver time, lost productivity, medical equipment, medications, out-of-pocket costs, and physician visits and tests were collected during monthly phone calls by a blinded research assistant and from daily diaries completed by participants. Program costs for both groups were included as well. Quality of life (QoL) information was collected via EQ-5D-5L at baseline, 6 and 12 months. Unit costs (2018 CAD) were applied to health system resources to calculate total, median±standard deviation (SD) and minimum-maximum (min-max) costs of the intervention and control groups, as well as the median cost per patient. The incremental cost-effectiveness ratio (ICER) between the two groups was also calculated.
Results: The study included 141 women (mean age=76±6.40y for intervention, 77±7.28y for control) and overall total costs were $664,923 and $614,033, respectively. The top three cost drivers from the resource utilization collected were caregiver time ($250,269 and $240,811), medications ($151,000 and $122,145) and adverse events ($58,807 and $71,981). The mean cost per intervention patient was $9,365±$9,988 (median=$5,054, min–max= $1,210–$57,774), and the mean cost per control patient was $8,772±$9,718 (median=$5,203, min–max = $931–$51,327). The mean EQ-5D index score per patient was 0.81±0.11 (median=0.81, min–max =0.54–1) and 0.79±0.13 (median=0.80, min–max= 0.33–1) respectively. The difference in

quality adjusted life year (QALY) (0.02) was used to calculate the ICER, and the ICER was determined to be $29,650.

Conclusions: Results from this preliminary study of 141 women in the B3E study indicate a variety of health resources are being utilized over a 12-month period.

10. Time to Discontinuation of Biologic Therapy by Mechanism of Action in Rheumatoid Arthritis: Results from The Ontario Best Practice Research Initiative (OBRI) Cohort

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Background: Time to discontinuation of biologic therapy may be related to mechanism of action. We aimed to compare drug survival of tumor necrosis factor inhibitors (TNFi) versus non-TNFi in an observational rheumatoid arthritis cohort.

Methods: Patients in the Ontario Best Practice Research Initiative (OBRI) who started their first biologics on or any time after enrolment were included. Time to discontinuation due to (1) any reason, (2) non-response, physician, and patient decision, (3) non-response, and (4) adverse events (AEs) were assessed using Kaplan-Meier survival and Cox proportional hazards regression analysis.

Results: A total of 796 patients were included of whom 130 (16.3%) received non-TNFi and 756 (83.7%) received TNFi. Over a mean follow-up of 2.4 years, biologic discontinuation was reported for 291 (36.6%) due to any reason, 229 (28.8%) due to non-response, AEs, physician, and patient decision, 110 (13.8%) due to non-response, and 81 (10.2%) due to AEs, respectively. There was a significant difference in time to discontinuation due to any reason (Logrank p=0.0002); non-response, AEs, physician, and patient decision (Logrank p=0.04) between groups. After adjusting for potential confounders, difference remained significant for any reason [HR: 0.62 (0.46-0.84)] and non-response, AEs, physician, and patient decision [HR: 0.67 (0.47-0.94)].

Conclusions: The analysis demonstrates that patients initially started on non-TNFi are significantly more likely to discontinue their therapy earlier for any reason and due to non-response, AEs, physician and patient decision compared to TNFi therapy. Lack of response is likely not driving this, whereas patient and physician preference likely influenced the results.

11. Collection of anti-rheumatic medication data from both patients and rheumatologists shows strong agreement in a real world clinical cohort: results from the Ontario best practices research initiative (OBRI)

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Background: Collection of Anti-Rheumatic Medication (ARM) information from both patients and rheumatologists is considered a strength for Rheumatoid Arthritis (RA) registries. However, it is important to assess the agreement between these two data sources.

Objectives: To examine the agreement of ARM use between self-reports and rheumatologist reports in the Ontario Best Practices Research Initiative (OBRI).

Methods: Patients enrolled in the OBRI on or after Sep 1st 2010 with the ARM use reports from two sources within 60 days of each other were included. ARM included conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs) and biologic DMARDs (bDMARDs). Cohen's Kappa statistics of agreement between the two data sources were calculated. A multivariate backward stepwise logistic regression was also used to exam the impact of different factors on ARM use agreement between two data sources.

Results: 2,154 patients (78.7% female) were included with a mean (SD) age of 57.8 (12.6) year. There was a good agreement (Cohen's Kappa=0.61-0.80) between two sources. Increased HAQ-pain index (OR: 0.66; 95% CI: 0.60-0.73) and physician global score (OR: 0.95; 95% CI: 0.92-0.98) were significantly associated with the lower agreement. By contrast, post-secondary education (OR: 1.20; 95% CI: 1.02-1.40), and seeing an academic rheumatologist (OR: 1.47; 95% CI: 1.25-1.73) were significantly associated with the higher agreement.

Conclusions: The results of this analysis suggest that ARM reports from the two data sources have strong agreement in the OBRI. This agreement is even better for patients who have post-secondary education and are being treated by an academic rheumatologist.

12. Physician characteristics associated with opioid overdose hospitalization and death among patients with long-term opioid use: a retrospective cohort study

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Background: We investigated whether the physician characteristics of sex, medical school graduation year, high practice volume, or prescribing behaviour were associated with hospitalization and death involving accidental opioid overdose among patients with long-term prescription opioid use.

Methods: We conducted a longitudinal cohort study with monthly repeated outcome measures, using administrative health data in British Columbia. The study included patients with >=180 days of continuous prescription opioid use at the start of any month during 2013-2015, excluding patients with a history of long-term care, palliative care or cancer. We used multivariable Poisson regression to estimate the association of physician characteristics and patient outcomes.

Results: Our analyses included 136,565 patients and 8,721 physicians. The baseline rates of hospital admissions and deaths involving accidental overdose were 4.0 (95% CI 2.2 to 7.2) per 10,000 person-years and 1.9 (95% CI 0.6 to 6 .1) per 10,000 person-years, respectively. Graduation during a period of increasing promotion and use of opioids for chronic non-cancer pain (1996-2010) was associated with opioid overdose hospitalization (rate ratio (RR) 1.42; 95% CI 1.06 1.91) and opioid overdose death (RR 3.02; 95% CI 1.61 5.68); graduation in 1975 or earlier was associated with opioid overdose hospitalization (RR 1.52; 95% CI 1.072.15).

Conclusions: Physician graduation during a period of increasing promotion and use of opioids for chronic non-cancer pain may have increased risk of hospitalization and death involving accidental opioid overdose among patients with long-term opioid use. Longer time in practice may also be a risk factor for opioid overdose hospitalization.

13. Canadian Patients Attitudes and Preferences for Original and Similar Biologic Medicines: 3-Year Comparison

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Objectives: In Canada, similar biologic medicines are available across many conditions, recently including diabetes and cancer. For the past three years, the Consumer Advocare Network has conducted an annual survey of patient knowledge, attitudes and usage preferences. Issues include: perceived effectiveness, adverse effects, switching,

interchangeability, pharmacovigilance, cost, and informed decision making. Over the years, differences among patient groups have emerged as important influences, including continuous/episodic use, primary/secondary use, and variability of condition. Biologics require patient engagement for appropriate use; as Canadian drug plans consider mandating policies like switching, patient attitudes and behavioural responses must be considered.

Methods: In 2016, an electronic survey with forced choice, rating, and open-ended questions was sent to about 2000 Canadian patients across diseases, asking about biosimilar knowledge, attitudes and preferences. In 2017 an updated version was sent to an expanded pool, and in 2018, a revised survey was distributed. We compared factors influencing acceptabiity and usage of biosimilars from 200 responses (2016), 370 (2017), and 300 (2018).

Results: The trend over three years has been increased knowledge and more positive attitudes about biosimilars. Patients using biologics continuously versus occasionally are more negative about switching (70% vs.20%). Diabetes and gastrointestinal patients are more concerned than arthritis. Cancer patients are most concerned about safety and effectiveness.

Conclusions: Patients remain resistant to forced switching to biosimilars, with implications for adherence to and confidence in their use.

14. Case Study: Real World Evidence Supporting Reimbursement Decision Making using the Canadian Kidney Cancer information system (CKCis).

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Background: On April 18, 2017, the pan Canadian Drug Review (pCODR) posted a Request for Advice (RFA) for axitinib (Inlyta) for metastatic renal cell carcinoma (MRCC): Is there evidence to fund axitinib as an alternative to everolimus for the second-line treatment of metastatic clear cell renal carcinoma? In 2009, the Kidney Cancer Research Network of Canada (KCRNC), the research arm of Kidney Cancer Canada (KCC) established the Canadian Kidney Cancer information system (CKCis), a centralized database to collect data from medical centers across the country. CKCis now contains retrospective and prospective de-identified patient data from over 9500 consented patients who have been diagnosed and treated for RCC.

Methods: KCC requested that CKCis investigators make as a research priority the RFA question. A cohort of patients who were pretreated with either sunitinib or pazopanib were identified where axitinib was given second line in 108 patients while everolimus was used in 229 patients.

Results: Time to treatment failure (TTF) was found to be longer in the axitinib group with Overall Survival (OS) similar in both groups. This Real World Evidence was submitted for review to pCODR by KCC.

Conclusions: Conclusion of CKCis Investigators: Axitinib should be considered an option for all patients in Canada post 1stL VEGF-Targeted Therapy without the limitations of the existing pCODR recommendation. CODR Conclusions: The Clinical Guidance Panel is of the opinion that there is appropriate real world evidence and expert judgment to justify axitinib as an equal alternative to everolimus in the second line setting.

15. Real world treatment patterns and survival of stage IV non-small cell lung cancer (NSCLC) in Ontario, Canada

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Objectives: The majority of NSCLC patients are diagnosed with Stage IV so it is important to understand which patients are treated with systemic therapies and to what benefit.

Methods: This longitudinal, population-level study determined treatment patterns and survival in Stage IV NSCLC patients diagnosed between April 1, 2010 and March 31, 2015 from the Ontario Cancer

Registry. Individuals were further identified as having non-squamous disease, and those who received an EGFR-TKI (afatinib, erlotinib, gefitinib) were assumed to be EGFR mutation-positive (EGFR+). Survival was calculated from date of diagnosis to death.
Results: There were 24,729 individuals diagnosed with NSCLC. Approximately half (12,159; 49.2%) had stage IV disease, including 10,103 with non-squamous disease, of whom 508 were categorized as EGFR+. The mean age for the stage IV non-squamous and EGFR+ cohorts were 68.7 ± 11.0 years and 69.1 ± 10.4 years, respectively; 49.3% and 60.8% were female, respectively. The most frequent treatments for stage IV non-squamous patients were palliative radiotherapy (RT) (46.7%) and systemic therapy (14.9%) while 26.7% received no treatment. 75.6% of the EGFR+ cohort received gefitinib, with the majority receiving no subsequent treatment (44.6%). Mean and median survival times (IQR) for the stage IV non-squamous patients were 0.9 ± 0.0 years and 0.4 (0.2-1.0) years, respectively. Mean and median survival times (IQR) for the EGFR+ cohort were 1.9 ± 0.1 years and 1.5 (0.9-3.0) years, respectively.
Conclusion: Few patients with Stage IV non-squamous NSCLC received systemic therapy. Survival was generally very poor, but better in the subgroup of EGFR+ patients.

16. Evaluation of the Fentanyl Patch-for-Patch Program in Ontario, Canada

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Background: The rising impact of opioid use is a major public-health concern, especially for fentanyl given its high potency and potential for overdose. To curb the misuse and diversion of fentanyl patches, an early Patch-for-Patch (P4P) program was implemented in Ontario between 2012 and 2015. The P4P program requires that patients must return their used fentanyl patches to a pharmacy before receiving a refill.
Methods: We conducted a cross-sectional time-series analysis among counties that implemented the P4P program using Ontario claims-data. We zeroed all intervention months and looked at outcome rates in the 5 years prior and 12 months following the launch of the P4P program. Outcomes included monthly rates of prescriptions dispensed for fentanyl and non-fentanyl opioids, and opioid toxicity-related hospital emergency department visits and hospital admissions. We modeled each outcome using ARIMA models and tested the impact of the P4P program using a ramp function.
Results: We analyzed 16 counties that implemented the early P4P program. Introduction of the P4P program resulted in a significant decline in the number of fentanyl patches dispensed (from 1,277 to 888 patches per 10,000 population; p=0.04). There was no significant change in the rate of non-fentanyl opioids dispensed (p=0.32) or opioid toxicity related hospitalizations and emergency department visits (p=0.4) following implementation of the program.
Conclusions: Implementation of a P4P program in select counties in Ontario reduced the number of fentanyl patches dispensed, but did not have any measurable impact on rates of opioid toxicity-related hospitalizations and emergency department visits.

17. Aromatase Inhibitors and Risk of Cardiovascular Outcomes in Post-Menopausal Women with Breast Cancer

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Background: Aromatase inhibitors (AIs) and tamoxifen are common treatments for estrogen-receptor positive breast cancer. However, data from trials suggest that AIs may increase the risk of cardiovascular outcomes, when compared with tamoxifen. Thus, to address this safety concern, we assessed whether use of AIs is associated with an increased risk of cardiovascular outcomes in the setting of real-world clinical practice.
Methods: Using the United Kingdom Clinical Practice Research Datalink linked to the Hospital Episodes Statistics and Office for National Statistics databases, we identified patients newly-diagnosed with post-menopausal breast cancer who were newly-treated with either AIs or tamoxifen between 1998 and 2015, and followed until 2016. Cox proportional hazards models using inverse-probability-of-treatment and censoring weighting were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) of fatal and non-fatal myocardial infarction (MI) or ischemic stroke associated with use of AIs when compared with tamoxifen.
Results: A total of 7,813 and 9,170 patients were newly-treated with AIs and tamoxifen during the study period, respectively. The use of AIs was associated with a 54% increased risk of MI, when compared with tamoxifen (4.1/1000 vs 1.9/1000 person-years; HR: 1.54, 95% CI: 1.04-2.27). In contrast, use of AIs was not associated with an increased risk of ischemic stroke, when compared with tamoxifen (5.1/1000 vs 3.3/1000 person-years; HR: 1.16, 95% CI: 0.83-1.61).
Conclusion: In this study, use of AIs was associated with an increased risk of MI but not ischemic stroke, when compared with tamoxifen in post-menopausal women diagnosed with breast cancer.

18. Does Active Identification of Patients Nearing End of Life Change Use of Palliative Care and Home Care Services?

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Objective: To evaluate whether active identification of patients who could benefit from a palliative approach changes the use of palliative and home care services.
Methods: From 2014 to 2017, Cancer Care Ontario implemented the INTEGRATE study among 4 cancer and 4 primary care centres. Physicians identified patients likely to die within 1-year and benefit from palliative care. INTEGRATE patients were 1:1 matched to non-intervention controls selected from provincial healthcare administrative data using propensity score-matching. Palliative and home care services utilization was evaluated within 1-year after the index date, censoring on death, or March 31, 2017. Cumulative incidence function was used to estimate the probability of having used services, with death as a competing event. Rate of service use per 360 patient-days was calculated. Palliative and home care was analyzed.
Results: Of the 1,187 INTEGRATE patients, 1,185 were matched to a control. The intervention and control groups were well-balanced on demographics, diagnosis, comorbidities, and death status. The probability of using palliative services in the intervention group was 81.3% (95% CI: 78.9% to 83.5%), significantly higher than controls (63.5%, 95% CI: 60.6% to 66.2%). The intervention group had a statistically higher number palliative visits (29.7 vs. 19.6 per 360 patient-days) and greater probability of receiving home care (82.5% vs. 56.8%) than controls. Rate of palliative visits in the intervention group (67.0 per 360 patient-days) was doubled than controls (33.2 per 360 patient-days).
Conclusion: Physicians actively identifying patients benefiting from palliative care resulted in increased use of palliative and home care services.

19. Prioritization of Oncology Drugs: What factors lead to priority status?

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Background: At the time of their pan-Canadian Oncology Drug Review (pCODR) submission, Submitters may request a priority review (PR). This request has an impact on the order of review, and placement on the pCODR Expert Review Committee (pERC) meeting agenda. PR requests are assessed by a panel of pERC members and priority status is either granted or not.
Objective: To provide a qualitative assessment of PR requests submitted to pCODR, with the aim of understanding what factors lead to prioritization.
Methods: Data from 53 pCODR submissions that have requested PR were explored using qualitative content analysis.
Results: 32 submissions received priority status, 21 submissions did not. Factors related to clinically meaningful outcomes (e.g., overall survival [OS], toxicity, progression-free survival [PFS]), promising evidence (e.g., OS, PFS, quality of life [QoL]), availability, and novel drugs were commonly mentioned in the panel's conclusion for granting priority status. Deterrents to prioritization were not having clinically meaningful outcomes or an urgent unmet need, availability of other treatment options, and uncertainty of evidence (related OS, QoL, safety). The decision to grant priority status does not automatically translate to a positive funding recommendation; five submissions with priority status did not receive positive funding recommendations.
Conclusions: A range of factors contributes to priority status being granted, premised on a limited set of values deemed relevant to technology prioritization. Future research will 1) characterize the determinants of technology prioritization using quantitative measures and 2) explore the normative basis for prioritization through comparative analyses of priority-setting criteria among HTA institutions.

20. Factors affecting ototoxicity in head and neck squamous cell carcinoma (HNSCC) patients treated curatively with cisplatin-based chemoradiation.

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Purpose: To estimate prevalence of hearing loss among HNSCC patients treated with cisplatin-based chemoradiation, and assesses need for baseline and follow-up hearing tests.
Methods: At Princess Margaret Cancer Centre, a prospective observational study assessed HNSCC patients receiving cisplatin-based chemoradiation. Hearing tests was tested at baseline and follow-up (0.7-18.5 months after treatment initiation) at physician's discretion. Significant ototoxicity was defined as a grade 2 audiometric change from baseline to post-treatment (CTCAE v.4.02) in one or both ears.
Results: Of 642 eligible patients (years 2008-2015) enrolled, 549 received definitive chemoradiation and 93 post-operative chemoradiation. Median age was 57.5 years; 114(18%) were female; sites included oropharyngeal (OPC; 421(66%)), oral cavity (OC; 105(16%)), laryngeal (56(9%)), hypopharyngeal (34(5%)) and unknown primary treated as HNSCC (26(4%)). 63(10%) were stage I-III and 576(90%) were Stage IV. Only 246 patients received both baseline and follow-up hearing tests, of which 142 (22% of 642) exhibited significant ototoxicity (94 bilateral/48 unilateral). None received prolonged courses of other ototoxic agents to explain hearing loss. Hearing loss was significantly higher (each $p<0.001$) for OPCs (27% of 421) compared to all others (13% of 221); high dose (24% of 557) vs. low-dose weekly cisplatin (6% of 78); and definitive (24%) vs. post-op chemoradiation (9%).
Conclusions: Hearing loss in 22% of HNSCC patients is clinically significant. The true proportion of hearing loss will be higher, as only 38% had baseline and follow-up hearing tests, often triggered by symptoms. Baseline and follow-up hearing tests

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should be routine, and primary preventive hearing loss strategies should be emphasized.

21. Migraine treatment patterns and opioid utilization among chronic and episodic migraine patients identified by a clinician-administered semi-structured diagnostic interview

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Background: The objective was to describe migraine treatment patterns and opioid utilization in chronic migraine (CM) and episodic migraine (EM) patients.
Methods: Eligible patients were enrolled from a large medical group, 18 years, and had 1 claim with a migraine diagnosis in the 12 months prior to screening. A physician-administered Semi-Structured Diagnostic Interview, which included questions related to headache symptoms, frequency, disability, medication use, and diagnosis, was used to classify patients as CM or EM. Acute treatment for migraine, preventive treatment for migraine, opioid treatment, and baseline characteristics were assessed in the 12 months prior to the study enrollment date.
Results: Of the 192 patients, 129 had CM and 63 had EM. The CM cohort had a mean age of 49.4 (SD=12.6) years and was 93.8% female. The EM cohort had a mean age of 48.9 (SD=15.4) years and was 82.5% female. 67.4% of CM and 55.6% of EM patients had 1 claim for both acute and preventive medications. 53.5% of CM and 36.5% of EM patients had 1 opioid claim (P<0.05); the mean number of opioid claims was 4.0 (SD=7.1) among CM and 2.8 (SD=8.2) among EM patients (P<0.05). 33.3% of CM and 15.9% of EM patients had 3 opioid claims. 13.2% of CM and 7.9% of EM patients had a pain diagnosis code.
Conclusions: Over half of CM patients and about a third of EM patients received an opioid prescription in the past year. Treatment patterns, particularly in CM patients, indicate opportunities for better management.

22. Pharmaceutical outcome-based pricing and reimbursement agreements: lessons learned from key international markets in Australia, Canada, Europe and the United States.

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Background: Health technology assessments are used by many jurisdictions worldwide to measure the value of new medicines. However, even after undertaking such reviews, many questions remain at the forefront of payers™ minds: How can uncertainty at launch regarding a new drug's real value be overcome? What is needed to ensure a medicine is used by the right patients in the real world? How can spending on the drug be contained for the patient population? Payers in various markets are currently exploring the use of outcomes-based pricing and reimbursement arrangements (OPRAs) to mitigate risks at launch and expedite patient access.
Methods: A comprehensive literature review of the trends, challenges, and opportunities in key international markets was conducted by the authors to provide clarity on the feasibility of such innovative outcomes-based agreements. Specifically, the payer reimbursement environment in Australia, Canada, Europe, and the United States was explored for this analysis.
Results: Although there was congruence as to the therapies that are appropriate for negotiation of such agreements, jurisdictions vary significantly on levels of experience and methodologies/data sources used. Challenges include system limitations,

resource availability, administrative burden, and the presence of existing agreements.
Conclusions: Given the variability in health systems, resources, and priorities, it is difficult to generalize learnings from one market and apply them to another. The authors have, therefore, developed a checklist of questions to support payer decision making in identifying when the use of OPRAs is most appropriate.

23. Clinical atherosclerotic cardiovascular disease (ASCVD): patient attitudes and awareness in Canada

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Background: As a leading cause of morbidity and mortality in Canada, cardiovascular (CV) disease has a profound effect on the lives of patients. The purpose of this study was to describe patient characteristics, treatment patterns and disease awareness of Canadian patients with dyslipidemia receiving lipid-lowering therapy (LLT).
Methods: A physician and patient (pt) survey was conducted in Canada from January to April 2017 through the Adelphi Dyslipidemia Disease Specific Programme. Participating physicians provided information on treated dyslipidemia pts, with the same pt completing Pt-reported forms containing questions on their condition, its impact and disease awareness. Pts with ASCVD were systematically over-sampled. Key outcome measures included: pt characteristics, treatment patterns and pt disease awareness.
Results: The study included 67 physicians, providing data on 230 ASCVD and 367 non-ASCVD pts. ASCVD pts were older and were more often diagnosed by a cardiologist. ASCVD pts had more comorbidities, and were taking higher dose statins. LDL-C was not optimized in all patients (mean 2.38mmol/L). Despite a high disease burden, disease awareness was low; only two thirds of pts recalled discussing CV risk with their doctor and one fifth knew their LDL-C values. Finally, ASCVD pts were more likely to have their work productivity, daily activities and quality of life (QoL) impacted than non-ASCVD pts.
Conclusion: Canadian pts with dyslipidemia may not be optimally managed or educated about their disease, and ASCVD pts have worse QoL than non-ASCVD pts. Further efforts are needed to improve patient education and disease awareness.

24. Innovation for whom? A systematic literature review on incidence and prevalence of severe migraine subtypes in North America to understand the market for emerging migraine therapies

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Objectives: Migraine is the second most burdensome disease globally. The only Health Canada approved therapy with an indication for migraine is Botox; additional treatment options are needed. Monoclonal antibodies (MABs) are potential prophylactic treatments for migraine, currently in phase III development, specifically for severe migraineurs with high frequency episodic (HFEM) and chronic migraine (CM) subtypes. An understanding of the epidemiology of severe migraine subtypes is needed to estimate the patient populations potentially eligible for these new treatments.
Methods: A systematic literature review was performed with the following strategy (run in EMBASE on 09/01/2018): terms for HFEM and CM populations, observational study design filter, outcomes of interest (i.e. incidence and prevalence), and publication date restriction 2008-2018. Epidemiological studies presenting incidence and prevalence data for HEFM and CM in North America were included.
Results: Of 371 unique hits, inclusion criteria was met by four cross-sectional survey studies from the United States reporting prevalence data for CM. The total number of returned surveys across the four studies was 249,277. The prevalence of CM in the

general population varied among included studies, ranging from 0.025% to 1.79%. Where reported, the prevalence of CM was higher in females and peaked at midlife. No epidemiologic data on HFEM were identified in North America.
Conclusion: Limited data exists regarding the incidence and prevalence of severe migraine subtypes, especially related to HFEM. No publications on the epidemiology of HFEM or CM in Canada were identified. Further research is needed to assess the epidemiology of the migraine subtypes.

25. Population-based study of orchiectomy treatment for prostate cancer in Quebec

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Background: Androgen deprivation therapy (ADT) can be delivered either surgically by orchiectomy or medically via luteinizing hormone-releasing hormone (LHRH) drugs. They are considered therapeutically equivalent in the treatment of advanced prostate cancer (PCa). The objective is to describe the use of orchiectomy for PCa and analyze factors associated with orchiectomy treatment over medical castration in Quebec.
Methods: The cohort consists of PCa patients from 2004-2012 and treated by ADT (either by LHRH drugs or by orchiectomy), extracted from a random sample from Quebec public healthcare insurance databases. The primary study outcome was the use of orchiectomy. Multivariable logistic regression analysis was performed to identify variables associated with orchiectomy treatment.
Results: We identified 7096 patients treated by ADT, of which 106 (1.5%) underwent orchiectomy. Following multivariable analyses, age (odds ratio [OR] 1.60, 95% confidence interval (CI), 1.06 -2.43) and Charlson comorbidity score (OR 1.09, 95%CI 1.01-1.17) were associated with increased odds of orchiectomy. Conversely, local radical treatment prior to ADT initiation (OR 0.18, 95%CI 0.07-0.46) and residence in a region with university-affiliated hospitals (OR 0.39, 95%CI 0.26-0.58) were associated with lower odds. Also, year of ADT initiation was associated with lower odds of orchiectomy (OR 0.88 for each increasing year, 95%CI 0.81-0.95).
Conclusion: A minority of PCa patients are treated by orchiectomy in Quebec. These men were likely to be older, more comorbid, not treated by local radical treatment, living in a region not serviced by a university-affiliated hospital, and initiated ADT in earlier years compared to patients treated by medical castration.

26. Systematic review and critical assessment of the literature on methodologies of indirect comparison of health technologies: Matching-Adjusted Indirect Comparisons (MAIC)

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As more therapeutic options emerge within the same therapeutic area, there is often a lack of evidence from head-to-head clinical trials that directly compare the safety and efficacy of a drug with the standard of care. Several statistical methods have been developed to allow for indirect comparison between different therapeutic alternatives that affect the same therapeutic area. Among these, one of the most commonly considered by regulatory bodies is the method of Matching-Adjusted Indirect Comparisons (MAIC). The goal of this study was to evaluate the applications of the MAIC method by HTA in order to understand its usefulness to health care decision making. The research was performed through a systematic review of the literature using the MEDLINE electronic database (Pubmed) and included data from HTA databases (specifically CADTH, NICE, SMC, and PBAC). Publications that reported the details of the MAIC methodology for various therapeutic areas were captured. Per PRISMA 2 guideli ne methodology, 50 studies identified and 11 were

included following screening. Of these, 2 were CADTH-specific assessments: Intuniv XR (ADHD) and Daklinza (Hepatitis C). Indirect comparisons represent a valuable tool for comparing technologies in the absence of head-to-head trials. Their quality will depend on several factors including the method of analysis, and the validity of the underlying assumptions. The MAIC method can provide useful information to support HTA decision-making when a head-to-head trial compared to standard of care is unavailable.

27. Clinical and Economic Burden of Atherosclerotic Cardiovascular Disease (ASCVD) in Ontario, Canada

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Objectives: Atherosclerotic cardiovascular disease (ASCVD) is a leading cause of morbidity, mortality, and economic burden in Canada. The objectives of this study were to characterize patients who experienced a primary ASCVD event and to quantify subsequent events and associated costs within a 10-year period.
Methods: Institute for Clinical Evaluative Sciences (ICES) datasets were used to identify adult patients with a primary ASCVD event using ICD-diagnostic codes for hospital admissions in Ontario. Patients were included in the study cohort if they had a primary event from April 1st 2005 to March 31st 2014. Data were collected for second and subsequent hospitalization and outpatient event(s) (2005-2015). Specific ASCVD events of interest were myocardial infarction (MI), stroke, and transient ischemic attack (TIA).
Results: The mean age of the cohort was 65 years and 54% of patients were male. Hypertension (64%) and diabetes (27%) were the most common comorbidities. The annua l incidence of a primary MI, stroke or TIA event generally decreased or remained stable over time, whereas the incidence of subsequent events trended upwards. The total mean annual cost per patient in the first year post-primary event was $14,179, $36,899, and $51,892 for TIA, MI, and stroke, respectively, and generally decreased over time.
Conclusion: Patients in Ontario who experience a primary ASCVD event remain at high risk for future episodes. Further analyses to identify populations who may benefit from intensified risk reduction strategies are warranted.

28. Moving towards universal coverage of direct-acting antiviral therapies for hepatitis C infection in Canada: an environmental scan of provincial and international jurisdictions

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Background: Direct-acting antivirals (DAAs) have become the standard treatment for patients with chronic hepatitis C infections because of their high cure rates and favourable side effect profiles; however, access to this new class of agents has been limited because of its high cost. While public payers across Canada have implemented strict criteria for drug coverage in order to contain expenditures, efforts have been made to provide treatment coverage as to improve access to medication for this high-burden condition. This environmental scan compares recent coverage criteria across national and international jurisdictions.
Methods: Coverage criteria for Daklinza, Epclusa, Sunvepra, Galexos, Harvoni, Sovaldi, Holkira Pak, Zepatier, Maviret, Technivie, and Vosevi were reviewed by accessing Canadian provincial drug formularies. International coverage (e.g., Europe, Australia, United States, Egypt, India) was reviewed by searching available literature.
Results: Coverage criteria vary across Canada but all provincial payers (except PEI) provide coverage for Daklinza and Zepatier. By April 2018, all Canadian jurisdictions, except Nova Scotia, New Brunswick, and Newfoundland & Labrador, had removed

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the stage 2 liver fibrosis requirement for patients to be eligible for coverage. Internationally, patient's access to DAAs differs significantly. Many jurisdictions restrict DAA prescribing authority to specialists and request documentation of chronic hepatitis C. In Australia all patients appear to have unrestricted access to DAAs. In the US, considerable gaps of coverage are identifiable and patients might face significant financial burden to receive treatment.

Conclusion: DAAs appear to be generally accessible through public drug plans in Canada compared to other countries.

29. Longitudinal changes in relative market share proportions of biologic and targeted synthetic disease-modifying anti-rheumatic drugs for treatment of rheumatoid arthritis: descriptive data from the Ontario best-practice research initiative database

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Background/Purpose: For patients with Rheumatoid Arthritis (RA) without adequate clinical response to conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), the next therapy is either biologic DMARDs (bDMARDs) or targeted synthetic DMARDs (tsDMARDs). bDMARDs include tumour-necrosis factor inhibitors (TNFi) or non-TNFi classes. Since inception of Ontario Best Practice Research Initiative (OBRI), new treatment options have become available. We describe evolving use of non-TNFi vs. TNFi in Ontario practices from 2008-2017.

Methods: Adult patients with RA enrolled in OBRI who started bDMARDs/tsDMARDs anytime during, or up to 30 days before, enrollment were included. The yearly proportion of the population treated with TNFi and non-TNFi therapy was measured for (i) all patients and (ii) those initiating their first bDMARD/tsDMARD. TNFi included: Etanercept, Adalimumab, Certolizumab, Golimumab, and Infliximab. Non-TNFi included: Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

Results: A total of 1,057 patients were included of whom 653 were bDMARD/tsDMARD naive. In 2008, the relative non-TNFi use was 3/56 (5.4%) in all patients and 0/31 (0%) in treatment-naive patients. By 2016, relative use was 224/679 (33.0%) in all patients and 17/56 (30.4%) in treatment-naive. This was followed by 144/426 (33.8%) and 4/15 (26.7%), respectively in 2017.

Conclusion: This descriptive analysis shows an increase in non-TNFi therapy use. The overall trend towards greater use of non-TNFi therapies as first line advanced therapeutics may be partially explained by recent guidelines allowing clinicians to select either class as first line advanced therapies. Future analyses evaluating patient-, disease- and concomitant drug use-specific determinants of physician decision-making will be conducted.

30. Higher drug cost for pregabalin/gabapentin shouldn't dissuade clinicians from prescribing this intervention in spinal cord injured individuals for neuropathic pain

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Background: Canadian guidelines for treatment of neuropathic pain in spinal cord injury (SCI) recommend pregabalin or gabapentin as first-line therapy followed by amitriptyline. To understand the

economic impact of this recommendation we evaluated the health care costs of SCI individuals with neuropathic pain prescribed pregabalin/gabapentin compared to amitriptyline.

Methods: Former patients of a tertiary SCI rehabilitation facility in Ontario, Canada were recruited to participate in a one year prospective study evaluating health care utilization, costs and health outcomes. Participants were over 18 years of age, C1-T12, AIS A-D, injury duration greater than 1 year with neuropathic pain and attended quarterly phone follow-up. Information collected include: hospitalizations, physician visits, other health care practitioner visits, drugs prescribed and equipment. Data was converted to 2016 Canadian costs using publicly available sources.

Results: Seventeen individuals were prescribed pregabalin/gabapentin and 7 amitriptyline. Median monthly cost for pain-related prescription drugs was $102 for pregabalin/gabapentin and $66 for amitriptyline. However, total median monthly healthcare costs were $1,987 for pregabalin/gabapentin and $3,357 for amitriptyline. Greatest cost differential was observed in emergency department ($1,211 for amitriptyline and $0 for pregabalin/gabapentin) and mobility equipment/device ($207 for amitriptyline and $0 for pregabalin/gabapentin). There was no difference in physiotherapy and occupational therapy costs. Results were limited to self-report of costs for a small case series in Ontario.

Conclusions: Higher prescription drug costs for pregabalin/gabapentin were not the primary cost driver for monthly healthcare costs. Higher total healthcare costs for amitriptyline were driven by higher emergency department visits and mobility equipment/device purchases.

31. Health Utilities Index Mark 3 scores for major chronic conditions: population norms for canada based on the 2013-2014 Canadian Community Health Survey

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Background: Utility scores are frequently used as preference weights when estimating quality-adjusted life-years within cost-utility analyses or health-adjusted life expectancies. Though previous Canadian estimates for specific chronic conditions have been produced, these may no longer reflect current patient populations.

Methods: Data from the 2013-2014 Canadian Community Health Survey were used to provide Canadian utility score norms for seventeen chronic conditions. Utility scores were estimated using the Health Utilities Index Mark 3 (HUI3) instrument and were reported as weighted average (95% confidence intervals [95% CI]) values. In addition to age and sex-stratified analyses, results were also stratified according to the number of reported chronic conditions (i.e., "none" to "≥5"). All results were weighted using sampling and bootstrapped weights provided by Statistics Canada.

Results: Utility scores were estimated for 123,654 (97.2%) respondents (weighted frequency = 29,337,370 [97.7%]). Of the chronic conditions that were examined, "Asthma" had the least detrimental effect (weighted average utility score = 0.803 [95%CI 0.795 – 0.811]) on respondents' utility scores and "Alzheimer's disease or any other dementia" had the worst (weighted average utility score = 0.374

[95%CI 0.323 – 0.426]). Respondents who reported suffering from no chronic conditions had, on average, the highest utility scores (weighted average utility score = 0.928 [95%CI 0.926 – 0.930]); estimates dropped as a function of the number of reported chronic conditions.
Conclusion: Utility score differed between various chronic conditions and as a function of the number of reported chronic conditions. Results also highlight several differences with previously published Canadian utility norms

32. The development of a chronic disease incidence prediction model for Ontario public health planning

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Background: Informed decision-making by public health officials is needed when planning for the future burden of chronic disease in the population. A prediction model that accurately predicts the incidence of chronic disease in a jurisdiction based on current population characteristics would be invaluable towards decision-making.
Methods: The Ontario version of the Canadian Community Health Survey was linked to health administrative data to predict the incidence of chronic disease over a fifteen-year period. Sixteen variables, including: modifiable lifestyle behaviors (e.g., alcohol, smoking, poor diet and physical inactivity), sociodemographic factors (e.g., age, ethnicity, income) and other health-related factors (e.g., body mass index) were used as predictors. Sex-specific prediction models were developed using Weibull regression models for males and females separately. The performances of the prediction models were evaluated based on measures of overall predictive accuracy, discrimination and calibration.
Results: The derivation cohort consisted of 47,960 females and 38,267 males. For both sexes, the overall predictive performance and discrimination improved when sociodemographic and other health-related predictors were added to the base model consisting of only modifiable lifestyle behaviors. Using the male model as an example, Nagelkerke™s R2 (0.036 to 0.152) and the Harrell's c-statistic (0.627 to 0.778) improved with more predictors; however, calibration as measured with the Greenwood-Nam-D'Agostino statistic (p-value <.0001) and calibration plots indicated underfitting in lower-risk groups.
Conclusions: Overall, the derivation models predicted the incidence of chronic disease well for both sexes. The next steps are to further improve the predictive accuracy of the model followed by model validation.

33. Patient preferences among individuals with type 2 diabetes for attributes of diabetes medications: a discrete choice experiment

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Objective: To estimate the trade-offs that patients with type 2 diabetes (T2D) make between attributes of glucose-lowering medications using a discrete choice experiment.
Methods: Eight relevant attributes were identified using a literature review, focus groups and interviews with patients and clinicians. A sample of Canadians with T2D, recruited through a survey company, completed 14 choice tasks. A multinomial logit model was used to estimate the weights of each attribute. Willingness-to-pay was used to assess trade-offs between attributes.

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Results: A total of 513 individuals completed the survey. Average age was 59 years (SD=12), 59% were male, 55% had tried two or more oral medications, and 62% had diabetes for at least 6 years. All attributes were found to significantly influence choice. On average patients were willing-to-pay a monthly cost for their therapy of: $135 to achieve three additional years of life; $48 and $36 for a 20% reduction in their risk of macrovascular and microvascular events respectively; $37 for a 1% drop in HbA1C; $32 for a 50% less risk of severe hypoglycemia over 10 years; $28 for a 50% less risk of a minor side effect; and $19 for a 50% less risk of a rare but serious side effect over 10 years.
Conclusion: All eight examined attributes were shown to significantly influence choice with cost and life expectancy carrying the most weight, and serious and minor side effects carrying the least weight.

34. Predictors of hip fracture among patients with inflammatory arthritis receiving chronic oral glucocorticoid therapy

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Objective: Oral glucocorticoids (GCs) rapidly induce bone loss and increase fracture risk. Predictors of fracture among oral GC users have not been examined by underlying indication. We aimed to identify predictors of hip fracture risk among patients with inflammatory arthritis receiving chronic oral GC therapy.
Method: We identified patients with inflammatory arthritis (gout, lupus, polymyalgia rheumatica, rheumatoid arthritis) aged 66 or more years taking oral GCs using Ontario public healthcare administrative data, 1998/01/01-2014/09/30. We included patients who dispensed 2 oral GC prescriptions totalling 450 mg prednisone equivalent using a 6-month ascertainment window. GC exposure was quantified during the ascertainment window by dose (mean daily, cumulative) and pattern (continuous, intermittent or sporadic). Index date was defined at the end of the ascertainment window. Medical and pharmacy claim were used to define fracture risk factors within the year prior to index. We used Cox proportional hazard models to identify predictors of hip fracture within 1 year following the index date.
Results: We identified 23,065 eligible patients (mean age=74.6 years, SD=6.4; 64% women). Average daily dose, cumulative dose and pattern of GC use were not associated with fracture risk. Rather, older age, rheumatoid arthritis, fracture history, stroke, antidepressant use and opioid use were associated with increased hip fracture risk and male sex was protective.
Conclusion: Controlling for GC exposure, risk factors for hip fracture parallel those commonly reported among patients without inflammatory arthritis. Of interest, among patients with inflammatory arthritis, patients with rheumatoid arthritis are at highest risk of hip fracture.

35. Disinvestment decision-making using value of information analysis: a hypothetical case study

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Background: Prudent health technology management involves allocation of financial resources toward technologies with high assessed value and away from those of low assessed value. Value of information (VoI) analysis may be practical for prioritizing cost-ineffective technologies for disinvestment.This research illustrates an application of VoI analysis to select the most appropriate disinvestment candidate using cost-effectiveness models of everolimus for advanced breast cancer (ABC) and bevacizumab for platinum-resistant ovarian cancer (PROC) in Canada.
Methods: The following comparative per-patient and population-level VoI analyses were conducted. Expected value of perfect information (EVPI) was estimated to assess the value of reducing cost-effectiveness uncertainty. Expected value of perfect information for parameters (EVPPI) was assessed to identify the type of additional research required

to reduce uncertainty. Expected net benefit of 1 sampling (ENBS) was calculated to estimate the overall value of disinvesting each health technology, respectively. The technology with highest ENBS should be prioritized for disinvestment.

Results: Per-patient EVPI of everolimus for ABC ($9,378) was higher than that of bevacizumab for PROC ($2,531). Analyses of EVPPI indicated that clinical trials were the most appropriate method for reducing uncertainty. The population-level ENBS was found to be substantially higher for everolimus ($1,615,253,171) compared with bevacizumab ($10,320,497).

Conclusion: Results suggested that bevacizumab for PROC should be prioritized for disinvestment over everolimus for ABC. Decision-making uncertainty may be minimized by prioritizing disinvestment candidate technologies according to the likelihood that additional information changes cost-ineffectiveness status. In this way, VoI analysis may be a useful analytical guide for informing healthcare technology management.

36. Disease-specific costs of non- metastatic and metastatic castration-resistant prostate cancer in Quebec

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Objectives: Estimate the disease specific costs of prostate cancer patients during the health states of nonmetastatic castration-resistant prostate cancer (NM-CRPC) and metastatic castration-resistant prostate cancer (M-CRPC).

Methods: This cohort analysis contains 211 prostate cancer patients from the MUHC. An algorithm of detecting NM-CRPC and M-CRPC was based on increases of prostate specific antigen (PSA) levels after castration and the detection of metastasis. The usage of imagery tests, hospital visits and treatments was extracted from the patients files and the mean usage per resource was calculated for 30 days in the given health state. Resources price were obtained from the RAMQ List of Medications when available, when unavailable prices were obtained from the MUHC internal prices lists. This cost analysis was performed by health care system perspective.

Results: Mean duration of NM-CRPC was 26.07 months while duration of M-CRPC was 20.79 months, with 62 and 6 8 patients per health state respectfully. The average disease specific resource utilisation per patient for 30 days was $786 for NM-CRPC and $2,210 for M-CRPC health states with the cost driver being chemotherapy or prescription drugs different than ADT. The total average cost for NM-CRPC health state was $20,457 compared to $45,956 for M-CRPC health state.

Conclusions: The disease specific resource utilisation costs for a patient in M-CRPC are significantly higher than the costs of NM-CRPC. This being said it would be interesting to study the total healthcare costs from a societal perspective in order to improve the cost management of PCa.

37. The use and effects of ehealth tools for patient self-monitoring and reporting of outcomes following medication use: a systematic review

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Background: ehealth tools are becoming increasingly popular for helping patients self-manage chronic conditions. Little research has examined the effect of ehealth tools for patient self-reporting on medication management. This review aims to evaluate whether ehealth tools featuring patient self-reporting of symptoms and adverse effects are effective at promoting medication changes and improving patient outcomes.

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Methods: MEDLINE, EMBASE and CINAHL were searched from Jan 1, 2000 through to April 25, 2018. References were also searched. Title, abstract and full text review, as well as data abstraction and risk of bias assessment were performed in duplicate. Due to high heterogeneity, results were not meta-analyzed, and instead presented as a narrative synthesis.
Results: Thirteen randomized controlled trials (RCTs) and one open-label intervention were included, from which eleven unique ehealth tools were identified. Four RCTs found statistically significant increases in positive medication changes as a result of using ehealth tools. Eight RCTs found improvement in patient symptoms following ehealth tool use, especially in adolescent asthma patients. Three RCTs showed that ehealth tools may improve patient self-efficacy and self-management of chronic disease. Little or no evidence was found to support the effectiveness of ehealth tools at improving medication recommendations and reconciliation by clinicians, medication-use behaviour, health service utilization, quality of life, or patient satisfaction.
Conclusions: Initial evidence showing ehealth tools may improve patient symptoms and lead to medication changes is promising, however more high-quality research is needed to explore how ehealth tools can be used to effectively manage use of medications to improve patient outcomes.

38. The pan-Canadian Pharmaceutical Alliance: how policy, governance and process changes are affecting public drug plan reimbursement

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Increasingly, the pan-Canadian Pharmaceutical Alliance (pCPA) has become the key forum for interjurisdictional dialogue and action on pharmaceutical policy issues. Since its generic pricing agreement achieved earlier this year, the alliance has turned more of its attention to single-source medicines, leading to the launch of new brand process guidelines in June 2018. This presentation will: 1) explore how the evolving pCPA is affecting the Canadian pharmaceutical marketplace; 2) examine what recent developments tell us about the future state of public reimbursement for medicines; and 3) consider what else may lie ahead for the pCPA. In addition, we will identify issues arising from the process guidelines, including gaps and opportunities. This presentation will update CAPT members on the latest data regarding pCPA's negotiations and their impact on the public reimbursement of new innovative medicines in Canada. It will build on 3Sixtyâ€™s previous analyses that were presented at CA PT 2016. Among the relevant trends we will explore are the impact of Quebec's participation in pCPA negotiations on the availability of new innovative medicines in that province, therapeutic class negotiations, the growing number of negotiations that lead to closed files without agreement and how long new medicines wait in the queue before negotiations are undertaken. We will also review the political, health policy, economic and legal aspects of the pCPA and provide a number of considerations for how pCPA can continue to evolve in the context of other national issues, such as national pharmacare.

39. Prevalence and characteristics of hospitalized patients on opioid therapy and risk of re-admissions and emergency department visits associated with opioid use in the 90 days post-discharge using Cox proportional hazards model

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Background: Canada is the world second largest consumer of opioids. As the number of opioid prescriptions has increased over the past two decades, the country has witnessed an increase

in hospitalizations resulting from opioid poisonings. Our main objective was to evaluate opioid use for patients admitted to surgical and hospital units at two tertiary hospitals in Montreal and their associated risk of emergency department (ED) visits and hospital re-admissions in the 90 days post-discharge.

Methods: Multiple sources of data were assembled and linked including patient demographics, medical services and prescription claims from the Quebec provincial healthcare databases to describe the clinical profile of patients on opioids. Time-varying opioid use was measured by using dispensing pharmacy records of filled opioid prescriptions post-discharge and was modeled as current, continuous and cumulative duration of use using Cox proportional hazards models. All analyses were adjusted for age, chronic conditions, concomitant medication use, and history of opioid use.

Results: Overall, half of the patients received an opioid prescription at discharge, the majority of whom had no history of opioid use in the one year prior to admission (67%). We found that opioid use was associated with a 19% increase in the risk of ED visits and hospitalizations and the risk increases when examining longer cumulative or continuous duration of use.

Conclusion: Our findings suggest that long-term use of opioids after hospitalization may increase the risk of re-admissions and ED visits and physicians may need to reassess the optimal duration of treatment with these drugs.

40. Calcium channel blockers and diuretics: A retrospective cohort study exploring a prescribing cascade

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Background: Calcium channel blockers (CCBs) are commonly prescribed for hypertension. While their safety profile is generally favourable, CCBs are known to cause peripheral edema, which can be distressing for patients and may result in prescription of a diuretic. Older adults are particularly susceptible to adverse events associated with diuretics (e.g., falls, hypokalemia, acute kidney injury). The extent to which diuretics are prescribed with CCBs at a population-level is presently unknown.

This study seeks to: (1) characterize the association between CCB use and the subsequent receipt of a diuretic and (2) identify drug, patient and provider factors that may be associated with this prescribing cascade.

Methods: A retrospective, population based cohort study was conducted using health administrative databases from Ontario, Canada between September 2011 and September 2016 to identify adults aged 66 and older with hypertension and/or coronary artery disease. Individuals newly dispensed a CCB were compared to prevalent users of angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers. Individuals were followed for 90 days post-index date to identify receipt of a loop diuretic. Hazard ratios were estimated using Cox proportional hazard models adjusting for individual-level characteristics.

Results: Data analysis is ongoing but will be complete before the conference.

Conclusions: Specific conclusions will be submitted subsequently. Due to widespread use of CCBs and the frequency of CCB-induced peripheral edema, we expect a large proportion of the population may be at risk of experiencing the CCB-diuretic cascade. Knowledge of the pervasiveness of this cascade and contributing factors can inform clinical and policy strategies to improve medication safety.

41. Productivity losses after acute coronary syndrome events in Canada: an interim analysis

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Background: The impact of an acute coronary syndrome (ACS) event on a patient's productivity is not well characterized. This study describes the productivity loss following hospitalization for an ACS event in Canada. This interim analysis was conducted to investigate early trends in the study findings.
Methods: Patients were enrolled across three sites in Canada during a routine ambulatory cardiologist visit 4-18 months post-index ACS hospitalization (myocardial infarction or unstable angina). At enrollment, study candidates were < 65 years old, had returned to work 4 weeks following their index ACS hospitalization, and were on a lipid lowering therapy prior to or at index hospitalization. Baseline characteristics were collected from medical records, while productivity loss was collected using a validated survey.
Results: An interim analysis of the study was performed on 44 patients (91% myocardial infarction, 9% unstable angina). Enrolled patients were almost exclusively male (96%), on average 53.6 years old, and had an average BMI of 29.1 kg/m2. The total annual lost productivity from a societal perspective was 57.5 (SD 56.3) workdays. This was composed of 45.8 (SD 48.8) days due to missed work, 8.8 (SD 24.8) days due to presenteeism, and 3.0 (SD 19.6) days attributed to caregiver help.
Conclusion: The results suggest that days taken off work after discharge are significant for patients who have experienced an ACS event, and the societal impact of ACS is high. This study is likely to have underestimated the impact, as the study population is of working-age and relatively healthy.

42. Persistence of pharmaceutically-derived cannabinoid use in Manitoba

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Aim: This study aims to assess the persistence of use of pharmaceutically-derived cannabinoid agents and assess the potential socio-demographic characteristics and medical conditions associated with discontinuation of use.
Methods: This study used administrative data from April/1st 2004 to March/31st 2017, from the Manitoba Population Research Data Repository located at the Manitoba Centre for Health Policy (MCHP), University of Manitoba. Incident users were included and followed for one year from the date of first prescription dispensation. Data were analyzed, using a competing risk regression model (Cause-specific hazards model), with death from any cause as the competing risk, to assess factors that may affect discontinuation rates. Time to discontinuation, in days, was the dependent variable.
Results: Among 7050 pharmaceutical cannabinoid users, 6835 were incident users. The mean (SD) age of users was 52.5(15.2) and 59.3% were females. Only 15.2% of incident users continued using cannabinoids after one year. The final regression model showed that age and income status had a significant effect on persistence of cannabinoid use. Among all medical conditions included, fibromyalgia, osteoarthritis, and substance abuse disorder had a significant effect on discontinuation rates with hazard ratios (95%CI) of 0.86 (0.81-0.92), 0.85 (0.76-0.94), 0.91 (0.84-0.98), respectively.
Conclusion: In a naturalistic setting, the persistence of prescription cannabinoid use was affected by age, income, and specific medical conditions of the incident user. The reason for these observed differences is uncertain and warrants further investigation.

43. Prevalence and risk factors associated with persistent use of opioids after surgery: a meta-analysis

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Objectives: Opioids are commonly prescribed to manage acute pain after the surgery; however,

about 10% continue to consume opioids beyond 90 after the surgery. We will conduct a systematic review and meta-analysis of observational studies to establish the rate of persistent opioid use after surgery, and explore risk factors associated with opioid use beyond 90 days after surgery.

Methods: We will report our systematic review according to the PRISMA guidelines. We will develop comprehensive search strategies with no language restriction, for MEDLINE, PsychINFO, EMBASE and CINAHL in collaboration with an expert librarian. Literature screening and data extraction will be performed by teams of reviewers, independently and in duplicate. When possible, we will pool the association of all predictors reported by two or more studies with persistent opioid use after surgery. We will report our results as odds ratios, absolute risk increase, and associated 95% confidence interval s (CIs). We will explore heterogeneity and publication bias by the visual inspection of forest plot and funnel plots, respectively. We will explore heterogeneity with a priori subgroup analyses (e.g. risk of bias, length of follow-up, type of surgery). The risk of bias will be assessed with criteria proposed by the Users Guides to the Medical Literature. The quality of evidence will be determined with the GRADE approach for each predictor.

Clinical Implications: Pain is important sequelae of surgery. Acute post-operative pain intensity and prolong opioid use correlates with PPSP; therefore findings of our study will enhance understanding to reduce the prevalence PPSP.

44. Leveraging CADTH's Scientific Advice Program for early feedback: from phase 2 studies to RWE

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Randomized controlled trials are considered the gold standard for evidence of clinical efficacy and safety for regulatory and HTA bodies and use in clinical practice. Designing the outright comparative development programs that maintain clinical relevance in rapidly advancing therapeutic areas is becoming increasingly challenging. CADTH's Scientific Advice program engages scientific experts, health economists, HTA, and patients early in the drug development process in order to provide an opportunity to adjust drug development plans based on advice from multiple stakeholders. Takeda is currently seeking scientific advice from the program for a drug in an area of high unmet need, currently in the protocol planning stage of phase II study development. Advice is being sought on the clinical development program, in order to increase the likelihood that this innovative medicine will be available for patients as soon as possible. Although CADTH's scientific advice process is non-binding, it has the potential to provide insight into possible areas of concern in the proposed study protocol and RWE collection when modifications are still possible. Takeda's experience with the program will be highlighted.

45. Management of post-traumatic stress disorder: a protocol for a multiple treatment comparison meta-analysis of randomized controlled trials

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Objectives: We will conduct a network meta-analysis of all randomized controlled trials (RCTs) evaluating therapies for PTSD to determine which therapies show evidence of promoting functional recovery (e.g. return to work), and the relative effectiveness of these treatments.

Methods: We will identify eligible trials, in any language, by a systematic search of PILOTS.

46. Proposed changes to the federal patented medicine pricing rules in canada: case study of a manufacturer's decision-making about regulatory submission

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Objective: To examine the proposed changes to the regulations and guidelines of the Patented Medicine Prices Review Board (PMPRB) and apply them to a case study of the decision-making process that the manufacturer of a new rare disorder medication is likely to go through when assessing whether to seek regulatory approval in Canada.
Methods: The current and proposed PMPRB guidelines are summarized and, using a hypothetical new rare disorder drug as an example, the potential manufacturer's decision-making regarding the impact of the proposed guidelines on its launch is examined.
Results: We assume the new drug will require an average price reduction to all payers to bring the effective price down by 80-90% due to the application of a new basket of comparator countries, pharmacoeconomic criteria and market size.
Conclusion: What should the manufacturer do about the drug's price? Some possible decisions are: (1) make a huge price reduction at regulatory approval, risking pricing in other countries, (2) launch at the desired price and face a PMPRB price investigation, (3) delay the launch in Canada until after other countries, and (4) not to seek regulatory approval in Canada. The high level of uncertainty being generated by the proposed changes in the PMPRB's guidelines will imperil the launch of all new medicines in Canada because it will significantly decrease the attractiveness of the country as a priority jurisdiction in which pharmaceutical companies seek regulatory approval for innovative new products.

47. Assessing the emotional, physical, and financial burden of caregivers for persons with dementia

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Objectives: Unpaid or informal caregivers play a key role in supporting persons experiencing cognitive decline; presently, literature on the burden of informal caregiving is limited.This study aims to examine emotional, physical and financial burden in informal caregivers of persons with dementia.
Methods: Participants are recruited as they accompany a patient for which they are the primary caregiver to a visit with a cognitive neurologist at Sunnybrook Health Sciences Centre.A convenience sample of 100-150 participants is currently being sought.Participants complete a questionnaire capturing demographics, the Zarit Burden Interview, and the Sunnybrook Costing Tool (SBT), designed to assess financial toxicity.In the absence of an appropriate tool to assess the financial burden of caregivers supporting persons with dementia, the Comprehensive Scale for Financial Toxicity from the FACIT Measurement System was modified to address issues in this population in a manner that is relevant.The patient's performance on the Mini-Mental State Exam (MMSE) was also recorded. Upon completion of recruitment, descriptive statistics will be applied to the data.
Results: At the time of writing 29 participants had been recruited to the study, over 60% of which are spouses of the patients and are female.A preliminary assessment of the score on the Zarit Burden Interview and the patient's MMSE score reveals a low level of burden in patients with greater cognition, as is expected.
Conclusion: Upon completion, this study aims to shed light on the burden of informal caregivers, and to better inform policies developed to support them.

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