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**“Patient Engagement and Outcomes:
Taking it to the Next Level”**

ABSTRACTS

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ORAL PRESENTATIONS

1. Serious Infections Associated with Tofacitinib in Rheumatoid Arthritis Patients Previously Treated with Methotrexate

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Objective: To compare serious infections associated with tofacitinib, disease-modifying antirheumatic drugs (DMARDs), tumor necrosis factor inhibitors (TNFi), and non-TNF biologics in rheumatoid arthritis (RA) patients previously treated with methotrexate (MTX).

Methods: We performed a retrospective cohort study with adult RA individuals, previously treated with MTX (continuing or not on MTX therapy), using MarketScan® Databases. Cohort entry was the date of first prescription of one of the medications under study between Jan/2011-Dec/2014. We required subjects to be continuously enrolled with medical and pharmacy coverage for 12 months before cohort entry and to be new users of biologics and tofacitinib. We defined serious infection as one associated with a hospitalization. We classified drug exposure into four groups using time-dependent approach: DMARDs; TNFi +/- DMARDs; non-TNF biologics +/- DMARDs; tofacitinib +/- DMARDs; or non-use (time within none of the previous groups). We estimated the rate of serious infection and hazard ratios (HR) with 95% confidence intervals (CI) to compare the exposure groups. We adjusted the analysis for covariates and potential confounders. Patients were followed from cohort entry until the earliest date of loss of coverage, death, end of the study, or the first hospitalized infection.

Results: We included 21,832 RA patients, 77.0% were female and the median age was 56 (interquartile interval 48-63) years. The incidence of hospitalized

infection was 3.66 (95%CI 1.08-3.01) for tofacitinib and the adjusted HR for was 1.81 (95%CI 1.08-3.01) compared to the non-use group.

Conclusion: Tofacitinib was associated with more hospitalized infections, but this could represent channelling bias.

2. Canadian Utility Norms Derived from the 2013-2014 Canadian Community Health Survey

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Background: Although many Canadian studies provide disease-specific and/or patient group-specific utility scores, utility score norms for the current community-dwelling Canadian population have not been produced. With Canadian guidelines for the economic evaluation of health technologies advocating the use of utilities reflecting those of the general population and for stratified analyses in the presence of result heterogeneity, there is also a need for age, gender and/or jurisdiction-specific utility score norms which could be used in these analyses.

Methods: We used data from the 2013-2014 Canadian Community Health Survey (CCHS). The Health Utilities Index Mark 3 was used to calculate utility scores. Mean (95%CI) and median (IQR) for utility scores were estimated. In addition to Canada-level measures, all utility score norms were stratified by respondents age, gender and/or province/territory of residence. Respondents answers were weighted and 95%CI

were computed using sampling weights and bootstrap weights provided by Statistics Canada to extrapolate the study findings to the Canadian population.

Results: Respondents of the 2013-2014 CCHS represented 30,014,589 community-dwelling Canadians (98% of the Canadian population), half of whom were women (50.6%) and with a weighted average age of 44.8 (95%CI 44.7-44.9). Main results indicated that the mean and median self-reported utility score for Canadians was 0.863 (95%CI 0.861-0.865) and 0.927 (IQR 0.838-0.972), respectively.

Conclusions: Results of this study provide utility score norms for multiple age, gender and jurisdiction-specific strata which are useful for future cost-utility analyses and which could serve as benchmark values for comparisons with future studies.

3. The Impact of OnabotulinumtoxinA on Opioid and Triptan Use in Chronic Migraine: A Longitudinal Claims-based Analysis

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Introduction/Background: OnabotulinumtoxinA (BO-TOX®) is the first Health Canada approved therapy for the prophylaxis of headaches in adults with chronic migraine (CM). Some CM patients use prescription opioids to treat headaches and there is a growing concern regarding opioid use and dependence in Canada. This study investigates whether inferred CM patients change opioid and triptan utilization after one year of onabotulinumtoxinA treatment.

Methods: Patients initiating 3-4 annual, 150-200 unit treatments of onabotulinumtoxinA between Nov 2011-Dec 2014 were identified in the QuintilesIMS longitudinal private drug plan claims database. Those with a history of using triptans, oral migraine prophylactic medications, and opioids in the year prior to initiating onabotulinumtoxinA were categorized as CM patients and included. Opioid and triptan use was measured

between months 13-24 post onabotulinumtoxinA initiation and compared to use in the 12 months prior to initiation. McNemar's and Wilcoxon signed-rank tests were used for statistical testing.

Results: 145 patients were included in the study: 81% female, average age of 45 years. 33% of patients ceased all opioid claims ($p < 0.001$) between months 13-24 post onabotulinumtoxinA initiation. A non-identical 33% of patients ceased all triptan claims ($p < 0.001$) between months 13-24 post onabotulinumtoxinA initiation. The average number of opioid and triptan claims decreased by 20% ($p < 0.001$) and 23% ($p < 0.001$) respectively.

Conclusion: As continued use of onabotulinumtoxinA is associated with a decrease in opioid and triptan prescription claims, further attention is warranted regarding the role that onabotulinumtoxinA plays in reducing the number of CM patients using these medications.

4. Profile of Canadian Adults with Type 2 Diabetes Mellitus (T2DM) and Factors Associated with Diabetes-Related Complications

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Objectives: Characterize profile of Canadians with T2DM, examine prevalence of related complications, investigate factors associated with related complications.

Methods: Data from Statistics Canada's Survey on Living with Chronic Conditions were analysed. Descriptive analyses present the prevalence of T2DM and related complications. Factors associated with related complications evaluated using logistic regression, sample weights and bootstrapping resampling methods.

Results: 2,341 respondents, mean age of 62.9 years and diabetes duration 10.6 years. Prevalence of related complications: eye (34.0%), foot/leg (24.4%), cardiovascular (22.6%), renal (15.7%), neuropathy (10.8%). Factors associated with complications: Eye: > 65 years (odds ratio [OR] 3.7, 95% CI 2.4-5.5, $p < 0.0001$); income < \$29,999 (OR 1.9, 95% CI

1.1-3.2, $p=0.01$), diabetes > 10 years (OR 2.3, 95% CI 1.6-3.5, $p<0.001$), cardiovascular complications (OR 1.8, 95% CI 1.1-2.9, $p=0.01$). Renal: diabetes 6-9 years (OR 3.0, 95% CI 1.4-6.3, $p=0.02$). Cardiovascular: male (OR 1.9, 95% CI 1.3-2.7, $p=0.0006$), eye complication (OR 1.9, 95% CI 1.2-3.0, $p=0.007$), foot/leg complication (OR 2.0, 95% CI 1.3-3.0, $p=0.002$). Foot/leg: cardiovascular complication (OR 2.0, 95% CI 1.4-3.1, $p=0.0006$). Neuropathy: income \$30,000-\$59,999 (OR 2.1, 95% CI 1.2-3.9, $p=0.03$); diabetes >10 years (OR 1.9, 95% CI 1.1-3.8, $p=0.01$), foot/leg complication (OR 7.0, 95% CI 4.1-11.8, $p<0.0001$), eye complication (OR 2.0, 95% CI 1.1-3.7, $p=0.006$). **Conclusions:** Presence of DM-related complications is multifactorial. Other diabetes-related complications were factors associated with DM-related complications.

5. Non-vitamin K Antagonist Oral Anticoagulants and Gastrointestinal Bleeding: A Systematic Review and Meta-analysis

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Background: With established efficacy and convenience, non-vitamin K antagonist oral anticoagulants (NOACs) are increasing in popularity; yet potential association with gastrointestinal (GI) bleeding remains uncertain. We conducted a systematic review and meta-analysis to better characterize this risk.

Methods: EMBASE, Medline, Cochrane and ISI Web of knowledge were searched through January 2016 for randomized trials comparing NOACs to conventional anticoagulation for approved indications. A meta-analysis was conducted with results reported as odds ratios (OR) with 95% confidence intervals (CI). The primary outcome was major GI bleeding. Secondary outcomes included clinically-relevant non-major (CRNM), upper and lower GI bleeding. A priori subgroup analyses by individual NOAC were performed.

Results: Forty-three trials were included, randomizing 166,289 patients. There was no difference in major (OR 0.98, 95%CI: 0.80 to 1.21), CRNM (OR 0.93, 95%CI: 0.64 to 1.36), upper (OR 0.96, 95%CI: 0.77 to 1.20) or lower GI bleeding (OR 0.88, 95%CI: 0.67

to 1.15). Dabigatran (OR 1.27, 95%CI: 1.04 to 1.55) and rivaroxaban (OR 1.40, 95%CI: 1.15 to 1.70) were associated with increased odds of major GI bleeding compared to conventional anticoagulation, whereas no difference was found for apixaban (OR 0.81, 95%CI: 0.64 to 1.02) or edoxaban (OR 0.93, 95%CI: 0.78 to 1.11). These subgroup findings were not observed in some sensitivity analyses.

Conclusions: Overall, major GI bleeding risk was equivalent between NOACs and conventional anticoagulation. Dabigatran and rivaroxaban, however, may be associated with increased odds of major GI bleeding. Further high-quality studies are needed to characterize GI bleeding risk among individual NOACs.

6. Newborn Blood Spot Screening for Galactosemia (GALT), Tyrosinemia Type I (TYRI), Homocystinuria (HCY), Sickle Cell Anemia (Hb SS), Sickle Cell/Beta-Thalassemia (Hb S/β-thal), Sickle Cell/Hemoglobin C Disease (Hb SC), and Severe Combined Immunodeficiency (SCID)

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This analysis was supported by a financial contribution from Alberta Health through the Alberta Health Technologies Decision Process, the Alberta model for health technology assessment and policy analysis. Seven conditions that are widely identified in screening programs across North America are not currently targets in Alberta's Newborn Metabolic Screening (NMS) Program. This analysis is to assess the cost-effectiveness of adding one or a combination of the seven conditions to the program. We created a care-pathway that captures diagnosis, sequelae, treatment and associated resources for each condition, based on which a Markov model was developed to assess costs and health benefits of screening compared to not screening. Direct medical costs, including costs of physician, dieticians, genetic counselling, medication, hospitalization, and laboratory services, were considered. The cost of education and social services for mental or developmental sequelae were included. The time horizon considered lifelong costs and benefits, starting from birth to 80 years of age. Health benefits

included life year. SCD (i.e. Hb-SS, Hb-S/ β -thal, and Hb-SC) alone would provide the greatest value among seven conditions, with an ICER of \$2,621 to produce additional life year. The option of adding all seven conditions to NMS program was associated with a cost per additional life year of \$8,155. Hence, decision-makers ought to consider only those combinations that had a cost less than \$8,155, because those combinations require less money to produce the same additional life year. Screening for any of the seven conditions or combination is associated with improvements in health benefits, but at additional cost increase. Expanding NMS program to include these conditions is ultimately dependent on both the availability of funding and the ability to increase service capacity and provision.

7. Outcomes Associated with Hospital Admissions for Accidental Opioid Overdose in British Columbia: A Retrospective Cohort Study

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Background: While a rise in opioid-related deaths contributed to the declaration of a public health emergency in British Columbia, serious morbidity related to opioid overdose has received less public attention. We investigated neurological, respiratory, cardiac and other adverse outcomes among patients hospitalized for accidental opioid overdose.

Methods: A retrospective cohort study of administrative data on BC residents between 2006 and 2015. The primary outcome was encephalopathy, and secondary outcomes were adult respiratory distress syndrome (ARDS), respiratory failure, pulmonary hemorrhage, aspiration pneumonia, cardiac arrest, ventricular arrhythmia, heart failure, rhabdomyolysis, paraplegia or tetraplegia, acute renal failure, death, and a composite

outcome defined by diagnosis of encephalopathy or any secondary outcome. We estimated whether risk of these serious adverse events increased during repeat hospital admissions compared to initial admissions for accidental opioid overdose and whether risk increased over time.

Results: 3% of accidental opioid overdose admissions included encephalopathy and 25% included ≥ 1 adverse events from the composite outcome. We found no evidence of increased risk of encephalopathy (odds ratio 0.58; 95% CI 0.14 to 2.51) or other outcomes during readmissions compared to initial admissions. Risk of respiratory failure with overdose hospitalizations was significantly higher in 2015 compared to 2006 (odds ratio 3.05; CI 1.15 to 8.08), but other risks were not.

Conclusion: In our study, the risk of respiratory failure associated with opioid overdose increased over time. However, no significant increase in the risk of encephalopathy or other adverse events in repeat versus initial hospital admissions for opioid overdose was observed.

8. The Impact of Metformin Interaction with Physical Exercise on HbA1c, Lipid Profile, Quality Of Life and Functional Capacity

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Background: Diabetes is a major cause of increased hospitalizations and premature death in Canada. Exercise is considered as first-line therapy, but pharmacological agents are often required, with metformin as first-line oral antidiabetic. Although a combination of metformin-exercise is recommended, it remains elusive if their effects are independent. Recent studies suggest their benefits might not be additive. Objective: To investigate the impact of metformin-exercise interaction on HbA1c, lipid profile, quality-of-life and functional capacity.

Methods: A retrospective cohort study using data from Cardiac Wellness Program in Moncton, New-Brunswick between 2003-2016. The primary outcomes were change in HbA1c, lipid profile, quality-of-life and functional capacity using 6-minute walk test (6MWT) over the 12 weeks of cardiovascular rehabilitation. Metformin was measured through recorded prescriptions and exercise was measured using the average weekly exercise minutes. Directed acyclic graphs were used to identify potential confounders which were accounted for with multiple linear regression models.

Results: The cohort included 410 admissions (mean age: 65 years) from 86 metformin users and 324 non-users. The average exercise minutes/week was 102.5 ± 48.4 among metformin users and 109.2 ± 59.2 among non-users. The adjusted interaction coefficient for metformin-exercise was significant for the change in 6MWT (0.418, 95% confidence interval: 0.046, 0.769), but not for other outcomes.

Conclusion: Unlike small trials suggesting deleterious impact of exercise on metformin effect, the current study suggests that among real-world patients, such effect is absent. Moreover, the combination of metformin and exercise led to greater gains in functional capacity than was expected from adding the individual effects of each treatment.

9. Cost-Utility of Novel Tests after a Negative Prostate Biopsy

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Background: Transrectal Ultrasound-Guided Biopsies (TRUSGB) are today the main approach of diagnosing

prostate cancer but overdiagnosis and sampling errors are major limitations. Magnetic Resonance Imaging-Guided Biopsies (MRGB) have been researched and previously published as an alternative approach. In this study, two tests for use after an initial negative biopsy for better patient stratification were assessed: PCA3, ConfirmMDx.

Methods: A Markov model was used over 5, 10, 15 and 20 years. All tests were performed on patients referred to a second biopsy due to a remaining suspicion of prostate cancer after an initial negative biopsy. The Markov model considers the probability of harboring prostate cancer, diagnostic accuracy of the tests, the stratification of patients after performing the tests and probabilities of being assigned to different treatments. The included costs were direct cost in the Quebec health care system perspective.

Results: Introducing PCA3 resulted in cumulative effects at 7.24, 9.12 and 10.21 QALY after 10, 15 and 20 years. The corresponding values for Confirm MDx were 7.24, 9.13 and 10.21. The cumulative costs using PCA3 after 10, 15 and 20 years were \$11525, \$14951 and \$17480. The corresponding costs for ConfirmMDx were \$11706, \$15092 and \$17598. The costs and QALY were compared to the approach used today, TRUSGB, and the incorporation of MRGB. Both strategies, PCA3 and ConfirmMDx, demonstrated similar costs and QALYs as the standard strategy TRUSGB.

Conclusions: Introducing the new tests showed potential of use in clinical practice, demonstrating similar clinical and economic outcomes when compared to TRUSGB.

10. Hypoglycemia Episodes and Cardiovascular Adverse Outcomes in Patients with Diabetes: A Systematic Review

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Background: From a pathophysiological perspective, hypoglycemia is associated with sympathetic activation, endothelial dysfunction, vasoconstriction, QT

prolongation, pro-inflammatory and pro-thrombotic state. From a clinical and outcome perspective, several RCTs, observational studies and subsequently meta-analysis explored the relationship between hypoglycemia events and cardiovascular adverse outcomes. The results of these studies are inconsistent and paradoxical.

Objective: To conduct a systematic review on meta-analysis that explored the possible relationship between hypoglycemia episodes and cardiovascular adverse outcomes in patients with diabetes

Methods: A systematic review was conducted on literature that evaluated the relationship between hypoglycemia and cardiovascular events. PubMed databases were utilized for this search. Meta-analyses prior to October 15th, 2016 were extracted. Publications in English language were included. Bibliography mining was also done on relevant articles to be as inclusive as possible.

Results: Eight meta-analyses were found in English language that included both hypoglycemia and cardiovascular outcomes. Three meta-analyses studied the association between severe hypoglycemia and cardiovascular outcomes. Severe hypoglycemia was associated with a two-fold increased risk of cardiovascular outcome [Hazard Ratio (HR) between 1.91 and 2.33]. One meta-analysis illustrated a dose-dependent relationship between the severity of hypoglycemia and adverse vascular events. HR for mild hypoglycemia was 1.68 with 95 % confidence interval (CI) between 1.25 and 2.26. HR for severe hypoglycemia was 2.33 with 95 % CI between 2.07 and 2.61.

Conclusion: Meta-analyses studies illustrate that there is evidence of a relationship between hypoglycemia events and increase in cardiovascular adverse outcomes. This finding is consistent for both severe and non-severe hypoglycemia episodes.

POSTER PRESENTATIONS

11. Characterizing the Utilization of the Trillium Drug Program by an Oncology Patient Population

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Objectives: The Trillium Drug Program (TDP) is a provincial government program for Ontario residents for whom prescription medications pose a burden on their annual income. Cancer patients are of interest due to rising cost of antineoplastic medications. There is minimal information about TDP costs. The objective is to characterize these patients and to investigate TDP costs.

Methods: Individuals age < 65 with a cancer diagnosis from 2000-2009 came from the Ontario Cancer Registry. The Ontario Drug Benefit database was used to identify prescription medication claims to the TDP. We examined baseline demographics and claims-related characteristics.

Results: 19,029 cancer patients with a TDP claim were included in the study, 63% after their diagnosis. Nearly 60% were female, half were in the poorest two income quintiles and the majority resided in urban areas. Total TDP expenditure increased from \$3.4 million in 2000 to \$22.2 million in 2009. Antineoplastic drug expenditures increased from \$130,000 (4% of total) in 2000 to \$11 million (50% of total) in 2009. Though most cancer types had similar pre-diagnosis TDP expenditures, average costs following diagnosis differed: lung, colorectal and breast cancer patients: < \$200/month; prostate, kidney, myeloma and lymphoma patients: \$400/month; and leukemia patients: over \$1,500/month, dominated by imatinib which accounted for \$5.4 million among only 173 patients.

Conclusions: Our study is one of the first attempts characterizing TDP utilization in an oncology population, showing utilization increasing over time and differing across cancer diagnoses. These results have public health policy implications as antineoplastic drug costs continue to rise.

12. Health Related Quality of Life in Adult Patients with Cutaneous T-Cell Lymphoma- A Preliminary Analysis

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Purpose: Cutaneous T-cell lymphomas (CTCL) are a group of Non-Hodgkin lymphomas primarily developing in the skin but can involve other organs. Individuals with more advanced disease can present with tumours, erythroderma, lymphadenopathy or visceral involvement. The diagnosis of CTCL can potentially have a large impact on quality of life (QoL) due to fear, uncertainty about the future, physical appearance and symptoms. Given that CTCL is currently incurable, it is important to recognize and address QoL issues.

Methods: Newly diagnosed patients were recruited at the one of the two sites: Sunnybrook Health Sciences Centre and the Odette Cancer Centre. Demographic data, disease stage, and duration of symptoms were recorded. Baseline QoL scores were measured using the EQ-5D, the FACT-Lym and the Skindex-29 scales. QoL was reassessed 6 months post diagnosis.

Results: Ten patients were recruited and consented to participate, and all patients completed the reassessment. 60% were male, and the average age at diagnosis was 48 years. At baseline, the majority of patients indicated that their new diagnosis had an overall minimal impact on QoL in areas such as social, emotional and physical well-being. At reassessment, 7 patients indicated they had some slight pain or discomfort. 60% of patients indicated they were slightly more concerned about their skin condition and had more anxiety about the future.

Conclusions: Preliminary data suggests there is some impact on QoL 6 months post diagnosis. Complete

statistical analysis will be conducted during the final analysis of the study.

13. Outcomes following Hospitalization for Accidental Opioid Overdose among Patients with Long-Term Opioid Use: A Retrospective Cohort Study

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Background: While case reports and other observational data provide some evidence about adverse events immediately following opioid overdose, less is known about health outcomes in the year following nonfatal opioid overdose. We investigated neurological, respiratory, cardiac and other adverse outcomes in the year following hospitalization for accidental opioid overdose among patients with a history of long-term opioid therapy (LTOT) in British Columbia.

Methods: A retrospective cohort study of patients with LTOT at any time between 2006 and 2015, based on administrative data. From a cohort of patients with LTOT, patients who were discharged following an accidental opioid overdose hospitalization were matched with up to 20 controls on sex and age within 2 years. Patients were followed for up to 1 year. The primary outcome was encephalopathy. Secondary outcomes were adult respiratory distress syndrome, respiratory failure, pulmonary hemorrhage, aspiration pneumonia, cardiac arrest, ventricular arrhythmia, heart failure, rhabdomyolysis, paraplegia or tetraplegia, acute renal failure, death, a composite outcome (encephalopathy or any secondary outcome), and "serious adverse events" (all-cause hospitalization or death).

Results: Fewer than 5 patients in each cohort (overdose patients and controls) experienced encephalopathy. Odds of the composite outcome (OR 2.15; CI 1.48 to

3.12) or a serious adverse event (OR 1.97; CI 1.62 to 2.39) were higher for patients in the year following overdose compared to controls.

Conclusion: Risk of serious morbidity and mortality may be elevated in the year following an accidental opioid overdose among patients with a history of long-term prescription opioid use.

14. Bone-Targeted Therapy Utilization among Metastatic Castration-Resistant Prostate Cancer Patients in a Real-World Setting

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Objectives: The aim of our study was to describe real-world BTT utilization and to identify factors associated with its utilization in mCRPC patients in Quebec.

Methods: We conducted a retrospective cohort study in two of the main McGill University hospitals. We selected patients treated for mCRPC in medical oncology departments from January 1, 2010, to June 30, 2014. Patients' charts were reviewed and relevant data was extracted. The cohort was divided into two groups according to mCRPC diagnosis year. The cut-off year chosen was 2012 as it corresponded to the RAMQ's public reimbursement of denosumab. Descriptive statistics were used to describe BTT utilization before and after 2012. Cox regression was used to identify predictive factors of BTT use.

Results: In our cohort, 308 patients treated for mCRPC were selected with 162 patients (53%) from 2010 to 2012 (pre-2012 group) and 146 (47%) from 2012 to 2014 (post-2012 group). In the pre-2012 group, 80% of patients had at least one prescription for a BTT comparatively to 84% in the post-2012 group. Factors that increased the likelihood of receiving a prescription for a BTT were: bone metastases (HR: 4.4; 95%CI: 2.6-7.5), bone and lymph nodes (HR: 4.7; 95%CI: 2.6-8.4) and visceral metastases (HR: 3.6; 95%CI: 1.8-7.2) at CRPC diagnosis, symptomatic disease at mCRPC diagnosis (HR: 1.5; 95%CI:

1.1-2.1), and mCRPC diagnosis after 2012 (HR: 1.5; 95%CI: 1.1-2.0).

Conclusion: Factors associated with BTT utilization were bone metastases at CRPC diagnosis, mCRPC diagnosis after 2012, and symptomatic disease at mCRPC diagnosis.

15. Cost-Minimization Analysis of Community Pharmacy-Based Point of Care Testing for Strep Throat in British Columbia

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Background: Point-of-care (POC) testing in community pharmacies to identify cases of severe sore caused by group A beta-hemolytic streptococci (strep throat), which require antibiotic treatment, will enable pharmacist-based care for this condition. Our objective was to conduct an economic evaluation of treating severe sore throat when POC testing for strep throat was offered in select British Columbia community pharmacies.

Methods: We conducted a cost-minimization analysis, from the public payer perspective, to estimate mean cost per patient of assessing and treating severe sore throat in two scenarios: 1) usual care where patients saw a physician in either a family physician's office, a walk-in clinic, or an emergency room (ER); and 2) a new scenario where patients received care in one of the three pathways described above or in a community pharmacy offering POC strep throat testing. One-way sensitivity analyses were conducted to account for uncertainty in the model.

Results: Mean cost per patient in each of the pathways in the base-case analysis was: 1) \$41.46 for family physician, 2) \$41.46 for walk-in clinic, 3) \$57.56 for ER, and 4) \$19.12 for community pharmacy. These results translate into savings of \$14.69 per patient for the new scenario. All sensitivity analyses yielded cost savings for the new scenario ranging from \$11.02 to \$18.37.

Conclusions: Funding POC testing for strep throat in British Columbia community pharmacies will lead

to cost savings within the public health care system. Similar analyses underway for Alberta, Nova Scotia and Ontario are expected to corroborate these results.

16. Canadian Study of Adherence Outcomes in HUMIRA® (Adalimumab) Patients: Three-Year Results from the Companion Study

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Objectives: HUMIRA® (adalimumab, ADL) is a TNF- α inhibitor indicated for various inflammatory autoimmune diseases. Patients receiving ADL can enroll in the AbbVie Care patient support program (PSP). This retrospective study assessed the impact of PSP services and patient characteristics on persistence and adherence to ADL over 3 years.

Methods: Upon probabilistic linkage to the IMS longitudinal pharmacy transaction database, PSP patients starting ADL between July 2010-August 2012 were tracked for 36 months to calculate persistence (end if >90 days without therapy). Cox and multivariable logistic regression models provided hazard ratios (HR)

and adjusted odds ratios (OR) to measure the association between patient characteristics/PSP services and persistence and adherence, respectively. Adherence was measured using the medication possession ratio (MPR) ($\geq 80\%$ MPR).

Results: In the overall cohort (N=4,772), older age groups had significantly greater odds of adherence (40-49, 50-59, 60-69, 70+; OR=1.3, 1.4, 1.4, 2.1; $p < 0.05$ for all comparisons) relative to the 30-39 years age group. In a subset of patients (n=2,866) who were persistent when ongoing care coach calls became available, those receiving this service were 65% less likely to stop therapy (HR=0.35, $p < 0.01$) and 38% greater odds to be adherent (OR = 1.38, $p < 0.01$) compared to those without it.

Conclusions: Ongoing care coach calls provided by the AbbVie Care PSP significantly correlate with greater patient persistence and adherence over 36 months. Patients aged between 30 and 39 years appear to have lower adherence compared to older age groups. These results may help refine services that improve treatment adherence.

17. A Smoking Cessation Initiative Across Ontario's Regional Cancer Centres: Early Successes and Continuing Challenges

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Background: Substantial evidence exists that quitting smoking after a cancer diagnosis can result in reduced all-cause and cancer-specific mortality, greater response to treatment, reduced toxicity, and decreased risk of recurrence and second primaries. Based on this evidence, Cancer Care Ontario (CCO) undertook a smoking cessation (SC) initiative for new ambulatory cancer patients in the 14 Regional Cancer Centres (RCCs) in 2014.

Methods: A committee of experts recommended a framework for cancer patients to be screened for tobacco use, advised on the benefits of quitting, and

referred to internal or external SC services for support. CCO's executive leadership supported the initiative, and regional SC "champions" were designated to lead its implementation locally. A minimum set of standardized performance metrics is captured by CCO, in order to monitor implementation and review with the RCCs in quarterly performance management sessions.

Results: In 2016, 60.6% of all new cancer patients were screened for tobacco use. Of those screened, 17.6% were current or recent (within the last 6 months) tobacco users. More than three-quarters of these individuals were advised of the benefits of SC (76.7%), and a referral to cessation services was recommended to over half (56.2%). Approximately 20% of smokers accepted the referral to SC services.

Conclusions: CCO, working collaboratively with the RCCs, led the province-wide implementation of a standardized SC intervention in a relatively short timeframe. Ongoing barriers experienced by the RCCs include lack of funding for Nicotine Replacement Therapy (NRT), limited financial resources to support the program, and physician buy-in.

18. A Cost-Utility Analysis Of Artificial Urinary Sphincter Versus Advance Male Sling In Post Prostatectomy Stress Urinary Incontinence: A Canadian Healthcare Perspective?

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Background: The artificial urinary sphincter (AUS) remains the gold standard for the treatment of post prostatectomy stress urinary incontinence (PPSUI). However, in recent years, minimally invasive, less expensive sling devices (Advance) are offered as potential alternative treatments. We sought to investigate the long-term cost-utility of the AUS compared with Transobturator Retroluminal Repositioning Sling (Advance sling) in the treatment of severe PPSUI.

Methods: A Markov model with Monte-Carlo simulation was developed to estimate the incremental cost-utility ratio (ICUR) of AUS vs. Advance sling from a

provincial payer perspective over a 10-year period. The Markov model included 4 states (wet, post-wet, dry and death). Uncertainty was analyzed using deterministic and probabilistic sensitivity analysis.

Results: AUS Implantation had a 10-year mean total cost of \$14,300 (SD±3,509) for 7.64 QALYs. On the other hand, Advance sling had a mean total cost of \$17,042 (SD±12435) for 6.53 QALYs. The cost-utility analysis showed that AUS becomes a dominant strategy when compared to Advance sling over 10 years. The incremental cost savings of AUS was \$2,742 with an added effectiveness of 1.11 QALYs. The probability of becoming wet after an Advance sling as well as the probability of going through AUS after an initial surgery with Advance sling demonstrate the most variability compared to base-case ICUR in one-way sensitivity analyses. (751,16\$ and 437,07\$, respectively).

Conclusions: Although the initial cost of sling is attractive, superior long-term outcomes are demonstrated with durable high success rate of AUS in men with severe PPSUI.

19. Comparative Safety of the Sodium Glucose Co-transporter 2 (SGLT2) Inhibitors: A Systematic Review and Meta-analysis.

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Background: Clinical guidelines recommend sodium glucose co-transporter-2 (SGLT2) inhibitors as the preferred second-line agents for glycemic control in type 2 diabetes in individuals with cardiovascular

disease. However, regulatory agencies have issued several serious safety warnings regarding these agents. **Methods:** We conducted a systematic review and meta-analysis of all randomized control trials comparing an SGLT2 inhibitor to placebo in adult patients with type 2 diabetes. The comprehensive literature search included PubMed, the Cochrane Library, EMBASE and International Pharmaceutical Abstracts. Outcomes of interest included serious safety events: acute kidney injury (AKI), diabetic ketoacidosis (DKA), urinary tract infections (UTI), bone fractures, and lower limb amputations. Random effects models using restricted maximum likelihood were used to estimate the pooled effect estimates.

Results: We screened 1350 citations of which 454 relevant abstracts were identified with 98 studies included in the final analysis. When compared to placebo, SGLT2 inhibitors were found to be significantly protective against AKI (6 studies / 88 events; OR = 0.61; 95% CI 0.40, 0.93; I²=0.0%), while no difference was found for UTI (76 studies / 3191 events; OR = 1.05; 95% CI 0.96, 1.14; I²=0.9%), DKA (8 studies / 6 events; OR = 0.82; 95% CI 0.23, 3.00; I²=0.0%), or bone fracture (19 studies / 399 events; OR = 0.94; 95% CI 0.76, 1.16; I²=0.0%). No studies reported on amputations.

Conclusions: Current evidence from RCTs does not suggest an increased risk of harm with an SGLT2 inhibitor over placebo with respect to the AKI, DKA, UTI or fracture.

20. Estimation of Non-severe Hypoglycemia Events (NSHE) Prevalence in Real-World Clinical Settings for Canadian Patients with Type 2 Diabetes Who Utilize Sulfonylurea (SU)

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Background: Several studies from Europe and North America reported that NSHE frequently occur in real world clinical settings but are infrequently reported to healthcare providers. Objective: To estimate the

prevalence of NSHE in real-world clinical settings for Canadian patients with type 2 diabetes who utilize sulfonylurea.

Methods: Data from literature, which evaluated the prevalence or incidence of NSHE in real-world clinical settings, were obtained. PubMed and Google Scholar databases were utilized for this search. An ecology of medical care for Canadian patients with diabetes who are utilizing SU was constructed to estimate the prevalence of NSHE in real-world clinical settings.

Results: The number of patients with type 2 diabetes in Canada who utilized SU during 2016 was estimated at 747,863 patients. The model incorporating data from real-world clinical settings estimated that 322,248 patients per year in Canada [maximum 498,323 patients, minimum 199,329 patients] were experiencing NSHE attributable to SU utilization. This model was constructed with the assumption of probability of only one episode of NSHE per annum per patient. Applying a model with compounded events of NSHE per annum, according to data from real-world clinical settings, could illustrate that 4,028,114 events of NSHE per year occurs in Canada attributable to SU use.

Conclusion: This modeling study illustrates that a large proportion of Canadian patients with type 2 diabetes utilizing SU are experiencing NSHE. Mostly NSHE are not reported to healthcare providers. This calls for better recording of these episodes and closer communication between the patients and providers.

21. Registration Issues in Phase III Randomized Controlled Trials of the Practice-Changing Novel Antithrombotic Drugs

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Background: Phase III randomized controlled trials must be registered on a public platform to prevent outcome-reporting bias. International standards require endpoints to be disclosed before enrolment of the first patient. Any modification should be duly justified in the eventual publication and in a registration platform

before the Primary Completion Date. We aimed to evaluate if trial-registration policies were followed in phase III trials regarding the new widely-prescribed antithrombotic agents.

Methods: Via PubMed, we searched for phase III, more-than-a-thousand-patient randomized controlled trials on the novel antiplatelet and anticoagulant drugs: prasugrel, ticagrelor, cangrelor dabigatran, rivaroxaban, apixaban and edoxaban. The included trials had to be published in high impact factor journals. We searched for major registration issues by assessing the data found on the public platform ClinicalTrials.gov and in the corresponding publications.

Results: We identified 38 trials published between 2008 and 2017. All trials were sponsored by the industry. Protocol was modified on ClinicalTrials.gov after the publication date in 31 (82%) trials. We documented major Endpoints Registration Issues: any endpoints, 35 (92%) studies; Primary Efficacy Endpoints, 28 (74%) studies; safety endpoints, 21 (55%) studies; Secondary Endpoints, 32 (84%) studies. For 19 out of 28 (68%) FDAAA applicable trials, results were not registered within one year of Primary Completion Date.

Conclusions: Despite legal, deontological and ethical obligations, trial-registration policies were generally not respected in major impact phase III trials regarding the new antithrombotic drugs. This practice complicates results generalization for real-life clinical application.

22. Prolaris and Decipher: Impact on Prostate Cancer Decision of Treatment

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Prostate Cancer Canada-Discovery Grant 2015

Background: In Canada, it is estimated that prostate cancer (PCa) will account for 21% of all new cancer cases in 2016. Inaccurate risk classification is a challenge due to the limited ability of current risk assessment tools and modalities in distinguishing indolent from aggressive cancers. There is a need for evidence-based testing that will improve stratification accuracy. Prolaris and Decipher are new promising tools that could decrease the uncertainties accompanying treatment decision.

Objective: This systematic review assesses the clinical utility of Prolaris and Decipher in PCa treatment after a positive biopsy and post-prostatectomy, respectively.

Methods: The Cochrane, Embase, Medline, and Web of Science databases were searched for clinical utility evidence.

Results: The search yielded 334 articles, of which seven met the inclusion criteria. Both tests demonstrated a change in treatment recommendations between pre- and post- testing. Overall, Decipher altered 36% of treatment decisions post-prostatectomy, and data showed an increase in recommendations for observation ranging between 20% and 42%. In particular, one study resulted in the reclassification for over 60% of high-risk patients to low-risk post-Decipher testing. On the other hand, in one study on Prolaris, a 47.8% change in treatment decision was noted, of which 72% was treatment reductions. Similarly, in another study based on a physician selected population, Prolaris lead to a 37.2% reduction in interventional treatment.

Conclusion: Prolaris improves treatment decision-making after a positive biopsy while Decipher does so in the post-prostatectomy setting. Further clinical utility and economic studies are warranted to provide further guidance.

23. Cost-Effectiveness of Sunitinib vs. Pazopanib in Metastatic Renal Cell Carcinoma (mRCC) In Canada Using Real-World Data.

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Objectives: Outside of controlled clinical studies, the understanding of the effectiveness and cost associated with targeted therapies for mRCC is limited in Canada. The purpose of this study was to assess the cost-effectiveness of targeted therapies for mRCC patients using real-world data from a Canadian database.

Methods: A Markov model with microsimulation was completed to analyse the cost-effectiveness. A time-horizon of 5 years was used and survival curves (Kaplan-Meier and direct adjusted survival curves) were used to estimate the transition probabilities between states. The costs of drugs were estimated by using the average duration of treatment in each line of therapy based on results from the database. Cost of management and progression of the disease were considered in the model. Deterministic and probabilistic sensitivity analysis were completed to assess the variability.

Results: The median overall survival when adjusted for confounding variables was 32 and 21 months for sunitinib and pazopanib respectively. This difference was statistically significant. ($p=0.02$) The total cost for the sunitinib strategy was \$210,257 and \$152,161 for the pazopanib strategy. There was a median survival difference of 0.71 life years and 0.421QALYs between both treatments. The Incremental cost effectiveness ratio between sunitinib and pazopanib is \$137,995/QALY and \$81,825/ LYG.

Conclusions: When using real-world data, sunitinib increases survival and is a cost-effective option compared to pazopanib with a ICER of \$81,825/ LYG.

24. Integrating Novel Screening Methods for Prostate Cancer, Cost-Utility Interventions

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Background: To find a higher proportion of the significant prostate cancers and reduce unnecessary biopsies, new screening tests are a possible solution. The available screening methods showing potential to reduce unnecessary biopsies are 4Kscore, Prostate Health Index (PHI). The aim of this study was to evaluate the cost-effectiveness of introducing these tests compared to the use of only Transrectal Ultrasound Guided-Biopsy (TRUSGB) and Magnetic Resonance Imaging-Guided Biopsy (MRGB).

Methods: To calculate the cost-effectiveness for the screening tests, a Markov model was developed to integrate new screening tests for prostate cancer. A systematic literature review was performed to get the necessary data. Quality-adjusted life years gained (QALY) and costs for the tests were estimated over a time horizon of 5, 10, 15 and 20 years. The rate of missed cancers of the test is also a part of the model, as well as direct medical costs.

Results: The costs for 4Kscore were \$6000, \$8300, \$10389 and \$11995 for the different time spans and for PHI \$7839, \$11164, \$14700 and \$17419 respectively. The cumulative effects for 4Kscore were 4.38, 7.42, 9.42 and 10.59 QALY and for PHI they were 4.33, 7.28, 9.18 and 10.25 respectively. Compared to the TRUSGB and MRGB strategies, the 4Kscore strategy was the dominating strategy, yet the PHI strategy demonstrated similar costs and QALYs as the TRUSGB strategy.

Conclusion: The new screening methods show potential in complementing the existing screening process for prostate cancer by improving the costs and QALY compared to TRUSGB and MRGB.

25. Patients Measuring the Impact of Canadian and Provincial Pharmacare Decisions: Patient-Centric Experience Measurement

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Background: Many patients/patient groups expressed an interest in providing quantitative measures to accompany their stories regarding their experiences and perceived value of different aspects of the Canadian and provincial pharmacare processes, decisions and outcomes which impact them. This presentation focuses on the approach patients/patient groups took to develop patient-centric indicators to measure their value and experiences with the current Canadian and Provincial pharmacare system decisions and programs.

Methods: Patient dialogues explored how best to 'measure' the different aspects of their pharmacare experiences and challenges. Surveys, focus groups and pilots were used to identify, test and validate indicators/measures which would provide the most convincing evidence of their experiences. Measures in the form of survey questions with scales and rankings were developed and piloted with patients/patient groups.

Results: Patients identified 36 indicators for pharmacare, aimed at macro (healthcare system), meso (practice and service delivery levels) and micro (individual patient/family/caregiver) levels. 92% of 424 survey respondents, 110 individuals in focus groups, 60 in pilots identified >4 major issues at the macro and meso levels regarding decisions for access and coverage, and outcomes including inequities. 56% identified two key issues at the individual level related to understanding drugs prescribed and their side effects.

Conclusion: Patients/patient groups having indicators and measures to standardize their evaluation of the healthcare system and drug programs will ensure that decision makers and practitioners get more concrete and consistent evaluation from greater numbers of patients regarding the impact of pharmacare decisions. This evidence will complement the patient stories.

26. The Risk of Fragility Fractures in New Users of Dipeptidyl Peptidase-4 Inhibitors Compared to Sulfonylureas and Other Anti-Diabetic Drugs: A Cohort Study

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Background: Mixed evidence exists for the effect of incretin-based therapies on osteoporosis in type-2 diabetes. We conducted a cohort study to determine the association between dipeptidyl peptidase-4 (DPP-4) inhibitors and common fragility fractures (upper extremity, hip, and spine).

Methods: Using UK-based Clinical Practice Research Datalink we identified adults without prior fractures receiving a new antidiabetic agent or a new type-2 diabetes diagnosis between 2007 and 2016. Primary analysis compared new users of DPP-4 inhibitors versus sulfonylureas (SU). The association between DPP-4 inhibitor use and incident fragility fractures was estimated using Cox proportional hazards ratio models. Deciles of high-dimensional propensity scores and other antidiabetic drugs were used as covariates.

Results: We identified 7,993 and 26,637 new users of DPP-4 inhibitors and SUs, respectively. Mean age was 58.8, 40% were female, mean diabetes duration was 1.3 years, and 42% had A1c >9%. Over 9 years (mean follow-up=1.2 years), the crude fracture rate was lower among DPP-4 versus SU users (2.9/1000 vs. 5.2/1000 person-years; P-value=0.007). After covariate adjustment, there was no significant difference in fracture risk (hazard ratio adjusted, aHR=0.78, 95% CI 0.50-1.21). Sensitivity analyses showed similar results when definition of DPP-4 inhibitor was varied; or different methods were used for confounding adjustment. DPP-4 inhibitors were associated with a significantly lower fracture risk versus thiazolidinediones (aHR=0.47, 95% CI 0.27-0.83); but not versus insulin (aHR=1.04, 95% CI 0.44-2.44).

Conclusions: DPP-4 inhibitors are not associated with an increased risk of fragility fractures versus SUs or insulin; however, are associated with a lower risk versus thiazolidinediones.

27. A Systematic Literature Review to Understand the Impact of Calcium-Containing Phosphate Binders and Sevelamer and on Mortality, FGF-23, Bone Related Disorders, and Cholesterol Levels in Patients with Kidney Disease

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Background: Phosphate binders are pivotal in the management of hyperphosphatemia in patients with kidney disease. Calcium containing phosphate binders (CPBs) may be effective and perceived to be less expensive but more likely to cause hypercalcemia compared with non-CPBs, such as sevelamer. Objectives: To compare the effects of phosphate binders on patients with chronic kidney disease (CKD) and bone mineral disorders in regard to mortality, FGF-23, bone related disorders and cholesterol levels.

Methods: A systematic literature search was conducted. Two independent reviewers identified and reviewed relevant references. Included were any peer-reviewed randomized studies that presented research on the impact of CPBs and sevelamer (hydrochloride or carbonate) on the outcomes of interest. Patients had to be >18 years with kidney disease. Papers published in any language after 1995 were accepted. Studies where outcomes of interest were part of pooled analyses or, post-hoc analyses were excluded.

Results: From the 1,690 identified references, data from 24 studies were summarized; 5, 5, 6, and 8 studies that reported outcomes for mortality, FGF-23, bone related disorders, and cholesterol levels, respectively. Most included studies reported advantages of sevelamer. This review included multiple outcomes compared to others that focused on fewer outcomes.

Conclusions: This research concludes that sevelamer has advantages in regard to the outcomes of interest and should therefore be considered preferentially to CPBs for the management of hyperphosphatemia in CKD patients. A CADTH Rapid Response suggested

that sevelamer is less costly and more clinically effective than calcium-carbonate in a subset of pre-dialysis or non-dialysis-dependent CKD patients.

28. Building Bridges: How Research Changes in Multi-Disciplinary Patient Inclusive Settings

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Objective: To describe how engaging patients and other disciplines can change conclusions in qualitative health services research.

Approach/Methods: A recent qualitative research project included a multi-disciplinary research team of health care professionals, engineers, information specialists, health systems specialists and patients. From this, two papers are being developed: 1) patient perspective on shared decision making; 2) healthcare professionals and health communication. Initial coding of patient and healthcare professional interviews was completed by the core research team. Then, a two-day research meeting with 11 multidisciplinary members of the research team, including a patient and a patient navigator, was organized to discuss and re-code data. Members coded four interviews individually prior to the meeting, and during the meeting placed and grouped them into emerging themes.

Results: Initial coding led to five emerging themes on healthcare professionals, the overall conclusion focusing on building electronic health records that facilitate care coordination. Group coding came to a slightly different conclusion: until pharmacists can see indications, and physicians gain insight into adherence, neither group will be fully able to provide the best care. Initial coding of patient interviews focused around how better tools are needed to facilitate the simplification of communicating health information and easing the burden on patients. After group coding, the conclusion ended very differently, centering around the influences on how decisions are made, with an emphasis on roles and power dynamics.

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Conclusions: More research needs to be done on how coding and conclusions change depending on who is included in the research team.

29. Effectiveness of a Diabetes Screening Intervention in the Canadian Workplace

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Background/Objectives: There is a lack of Canadian data on the effectiveness of diabetes interventions in the workplace. To better inform workplace stakeholders, the objective of this study was to evaluate the effectiveness of Motivaction™ a diabetes screening and education pilot program in the workplace.

Methods: The Motivaction™ program involves a voluntary web-based diabetes health risk assessment (CANRISK) combined with an opportunity for those eligible (i.e. being diabetic or having a CANRISK score >21) to attend two on-site biometric screening meetings with a registered nurse (RN), and four educational sessions by telephone with a certified diabetes educator (CDE). Biometric data as well as information on self-efficacy, lifestyle changes, productivity, quality of life, mental health and program satisfaction, were collected at baseline and six months.

Results: 577 attended the initial clinical visit with the RN. During this 1st session, 41% of employees were identified as being at risk of developing diabetes (HbA1c between 5.5% and 5.9%) and 22% were identified to be pre-diabetic (14%) or having diabetes (8%). Statistically significant reductions in HbA1c from baseline to study end were observed among those with pre-diabetes or diabetes. No statistical

differences were observed in terms of productivity or mental health although a statistical improvement was seen in employees' well-being. More than 90% of employees would recommend the Motivaction™ program to other employers.

Conclusion: This study provides a framework for future diabetes interventions in the workplace and demonstrates that workplace interventions can reduce employees' diabetes risk levels, and are valued by employees.

30. Variation in Prescribing Rates of Oral Antibiotics Among General Practitioner and Emergency Department Physicians in Newfoundland and Labrador, Canada

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Background: Choosing Wisely NL recently undertook a multiphase campaign aimed to reduce unnecessary outpatient antibiotic use. This study describes the variation in oral antibiotic prescribing among general practice (GP) and emergency department (ED) physicians.

Methods: In June 2017, Choosing Wisely NL launched a prescriber-focused antibiotic campaign, which included peer comparison reports provided to physicians with >25 total prescriptions registered with the NL Medical Association. Prescribing information was available for patients 65-years of age and older receiving NL provincial drug plan coverage.

Results: Between 1April2015 and 31March2016, there were 1,405,464 prescription records for seniors, initiated by 509 GP and 29 ED physicians, of which 47,328 (3.4%) were for an oral antibiotic. Of 498 physicians sent a custom report, 139 (28%) downloaded their report within 24-hours and 180 (36%) within

1-week. The average prescribing rate was 33 and 224 antibiotics per 1000 total prescriptions for GPs and ED physicians respectively. The rate ratio between the 90th and 10th percentile was 5.8 for GPs and 2.3 for ED physicians. After adjusting for differences in patient age, sex, and comorbidities, the 90th to 10th percentile rate ratio was 9.8 for GPs and 2.1 for ED physicians. The most frequently prescribed oral antibiotics were ciprofloxacin (18%), amoxicillin (17%), and azithromycin (11%) among GPs, and ciprofloxacin (22%), cephalexin (11%), and nitrofurantoin (10%) among ED physicians.

Conclusions: There is a 2 to 10-fold variation in prescribing of outpatient oral antibiotics for seniors among physicians in NL. Pre-specified evaluations at 6-months and 1-year post-campaign are planned.

31. Over 63,700 Ontario Seniors have Initiated Denosumab: User Characteristics and Persistence with Therapy

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Purpose: Denosumab was added to the Ontario Drug Benefit formulary for patients at high risk for osteoporotic fracture in February 2012. Each injection covers 6-months of therapy. We sought to describe new denosumab users and estimate persistence with therapy.

Methods: We identified Ontario seniors (aged ≥ 66 years) initiating denosumab therapy from 2012/02 to 2016/03. Patient characteristics were summarized based on medical and pharmacy claims, and stratified by residence in the community or long-term care (LTC). Persistence with therapy and return to therapy after discontinuation (>90-day gap) were summarized.

Results: We identified 63,780 (97% female, 13% LTC, 79% in urban areas) new users of denosumab; with an average of 1,300 (SD=183.0) patients initiating

therapy per month. Denosumab users residing in the community had a higher prevalence of bone mineral density testing (63% vs. 5%), yet were younger (mean age=78.3 years vs. 87.6 years), and had a lower proportion of hospitalizations (14% vs. 31%), or hip fractures (3% vs. 9%) compared to LTC patients. Prior osteoporosis drug use was high in both groups (78% community, 82% LTC) as was persistence with denosumab therapy. Patients persisted with therapy for an average of 1.7 years (SD=1.0). Overall, 70% persisted ≥ 1 year, 35% ≥ 2 years, and 15% ≥ 3 years. Of those that discontinued therapy, 17% returned within 4 years.

Conclusions: New exposure to denosumab is increasing at a steady rate among Ontario seniors. Patients persisted with therapy for an average of 1.7 years, and more than a third persisted for at least 2 years.

32. The Methodological Review of Budget Impact Analysis (BIA) Models to Update Canada's Pharmaceutical Bias Guidelines for New Drug Submissions to Public and Private Payers

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Background: over last decade, in the health technology assessment (HTA) process, the budget impact analysis (BIA) has become more important to the subsequent steps, including the adoption decision. The first Canadian BIA Guidelines was published by Patented Medicine Prices Review Board (PMPRB) in 2007. According to the results of a recent survey with regards to validate the practicality of the guidelines for policy makers, an update was recommended in order to reflect the changes that have occurred in the pharmaceutical industry. Objectives: the present study aimed to identify existing guidance documents

for conducting pharmaceutical BIAs around the world, to provide an overview of the most recent methodological features and recommendations.

Methods: BIAs guidelines were searched in MEDLINE, EMBASE, EconLit, CINAHL, Business source and the grey literature. Two reviewers independently selected the studies and extracted the data.

Results: After completing the title and abstract review of 2,890 records, and then screening of 50 full-texts, 19 articles were selected to be included in the final review and data abstraction. The main focus of the study was a comparative review of recommended model structures in BIAs guidelines published in different countries such as Netherlands, Belgium, Poland, Australia (PBAC), England (NICE), Canada (provincial and the PMPRB guidelines), as well as the latest version of the international society for pharmaco-economics and outcomes research (ISPOR) task force report.

Conclusion: This article presents a review of published BIA guidelines over last decade worldwide, and makes some relevant practical recommendations for the improvement of Canadian BIAs guidelines.

33. The Economic Costs of Industry-Sponsored Pharmaceutical Clinical Trials

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Purpose: In pharmaceutical clinical trials (CTs), stakeholders pay for study drugs and care services. Since a considerable volume of pharmaceutical CTs is sponsored by industry we conducted a study of the economic costs of these trials to a healthcare system to determine their magnitude in a single jurisdiction—the province of Alberta, Canada.

Methods: We used data from two centers for cancer and non-cancer CTs at the University of Alberta, Canada. For each type of trial (cancer, non-cancer), we investigated the average cost that the provincial

government or private payer would have to pay to deliver the services provided in these CTs. We extrapolated these results to all CTs in the province of Alberta based on information obtained from the registration website ClinicalTrials.gov.

Results: Using a sample of 40 non-cancer and 39 cancer drug CTs which were initiated in 2012, the total value of the non-cancer and cancer drug CTs examined were \$31.4 million and \$24.6 million, respectively. Drugs accounted for 83.3% and 93.2% of the total costs of the non-cancer and cancer drug CTs, respectively. The monetary value to the health system is \$784,462 per non-cancer and \$630,243 per cancer drug CT. The total province-wide cost was \$99.8 million (including open-label components).

Conclusions: Besides the major aim to test innovative pharmaceuticals to provide healthcare, industry-sponsored pharmaceutical trials represent a major economic contributor to clinical research and its further development.

34. An Observational Analysis of pan-Canadian Pharmaceutical Alliance (pCPA) Activities

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The pan-Canadian Pharmaceutical Alliance (pCPA) has been active since 2011 to negotiate confidential prices on behalf of provincial and federal public drug plans. This analysis examined characteristics of drugs considered for negotiation, and the time period required for negotiations, from inception to December 31 2016. The objectives were to observe (1) patterns of implicit prioritization and (2) the role of health economics at the pCPA. The dataset contained 171 drug indications from the pCPA archives: drugs which had been negotiated (125), and drugs with a decision not to negotiate (46). There was close but not perfect alignment between the health technology assessment (HTA) agency recommendation to list and the pCPA decision to negotiate. The incremental cost-effectiveness ratio (ICER) of negotiated drugs (as estimated by HTA agencies) was close to \$200,000/

QALY. The time period required to engage in negotiations was dramatically shorter for oncology versus non-oncology drugs, and also differed by therapeutic area within both classes of drugs. The time period for price negotiation was surprisingly similar for drugs recommended without a price condition as for those conditional on a price reduction. ICERs were influential to Common Drug Review recommendations (and were increasingly used to set a negotiation target) but were not meaningful for oncology drug HTA recommendations. ICERs did not influence the time period of negotiation for either oncology or non-oncology drugs. These findings reveal an implicit prioritization pattern at the pCPA, as well as an understanding of the role of health economics.

35. The Impact of Prescription Medication Cost Coverage on Optimal Adherence to Hypertension and Diabetes Medications: A Repeated Cross-Sectional Population-Based Study

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Funding for this study is solely provided from the research fund of Dr. Wasem Alsabbagh provided by the school of Pharmacy, Faculty of science, University of Waterloo. As a graduate student in Dr. Alsabbagh's research team, Mrs. Razan Amoud receives support from these funds.

Background: It can be difficult for patients who do not have prescription medication cost coverage to adhere to diabetes and hypertension medications. No previous studies have examined the time trend and impact of absence of coverage on adherence to oral diabetes and hypertension medications in Canada.

Methods: Using data from the Canadian Community Health Survey cycles 2007, 2008, 2013, and 2014, we looked at a representative sample of Canadians from the participating provinces that opted to include questions about coverage (Ontario and New Brunswick). We included adults (18 years or older) who had either hypertension or diabetes and had answered questions on both coverage and adherence to oral diabetes and

hypertension medications. We examined the time trend of coverage and adherence using descriptive statistics. Then, we will fit a multivariate-adjusted logistic regression model to estimate the odds of non-adherence to hypertensive or diabetes medications among individuals who do not have coverage in comparison to those who do.

Results: Our pseudo-cohort included 23,215 individuals. The weighted average age was 60 years and 20% did not have any coverage. This percentage increased slightly over the study period. Non-adherence was observed in 28% of the cohort.

Conclusion: The study in progress will report the time-trend and impact of coverage on medication non-adherence in a representative Canadian sample while identifying any underlying factors affecting this relationship. Study results will enlighten researchers and policy-makers about health inequality in Canada and the need for national change in drug coverage policies.

36. Non-Severe Hypoglycemia Events and Health-Related Quality of Life (HRQOL) in Patients With Diabetes: A Systematic Review

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Background: Non-severe hypoglycemia events impact health-related quality of life and well-being. This has been illustrated by several individual studies. A large number of patients with diabetes report feeling tired, irritable, less alert and having negative feelings following non-severe hypoglycemia events. Objective: To calculate HRQoL reduction due to non-severe hypoglycemia events in patients with diabetes. **Methods:** A systematic review was conducted on literature that evaluated HROoL correspondent to hypoglycemia. PubMed databases were utilized for this search. Studies published prior to November 1, 2016 were extracted. Publications in English language were included. Bibliography mining was also done on relevant articles to be as inclusive as possible.

Results: Non-severe hypoglycemic episodes reduce HRQoL significantly for different domains. The most impacted domain was mental health domain. Non-severe nocturnal hypoglycaemic episodes lead to a greater disutility compared to non-severe daytime episodes. Studies reported HRQoL in RCTs and real-world clinical settings by various tools which are dissimilar for cross comparisons. Most studies utilized generic (general) HRQoL such as EQ-5D and SF-36 rather than diabetes specific or hypoglycemia specific tools. Eight patterns of reporting and defining severe versus non-severe hypoglycemia episodes were recognized amongst studies.

Conclusion: This study illustrates that non-severe hypoglycemia reduces HRQoL. However, combined quantification of this impact is not possible due to utilization of different questionnaires and HRQoL measures. Also, definitions for severity of hypoglycemia episodes are dissimilar for combined estimation of the impact. This calls for developing similar HRQoL tools and definitions for hypoglycemia evaluation.

37. Comparison of Treatment Effect Estimates of Non-Vitamin K Antagonist Oral Anticoagulants versus Warfarin Between Observational Studies Using Propensity Score Methods and Randomized Controlled Trials

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Emerging observational studies using propensity score (PS) methods assessed real-world comparative effectiveness of non-vitamin K antagonist oral anticoagulants (NOACs) versus warfarin in patients with non-valvular atrial fibrillation (AF). We aimed to compare treatment effect estimates of NOACs between PS studies and RCTs. Databases and conferences were searched systematically. Primary

outcomes included stroke or systemic embolism (SE) and major bleeding. A random-effects meta-analysis was performed to pool the PS- and RCT-derived hazard ratios (HRs) separately. The ratio of HRs (RHR) from the ratio of PS-derived HRs relative to RCT-derived HRs was used to determine whether there was a difference between estimates from PS studies and RCTs. There were 10 PS studies and 5 RCTs included. No significant difference of treatment effect estimates between the PS studies and RCTs was observed: RHR = 1.11, 95% CI: 0.98 - 1.23 for stroke or SE; RHR = 1.07, 95% CI: 0.87 - 1.34 for major bleeding. A significant association between NOACs and risk of stroke or SE was observed: HR = 0.88, 95% CI: 0.83 - 0.94 for the PS studies; HR = 0.79, 95% CI: 0.72 - 0.87 for the RCTs. However, no relationship between NOACs and risk of major bleeding was found: HR = 0.91, 95% CI: 0.79 - 1.05 for the PS studies; HR = 0.85, 95% CI: 0.73 - 1.00 for the RCTs.

Conclusion: treatment effect estimates of NOACs versus warfarin in patients with AF from PS studies are found to be in agreement with those from RCTs.

38. New Tests and Interventions for Prostate Cancer Management - A Systematic Review

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Prostate Cancer Canada-Discovery Grant 2015

Background: In Canada, it is estimated that prostate cancer (PCa) will account for 21% of all new cancer cases in 2016. Inaccurate risk classification and the burden of unnecessary biopsies are a challenge due to the limited ability of current risk assessment tools in

distinguishing indolent from aggressive disease. There is a need for evidence-based interventions that could improve stratification accuracy, and allow a decrease in overtreatment and overdiagnosis.

Objective: This systematic review assesses and identifies new interventions with highest evidence of clinical utility that might be adopted in clinical practice.

Methods: The Cochrane, Embase, Medline, and Web of Science databases were searched for clinical utility evidence.

Results: The search yielded 2,940 articles, of which 46 met the inclusion criteria. We found clinical utility evidence on all tests except for Prostarix, Prostavision, and MiPs. The interventions demonstrated their utility in terms of change in treatment recommendations, decrease/increase in interventional treatment, decrease in biopsy, and risk reclassification. At diagnosis after a positive biopsy, use of ProMark, Oncotype, Prolaris, and MRI guide the use of active surveillance. Post-prostatectomy, use of NadiaProsVue, Decipher, and Prolaris aid in the decision of adding adjuvant therapy. Prior initial and repeat biopsies, PHI, 4K score, and MRI; and prior repeat biopsies ConfirmMDx, PHI, ProgenSA, 4K score, and MRI - improve prediction of biopsy outcome allowing a decrease in unnecessary biopsies.

Conclusion: This review suggests that implementation of these tests in clinical practice could assist in the achievement of personalized treatment of PCa.

39. Real-World Retention Patterns of Patients Treated with Infliximab (REMICADE®, INFLECTRA® or REMSIMA™) or Switched from Innovator to Biosimilar Infliximab in Germany

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Purpose: To compare the 6-month post-switch retention and 12-month overall retention of infliximab and biosimilar infliximab in Germany.

Methods: QuintilesIMS™ longitudinal health insurance prescription data from Germany was used to identify

patients with an initial claim of infliximab (REMICADE®, INFLECTRA® or REMSIMA™ between Feb 2015-Oct 2016. All patients must have had sufficient claims history and had > 2 claims of the drug within the analysis period. Retention was captured as the proportion of patients remaining on treatment at each respective time point, captured in 90-day increments.

Results: 6,491 patients had an infliximab claim between Feb 2015-Oct 2016. Patients on the innovator (n = 3,697) and biosimilar (n = 2,794) groups were comparable with respect to age, gender, prescriber and biologic status. 57% of patients initiated treatment with innovator infliximab while 43% initiated on a biosimilar. The majority (97%) of patients were within working age (18-65) and 82.8% of patients were biologic-naïve prior to initiating infliximab. After 6 months, 14.3% more patients who stayed on innovator infliximab remained on treatment compared to those who had switched from the innovator to a biosimilar (p<0.01). At 12 months, 9.4% more patients treated with innovator infliximab remained on treatment compared to those who had initiated and continued a biosimilar (p<0.01).

Conclusions: Significant differences were noted in real-world retention amongst patients treated with innovator or biosimilar versions of infliximab in Germany. Further investigation is needed to better understand these differences regarding impact of switching from reference drug to biosimilars.

40. Using Longitudinal Data to Understand the Impact of Card Programs on Patient Persistence and Compliance in Ontario

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QuintilesIMS supplied the time and materials needed to complete this analysis.

Anonymized longitudinal patient prescription data (QuintilesIMS; LRx) were examined to better understand the relationship between patient cards and the persistence, utilization, and compliance for a second line diabetes medication. The use of card programs has been increasing over time in Canada with use

by patients to minimize out of pocket expenses, and the acceptance of cards by pharmacists and physicians. Detractors point to the overall increased cost to the health care system while patient advocates suggest that these programs improve patient adherence. Anonymized patient data for a second line genericized diabetes molecule were examined for two cohorts (new start and ongoing patients) in Ontario in 2016. Patients were split into three groups for comparison; those who made use of a card for the brand, those who used the brand without a card and those who used a generic version. Patients who used cards had significantly higher persistence than those who used a brand or generic alternative, while there was no significant difference between brand and generic users. Preliminary analysis of ongoing patients shows that utilization in the period after card use was higher than in the period prior to card use, however a longer time horizon is required to assess the absolute impact. This analysis reveals that patient cards do have value in improving patient persistence after initiation, and suggests that long run adherence also improves with card use. The generalizability, clinical value, and long term outcome on patients of these findings are all areas for further investigation.

41. Risk and Liabilities of Working with Non-professional Language Interpreters in the Healthcare Sector and Its Potential Clinical Consequences

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Theme: Community inclusion and integration / risk management. Language and cultural differences are among the main barriers to equal access to healthcare services. Over 50% of Toronto’s population speaks neither English nor French at home. Communication is a critical tools used for the provision of quality healthcare services. My presentation will include a general overview of the interpreting

Profession: role of the interpreter, types of interpretation and facts. I will identify why interpretation

is important in the healthcare sector; which are the skills needed to be a professional interpreter and reasons why interpreters need to abide by a Code of Ethics and Standards of Practice. This presentation will provide recommendations to healthcare service providers on how to work with interpreters and with ISPs (Interpreting Service Providers). I will also discuss the challenges, risks and liabilities faced by healthcare service providers when serving patients with LEP/LFP (Limited English/French proficiency); risks that have been demonstrated may have clinical consequences and affect patient safety.

Project Outcomes / Learning Objectives: Inform healthcare service providers about the risk and liabilities of working with non-professional language interpreters and its potential clinical consequences. Inform healthcare service providers on how to effectively work with interpreters in the healthcare sector. Assist healthcare service providers to understand the challenges when dealing with non-English/French speaking patients. Provide a general overview of language interpretation services.

42. The Variation in the Definition of Hypoglycemia in Randomized Controlled Trials (RCTs): A Systematic Review on RCTs Conducted for SGLT-2 Inhibitors

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Background: Hypoglycemia is a dangerous side effect associated with diabetes pharmacotherapy. Medical organizations have tried to define hypoglycemia in clinical practice and RCTs with scientific statements and guidelines. Objective: To investigate the variation of the definition of hypoglycemia reported in RCTs.

Methods: Using PubMed, a systematic review was conductive by extracting data from RCTs on SGLT-2 inhibitors limited to the English language.

Results: The definitions of hypoglycemia in RCTs could be categorized into 13 different classes. Hypoglycemia was not defined nor reported in 55(35.5%) RCTs(n=155). Amongst the RCTs that reported

hypoglycemia, 20(20.0%) did not define the definition and 7(7.0%) defined the episodes as symptomatic. Additionally, 45(45.0%) RCTs defined hypoglycemia as <3.9mmol/L blood glucose level, 15(15.0%) used <3.5mmol/L, 1(1.0%) used <3.3mmol/L, 10(10.0%) used <3mmol/L, and 2(2.0%) used <2.8mmol/L. Of the RCTs that reported hypoglycemic episodes, 18(18.0%) used a combination of variables for defining severity, while 82(82.0%) did not. About 45(45.0%) RCTs used a combined definition of hypoglycemia including the threshold and/or symptoms and/or the requirement of assistance. However, 29(29.0%) utilized the threshold of blood glucose as the definition not associated with other variables.

Conclusion: This study demonstrates the diversity in the definition of hypoglycemia reported in SGLT-2 inhibitor RCTs. The implementation of a more comprehensive definition of hypoglycemia for all RCTs may result in less heterogeneity of the outcomes in evaluating safety and effectiveness of diabetic pharmacotherapy.

43. Canada's Health System Performance: The Case of Pharmaceuticals

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Objective: The aim of this study is to evaluate Canada's health system performance in terms of pharmaceuticals using a balanced scorecard approach.

Methods: Seven comparable indicators of Canada regarding the number of pharmacists per 100,000 population, pharmaceutical expenditure per capita, share of public pharmaceutical expenditure, business expenditure on research and development in pharmaceutical industries per capita, generic and patented drug price, and generic share of the pharmaceutical market, were relatively compared to the corresponding average and best numbers of the Organisation for Economic Co-operation and Development (OECD) countries.

Results: Canada generally performed slightly worse than the OECD's average (95.3%) but significantly

worse than the OECD's best (56.4%). Among 7 comparable indicators, 4 were over the OECD's average, but all were less than 84% of the best, indicating there are rooms for Canada's pharmaceuticals to improve. The worst 3 indicators of Canada in comparison with the OECD's best or average were the business expenditure on research and development in pharmaceutical industries per capita, the share of public pharmaceutical expenditure, and price of generic drugs. Within Canada, the average expenditure on pharmaceutical research and development per capita was \$22.0. Provinces spending the most were ON (\$29.9) and QB (\$27.5) and the least were P.E.I. and the territories (\$0.0). Canada's average share of public pharmaceutical expenditure was 36.6%. Provinces with the lowest public share were NB (28.0%) and NS (29.6%).

Conclusion: We suggest that this information should be considered when setting priority for planning of the country's health system with regards to pharmaceuticals.

44. Stepwise or Step-un-wise: The Evolution of COPD Therapy

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Objective: RCTs have demonstrated modest incremental benefit gained in patient-relevant outcomes with each step of further chronic obstructive pulmonary disease (COPD) medications added to short-acting bronchodilators. In the case of the addition of inhaled corticosteroids (ICS) harm in the form of pneumonia increases significantly. To address a potential benefit-burden imbalance, we sought to compare the evolving evidence base and clinical practice guideline recommendations against real-world medication choice and the resulting cost per patient of COPD medications.

Methods: A population-based cohort study of COPD patients was conducted in Manitoba using data from 1997-2014. Prescriptions for COPD medications were used to determine annual rates of utilization, total cost, and mean treatment cost per person-year for each year in the study period.

Results: In our cohort of 18,162 patients, there was a 198% increase in mean total medication cost/person/year over the study period. Contrary to current guidelines, ICS medications were dispensed as first medications in 28.2% of patients. The combination of ICS and LABA (long-acting beta-agonist) accounted for the majority of the cost increase. The total cost of ICS-LABA rose sharply through the study period, making up 54.4% of all costs in 2013/14. Tiotropium costs also increased substantially, accounting for 20.7% of total costs in 2013/14.

Conclusions: A dramatic increase in COPD inhaler costs per patient occurred over time despite clinical trial demonstrating only modest improvements in patient-relevant outcomes. Despite this and the noted harms also attributed to ICS, the combination of ICS and LABA was the overwhelming primary cost driver.

45. Pharmacological Pertinent Period of Effect (PPPE)

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Background: The period of time during which a patient is exposed to a drug does not necessarily correspond to the period during which the drug produces the adverse effect under consideration. We propose the term Pharmacologically Pertinent Period of Effect (PPPE) to address this time window. In 2000, rofecoxib, the first COX-2 inhibitor, was associated with a significant increase in the rate of myocardial infarctions (MI) in the VIGOR trial.

Methods: We systematically searched and reviewed the observational database studies that looked specifically at rofecoxib at the doses of 25 and 50mg daily and thromboembolic events.

Results: The 50mg observational studies, looking at current exposure, correctively identified the almost immediate increase in risk evident in the VIGOR Kaplan-Meier curves. The absence of an immediate increase in risk shown by the APPROVE trial was

also correctively identified by most observational 25mg studies. To our knowledge no observational study was done on the long-term cardiac toxicity of the 25mg dose. It would thus appear that the two doses of rofecoxib have different PPPEs. At 25 mg the PPPE appears after 18 months of regular and continuous intake. At 50 mg there are 2 PPPEs, one is immediate while the other one appears only after continuous administration.

Conclusion: The presumed PPPE should be formally discussed at the time of the design of a study. All the information on the drug-side effect combination should be taken into consideration in the selection of the most appropriate PPPE(s).

46. Determining the Economic Value of Adding Rituximab to Chemotherapy in Canada

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Objectives: Rituximab (R) is used to treat diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL) and chronic lymphocytic leukemia (CLL) along with *cyclophosphamide*, *doxorubicin*, *vincristine* and *prednisone* (CHOP). The objective of this study was to determine the five year survival and direct medical costs of rituximab and comparator groups using real world Canadian data.

Methods: Administrative data from the British Columbia (BC) Cancer Agency and Population Data BC was used. Individuals ≥ 18 years old and diagnosed with DLBCL, FL and CLL were grouped into three cohorts: "rituximab cohort" (diagnosed January 2001-December 2010 and received first-line R+CHOP/equivalent), "historical cohort" (diagnosed January 1995-December 2000 and received first-line CHOP/equivalent), and "no rituximab cohort" (diagnosed January 2001-December 2010, never received rituximab but received first-line CHOP/equivalent). Each cohort was further divided by histology type and (unadjusted) five year survival and total five year cost (2014 CAN\$) were calculated.

Results: 5,624 patients were ~60% male, mean age was 64.0 ± 14.1 years and 24.2% were stage IV. CLL had the best survival with 4.6 years for the rituximab cohort followed by FL=4.3 and DLBCL=3.6. The same trend was observed in the historical cohort: CLL=4.0, FL=3.7 and DLBCL=3.0 years as well as the no rituximab cohort: CLL=3.5, FL=3.4 and DLBCL=2.6 years. FL had the highest mean total five year cost for the rituximab cohort with \$81,557 followed by

DLBCL=\$79,084 and CLL=\$50,373. The same trend was observed in the historical cohort: FL=\$50,062, DLBCL=\$48,088 and CLL=\$39,299 whereas the no rituximab cohort found DLBCL=\$60,856, FL=\$41,032 and CLL=\$36,423.

Conclusions: Using BC administrative data, our study determined that rituximab provided better five year survival but at a higher cost.

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Witt D	37
Xie F	32
Yan C	6
Zagorski B	46
Zhang Y	37