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ABSTRACTS

"DRIVERS OF CHANGE: HOW HTA, EVIDENCE AND POLICY AFFECT PERCEPTIONS OF VALUE AND HEALTH CARE PRACTICE"

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CAPT-ACTP SUBMITTED ABSTRACTS

DRIVERS OF CHANGE: HOW HTA, EVIDENCE AND POLICY AFFECT PERCEPTIONS OF VALUE AND HEALTH CARE PRACTICE

November 2 - 4, 2014
Toronto

Oral Presentations
Sunday, November 2, 2014

(Note: Presenting Authors are underlined)

1

Impact of country-specific EQ-5D tariffs

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Funding Source: None

Objectives: Previous Canadian EQ-5D based cost-effectiveness studies commonly use UK or US valuations, as Canadian tariffs were only recently made available. The implications of using non-Canadian tariffs to inform decision-making are unclear. We aim to re-evaluate a previous cost-effectiveness study of therapies for metastatic pancreatic cancer, originally performed using US utilities, with weights from Canada and various countries to determine the impact of using non-country specific tariffs.

Methods: EQ-5D utilities were derived using tariffs from Canada, US, UK, Denmark, France, Germany, Japan, the Netherlands and Spain for the 10 health states in the pancreatic cancer model. Incremental cost-effectiveness ratios (ICERs) were generated, and probabilistic sensitivity analyses (PSA) were performed.

Results: Canadian utilities are generally lower than the corresponding US values and higher than those of UK. Compared to the Canadian-valued scenarios, US and UK estimates were statistically different for 5 and 10 scenarios, respectively. Overall, 60% (54 of 90) of the non-Canadian utilities were significantly different, clinically, from the Canadian values. Canadian ICERs were about 5% greater than those of the US and 9% lower than those of the UK. The minimum willingness-to-pay threshold at which the chemotherapy regimen GEM-CAP is the most cost-effective based on PSA was $5,239 less for the US and $11,986 more for the UK compared to the Canadian threshold value.

Conclusions: Using non-country specific tariffs, there are significant differences among the derived utilities, ICERs and PSA results. Past Canadian EQ-5D based cost-effectiveness studies and related funding decisions may need to be re-visited using Canadian tariffs.

Keywords: *EQ-5D; cost-effectiveness; pancreatic cancer*

2

A population based cross-sectional study of comparison of breast cancer stage at diagnosis between immigrant women and general population in Ontario

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Funding Source: Ontario Institute for Cancer Research (OICR) and Cancer Care Ontario (CCO)

Background: Immigrants often experience barriers to accessing timely breast screening and are at risk of presenting with advanced stage breast cancer. Given the high number of immigrants in Canada, it is important to determine the distribution of stage at diagnosis of breast cancer in this population.

Methods: We extracted stage at diagnosis of invasive breast cancer from the Ontario Cancer Registry (Jan 2007-Dec 2012). We used Citizenship and Immigration Canada data to classify all women according to immigration status. We used a validated surname algorithm to further classify women into South Asian and Chinese ethnicities. Logistic regression was performed to estimate the odd ratios (OR) of being stage 1 at diagnosis of breast cancer.

Results: Of 41,213 women eligible for study, 10.6% were immigrants and 89.4% were women in general population. Compared to general population, immigrants were younger at breast cancer diagnosis (51 years vs. 62 years) and belonged to a lower socioeconomic status (47.2% vs. 35.8%). The ORs of being stage 1 were 0.82 (95%CI 0.80-0.92, p = <0.0001) for all immigrants, 1.30 (95%CI 1.16-1.45, p = <0.0001) for Chinese and 0.82 (95%CI 0.70-0.96, p = 0.01) for South Asians.
Conclusion: Immigrant women in Ontario are less likely to be diagnosed with early-stage breast cancers. Raising breast cancer awareness and reducing access barriers is critical in these communities. Further research is warranted to understand the tumor biology in women with different ethnic origins.
Keywords: *Breast cancer; immigrants, ethnicity; Ontario*

3

Chronic diabetic ulcers of the lower limb: results from a double-blind, randomized controlled trial comparing wound care with adjunctive hyperbaric oxygen therapy to wound care alone

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Funding Source: Ontario Ministry of Health and Long-Term Care

Background: Few studies have used a double-blind approach to evaluate the efficacy of hyperbaric oxygen therapy (HBOT) in the treatment of diabetic ulcers. The goal of this study was to assess the efficacy of HBOT plus wound care compared with wound care alone with sham HBOT in preventing the need for major amputation in patients with chronic diabetes ulcers.
Methods: This single-centre, double-blind, randomized controlled trial recruited adult patients with non-healing diabetic lower limb ulcers. Patients were randomized to either receive active HBOT or sham HBOT 5 times per week for 6 weeks. Patients had 6 weeks of follow-up for wound evaluation and management. The primary outcome was having, or meeting the criteria for, a major amputation up to 12 weeks after randomization.
Results: One hundred and six (55 patients in placebo and 49 in HBOT) patients were randomized for the study. One minor amputation occurred in the placebo group but there were no major amputations in either group. Based on vascular surgeon assessment, 13 major amputations were recommended in the placebo group and 11 in the HBOT group (P=0.87). Complete ulcer healing was achieved in 12 (22%) and 9 (18%) in the placebo and HBOT groups, respectively.
Conclusion: At the end of the 12-week treatment period, HBOT does not appear to offer an additional advantage to comprehensive wound care for prevention of amputation or facilitating wound healing in patients with DFU. Longer-term data are necessary in order to evaluate the use of HBOT for this indication.
Keywords: *Hyperbaric oxygen therapy; health technology assessment; diabetes foot ulcer*

4

Anticholinergic drug burden in persons with dementia: the effect of multiple prescribers

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Funding Source: Canadian Institutes of Health Research (CIHR)

Background: Anticholinergic drugs may contribute to worsening confusion. Of concern is the use of anticholinergics in older adults with dementia who are also taking a cholinesterase inhibitor. Contact with multiple physicians could lead to this potentially inappropriate prescribing. We explored the association between anticholinergic burden and the number of physician contacts among older patients with dementia.
Methods: An Ontario population based cross-sectional study included older adults with dementia who were newly dispensed a cholinesterase inhibitor (April 2008 and March 2013). Physician exposure was determined by the number of physicians submitting claims for the patient within one year. The main outcome was anticholinergic drug burden in the year prior to cholinesterase inhibitor prescription.
Results: We identified 79,067 patients (mean age 81 years, 61% women) who saw an average of 8 unique physicians. After adjusting for potentially confounding variables, we observed an increased risk of higher anticholinergic burden (score of 2 or more) if they saw a greater number of physicians in the past year (adjusted odds ratio, 1.05; 95% confidence interval, 1.05-1.06; p-value <0.0001). Female sex, a low-income flag on the Ontario drug benefit claim, previous hospitalization and higher comorbidity were also associated with high anticholinergic burden.

Conclusions: Number of physicians was associated with an increased risk of higher anticholinergic drug burden in the year prior to cholinesterase inhibitor prescription. More comprehensive medication review for this vulnerable population prior to the prescription of cholinesterase inhibitors and better communication amongst physicians are important strategies to consider in improving prescribing practices.
Keywords: *Anticholinergics; dementia; cholinesterase inhibitors*

5

Health utility estimates of Canadian cancer patients

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Objectives: Health utility values (HUV) play an important role in health economic analyses, but comprehensive reference values do not currently exist for Canadian cancer patients. We generated HUVs from patients representing multiple disease sites using the recently introduced Canadian EQ5D valuations.
Approach: 983 non-CNS cancer outpatients completed the EQ5D-3L and visual analogue scale (VAS). Responses from the EQ5D-3L were used to generate HUVs (Canadian weights); VAS responses were recorded from 0-100. Subgroup scores were then calculated for each level of the Eastern Cooperative Oncology Group (ECOG) performance status, disease site and treatment intent. Significant differences between subgroups were assessed using Kruskal-Wallis one way analysis of variance.
Results: The mean (SD)[range] HUV and VAS scores were 0.82(0.15)[0.34-1.00] and 74(18)[0-100], respectively. Patients with ECOG scores of 0, 1, 2, and 3 had HUVs of 0.90(0.11)[0.46-1.00], 0.76(0.12)[0.19-1.00], 0.65(0.14)[0.12-1.00], and 0.56(0.21)[0.09-0.77], respectively; ($p<0.0001$), and VAS scores of 82(14)[0-100], 70(15)[20-100], 57(18)[5-100], and 45(27)[0-80]; ($p<0.0001$). Patients treated with a curative intent had HUVs of 0.83(0.15)[0.09-1.00], while palliative patients scored 0.77(0.13)[0.18-1.00]; ($p<0.0001$). Across disease groups, genitourinary cancer patients scored the highest HUVs of 0.87(0.15)[0.09-1.00], followed by head/neck, 0.83(0.14)[0.19-1.00]; gastrointestinal, 0.83(0.14)[0.12-1.00]; skin/ sarcoma, 0.81(0.16)[0.41-1.00], gynecologic, 0.80(0.12)[0.59-1.00]; hematologic, 0.80(0.17)[0.34-1.00]; breast, 0.80(0.18)[0.12-1.00]; and lung cancer, 0.78(0.14)[0.18-1.00]; ($p<0.0001$).
Conclusion: Patients with better performance status and those treated for cure had higher corresponding HUV and VAS scores. Future research will focus on collecting longitudinal data and characterizing utilities for specific disease sites based on stage and tumour subtype.
Keywords: *Health utility; EQ-5D; cancer*

6

Impact of a provincial drug plan policy limiting out-of-pocket payment for seniors: a population-based study in Saskatchewan, Canada

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Funding Source: Saskatchewan Ministry of Health

Background: In 2007, the Saskatchewan government implemented the Seniors' Drug Plan Benefit (SDP) that limited out-of-pocket payment to $15 per prescription for eligible individuals 65 years of age and older, for drugs listed on the Saskatchewan Formulary. We examined the impact of this new policy on medication utilization and cost using population-based provincial administrative databases.
Methods: Pharmacy claims data between 2005 and 2009 were used to calculate monthly measures of utilization and cost amongst beneficiaries aged 65 and above comparing with a younger group aged 40-60. An interrupted time-series analysis was used to test for differences in age-and sex standardized rates pre- and post-program. Overall and drug class specific analyses were conducted.
Results: Following implementation of the SDP policy, significant increases for individuals 65+ years were observed in total medication spending (+9.8%; 95% CI 3.7 - 16.0), government spending on medications (+45.9%; 95% CI 40.1 - 51.8), total medications dispensed (+6.0%; 95% CI: 3.1 – 9.0), and number of individuals receiving ≥ 1 dispensations (+3.9%; 95% CI: 2.1 – 5.8). However, no differences in these measures were observed for those aged 40 to 64.

Consistent increases were also observed for 10 out of 12 major drug classes for the 65+ age group.
Conclusions: Our study confirms that the SDP was associated with increased medication utilization. Government spending increased by 46%, while the total number of dispensations increased by 6%.
Keywords: *Medication utilization; out-of-pocket payment; copayment; reimbursement, policy*

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Prescription stimulant use and hospitalization for psychosis: a population-based case-crossover study

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Funding Source: The Canadian Drug Safety and Effectiveness Research Network and the Institute for Clinical Evaluative Sciences, which is funded by a grant from the Ontario Ministry of Health and Long-Term Care.

Background: Stimulant prescribing for symptoms of ADHD has increased dramatically over the past decade. We explored whether initiation of prescription stimulants was associated with hospitalization for psychosis, an adverse effect predicted by the pharmacology of these drugs.
Methods: We conducted a population-based study from October 1, 1999 to March 31, 2013 of Ontario residents aged ≤25 whose prescription costs were reimbursed by the provincial government. All subjects were hospitalized for psychosis within 180 days of commencing treatment with a prescription stimulant. We estimated the risk of hospitalization for psychosis within 60 days of commencing treatment, relative to a 60-day reference interval four months earlier. Each patient served as their own control.
Results: We identified 219 patients hospitalized with psychosis within 180 days of a first stimulant prescription. Hospitalization for psychosis was associated with stimulant initiation in the preceding 60 days (odds ratio [OR] 1.70; 95% confidence interval [CI] 1.31 to 2.27). The risk was higher in patients with a history of treatment with antipsychotic drugs (OR 2.00; 95% CI 1.36 to 3.11), but persisted in patients with no such history (OR 1.48; 95% CI 1.03 to 2.19). More than a third of patients hospitalized with psychosis resumed stimulant therapy after hospital discharge; of these, 38% (30 of 78) were readmitted with psychosis shortly thereafter.
Conclusions: Initiation of prescription stimulants is associated with hospitalization for psychosis in young people. Resumption of therapy and readmission for psychosis are common, suggesting a lack of aware ness of the causative role of these drugs.
Keywords: *Attention deficit hyperactivity disorder; stimulants; psychosis*

8

The efficacy and safety of electronic nicotine delivery devices (e-cigarettes) as a method for smoking cessation: a systematic review and meta-analysis

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Funding Source: None

Background: Smoking cessation is associated with significant health benefits, and e-cigarettes are increasing in popularity as potential cessation aids. In this review, we assessed the effectiveness and safety of e-cigarettes for smoking cessation (primary outcome), desire to smoke, withdrawal symptoms, and adverse events (secondary outcomes) in adult smokers
Methods: A systematic review of medical databases (MEDLINE, EMBASE, PsychINFO, CENTRAL) and grey literature was conducted. Two reviewers screened studies independently and in duplicate. All studies comparing e-cigarettes to other nicotine replacement therapies or no intervention (placebo) were included.
Results: Of the 569 identified citations, 5 studies proved eligible for inclusion. Participants were more likely to stop smoking when using nicotine e-cigarettes (43/489) versus placebo e-cigarettes (8/173), however this was not statistically significant (RR 2.02; 95%CI 0.97, 4.22). No pooled effect estimates of secondary outcomes were statistically significantly different, including desire to smoke (RR -0.22; 95%CI-0.80,0.36), irritability (RR -0.03; 95%CI-0.38,0.31), restlessness (RR -0.03; 95%CI-0.42,0.35), poor concentration (RR -0.01; 95%CI-0.35,0.32), depression (RR -0.01; 95%CI-0.22,0.20), hunger (RR -0.01; 95%CI-0.32,0.30), and average number of non-serious adverse events (RR -0.09; 95% CI -0.28,0.46). Only one study reported serious adverse events, however there was no apparent association between the reported events and the use of e-cigarettes.

Conclusions: The current evidence does not suggest that nicotine e-cigarettes are effective for long-term smoking cessation aids when compared with placebo e-cigarettes. However, the studies were small and of low quality, hence larger and higher quality studies are needed to inform policy decisions.
Keywords: *Meta-analysis; e-cigarettes; smoking cessation*

9

Retrospective evaluation of drug therapy recommendations made by pharmacists providing pharmaceutical opinion service in Ontario

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Funding Source: An unrestricted grant from Eli Lilly Canada

Background and Objectives: The Pharmaceutical Opinion (PO) Program is a service through which a pharmacist is compensated by the Ontario Public Drug Program when a drug related problem is identified, a recommendation to resolve the problem is made in consultation with the prescriber, and the situation is documented. The objective of this study was to examine the quality of the POs provided by pharmacists.
Methods: This study was an audit of PO documentation in 25 community pharmacies in Toronto, Orangeville and Caledon, Ontario. A random sample of 6-20 de-identified POs were collected from each store. Two clinical pharmacists used a pre-established structured rating form to extract data and rate each opinion.
Results: A total of 464 POs were obtained, 81% of which were from urban pharmacies. Patients were a mean of 68 (SD: 16.6) years of age and taking 6.8 (SD: 4.3) medications. Sixteen percent of the POs were ineligible for reimbursement since they addressed administrative rather than clinical issues. Over 43% of eligible POs addressed adverse drug reactions; another 30% concerned dosage issues. Thirty six percent of the POs identified a drug therapy problem but did not include a clinical recommendation to the prescriber. The majority (63%) of eligible POs were rated as poor or fair in overall quality.
Conclusion: This study found the PO program mainly associated with pharmacist – prescriber communication in the management of adverse events and medication dosage issues. Opportunities exist to improve the understanding of program criteria and quality of service provision by pharmacists.
Keywords: *Pharmacist services; drug therapy problems; service quality*

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Economic evaluation of sofosbuvir in hepatitis C: a Canadian perspective

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Funding Source: Gilead Sciences Canada

Objective: To conduct a cost-utility analysis of sofosbuvir (SOF) versus appropriate comparators, over a lifetime horizon, in patients with genotype (G) 1, 2 or 3 chronic hepatitis C virus (HCV) infection.
Methods: A Markov state-transition model described the progression of HCV over a lifetime horizon. Patients underwent treatment and moved to the cure state depending on the sustained virological response (SVR) rate observed in clinical trials. Without SVR, patients faced an annual probability of liver disease progression and mortality. Recent Canadian literature sources were used for health state utilities and costs. Adverse event costs were drawn from a retrospective HCV treatment analysis of the Quebec claims database.
Results: The incremental cost-effectiveness ratio (ICER) varied depending on the genotype subgroup and the perspective of the analysis. From the societal perspective, SOF was dominant (more effective and less expensive) over boceprevir and telaprevir for both treatment-naïve (TN) and treatment-experienced (TE) G1 patients (the majority of Canadian patients). From the health care system perspective, SOF was highly cost-effective (under $20,000/QALY) over boceprevir and telaprevir in G1 TN non-cirrhotic patients, dominant in G1 TN cirrhotic patients, and dominant in G1 TE patients. ICERS were below $60K/QALY from any perspective in G2/3 patients with interferon TE or interferon intolerance/contraindication –subgroups with no other treatment options.
Conclusion: SOF is a cost-effective strategy in the treatment of HCV. SOF provides a short, well-tolerated, highly efficacious regimen compared to the current standard of care, which is interferon -sparing for G1 patients and interferon -free for G2/3 patients.
Keywords: *Hepatitis C; economic evaluation; cost-effectiveness; sofosbuvir*

11

A Canadian cost-effectiveness analysis of transcatheter mitral valve repair with the MitraClip System in high surgical risk patients with significant mitral regurgitation

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Funding Source: The work reported in this manuscript was funded via a consultancy agreement between Cornerstone Research Group, Inc. and Abbott Vascular

Background: In patients with significant mitral regurgitation (MR) at high risk of mortality and morbidity from mitral valve surgery, transcatheter mitral valve repair with the MitraClip System is associated with reduction in MR, and improved quality of life and functional status compared with baseline. The objective was to evaluate the cost-effectiveness of MitraClip therapy compared with standard of care (medical management) in patients with significant MR at high risk for mitral valve surgery from a Canadian payer perspective.
Methods: A decision analytic model was developed to estimate the lifetime costs, life years, quality-adjusted life years (QALYs), and incremental cost per life year and QALY gained for patients receiving MitraClip therapy compared with standard of care. Treatment-specific overall survival, risk of clinical events, quality of life, and resource utilization were obtained from the Endovascular Valve Edge-to-Edge REpair High Risk Study (EVEREST II HRS). Health utility and unit costs (CAD $2013) were taken from the published literature. Sensitivity analyses were conducted to explore the impact of alternative assumptions and parameter uncertainty.
Results: The base case incremental cost per QALY gained was $23,433. Results were most sensitive to alternative assumptions regarding overall survival, time horizon, and risk of hospitalization for heart failure. Probabilistic sensitivity analysis showed a 92% chance of MitraClip being cost-effective compared with standard of care at a willingness-to-pay threshold of $50,000 per QALY gained.
Conclusions: MitraClip therapy is likely a cost-effective option for the treatment of patients at high risk for mitral valve surgery with significant MR.
Keywords: *Cost-effectiveness; mitral regurgitation; MitraClip*

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A descriptive analysis of the Ontario MedsCheck Annual pharmacy medication review service

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Funding Source: Government of Ontario, Blueprint for Pharmacy

Background: A Medscheck Annual (MCA) consultation is a medication review service funded by the Ontario government for people taking three or more prescription medications for chronic conditions. This study describes the demographic and clinical characteristics of MCA service recipients.
Methods: This cohort study leverages linked administrative claims data from April 1, 2007 to March 31, 2013. Descriptive statistics were calculated for recipient characteristics and stratified by age and sex. Trends over time were examined by plotting the number of services and unique patients by month.
Results: The MCA service was provided to 1,498,440 Ontarians (55% seniors, 55% female) over 6 years. One-third of recipients (36%) had two or more MCAs over the 6-year period. Service provision increased over time with a sharper increase after 2010. Ten percent of recipients had experienced a hospitalization or emergency department visit 30 days prior to their MCA service; and seven percent had high medication costs in the prior year ($4000+). Diagnoses of hypertension (68%), COPD or asthma (31%), diabetes (30%), psychiatric condition (28%) and arthritis (27%) were most common. Service recipients over 65 years old were most commonly dispensed an antihypertensive (81%), antilipidemic (64%), or a diuretic drug (49%) in the prior year and received an average of 12 prescription drugs.
Conclusions: Over a 6 year period, approximately one in nine Ontarians has received an MCA, with the majority having cardiovascular disease. Service delivery has increased over time; however, the number of persons receiving the service more than once is low.
Keywords: *Medication review; community pharmacy; administrative data*

Elevator Pitches
Sunday, November 2, 2014

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Hypertension treatment and cross-sectional relationship with peripheral and central blood pressure in non-diabetic participants from the CARTaGENE Cohort Study

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Funding Source: CIHR

Background: Thiazide diuretics (TZD) are cost-effective first-line therapy for mild to moderate uncomplicated hypertension; however they are less prescribed than other options. We aimed to compare TZD with different classes of antihypertensive medications in relation with peripheral and central blood pressure (BP).
Methods: We used cross-sectional data from the Quebec CARTaGENE project. Non-diabetic hypertensive participants, on monotherapy for hypertension were selected. Participants completed a questionnaire at baseline, including assessment of current medications, and underwent peripheral and central BP measurements. Multivariable linear models, adjusted for age, sex, body mass index, height, hypercholesterolemia, comorbidities, smoking, alcohol intake, heart rate, and duration of hypertension, were employed to compare BP control for TZD versus non-TZD antihypertensive medications. Separate adjusted models were constructed for each of the following outcomes: central and peripheral systolic BP, diastolic BP, mean pressure, pulse pressure, and augmentation index.
Results: Of the 1,194 hypertensive participants, 50% were on angiotensin converting enzyme inhibitors or angiotensin receptor blockers, 16% were treated with calcium channel blockers, 13% with β-blockers, and only 7.4% with TZD. In multivariate analyses we found that systolic BP was similar in both TZD and non-TZD groups (adjusted regression coefficient=0.31; 95% Confidence Interval=-2.06 to 2.68). No differences in other peripheral and central BP measures were noted between TZD and non-TZD groups.
Conclusions: We found that TZD use was not associated with significantly higher levels of both peripheral and central BP. These results provide additional support that TZD are at least as effective as other first-line medications for treating uncomplicated hypertension.
Keywords: *Hypertension; therapy; non-diabetic*

14

Hypofractionation versus conventionally fractionated radiotherapy for low-intermediate risk prostate cancer: clinical and economic evaluation.

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Funding Source: None

Background: Hypofractionated radiotherapy (HypoRT) uses larger daily fractions and shortens the overall treatment time compared to conventionally fractionated radiotherapy (ConvRT). This can improve therapeutic outcomes in prostate cancer and reduce the costs associated with radiotherapy.
Objective: To evaluate clinical outcomes and perform an economic evaluation of HypoRT versus ConvRT regimens.
Methods: The cohort consists of low- and intermediate-risk prostate cancer patients treated at the McGill University Health Center Radiation Oncology Department from Nov. 2002 to Jul. 2013. Biochemical failure was the main clinical outcome and defined as the nadir PSA level plus 2ng/ml. Kaplan-Meier analyses were performed to evaluate the time to clinical outcomes. Cox proportional hazards model was used to evaluate the association between the clinical outcomes of HypoRT versus ConvRT, adjusted for covariables.
Results: With a median follow-up of 90 months, the 8-year biochemical relapse-free survival rates were 93% for low risk patients treated with the HypoRT regimen, compared to 82% among intermediate risk patients receiving the HypoRT regimen, and to 67% for intermediate risk patients in the ConvRT group. A significant association was found between type of regimen and biochemical failure (HRHypo/Conv = 0.495; 95% CI 0.256-0.996). In addition, the cost estimates for the HypoRT regimen ranged from $5,718.80 to $6,254.00; compared to ConvRT, which ranged from $8,802.70 to $9,614.40.
Conclusion: This study highlights the potential therapeutic gains and cost savings of using a HypoRT regimen in patients with low and intermediate risk prostate cancer, versus ConvRT.
Keywords: *Prostate cancer; radiotherapy; cost-effectiveness*

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Performance of the disease risk score (DRS) in a cohort with policy induced selection bias

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Funding Source: CIHR Fredrick Banting and Charles Best Canada Graduate Scholarship Doctoral Award (GSD-11342)

Background: Selection bias can arise when a new medication enters the market and is associated with higher utilization in sicker patients. The disease risk score (DRS) may be a useful tool in comparative effectiveness research with newly marketed products.
Objective: To examine the performance of the DRS in a cohort with selection bias.
Methods: We leveraged an established cohort of female new users of oral bisphosphonates (alendronate and etidronate) ages ≥ 66 years from 2001 to 2008. This cohort has shown past evidence of selection bias with higher baseline fracture risk among alendronate users. We compared 1-year hip fracture rates using Cox-proportional hazard models with alendronate as the referent group. Traditional multivariable analysis was used as the base analysis. DRS were created and divided into equal quintiles, and examined using stratification and as covariates in the model. Percent variation from the base analysis was calculated to assess performance. Sensitivity analysis for trimming and outcome-definition was completed.
Results: The cohort analyzed had 170,862 subjects with 2,740 events. The base analysis yielded non-significant differences (HR=0.99; 95% CI 0.90-1.10). Variation from the base analysis was found (-1.1% to -18.4%), with the greatest variation seen with DRS based analyses. Sensitivity analyses with trimming and outcome-definitions did not vary our results greatly.
Conclusion: Selection bias was found to impact DRS-based estimates. The DRS exaggerates differences favouring older drugs with unrestricted access. Researchers using the DRS method should be mindful of possible policy-induced bias as it can greatly impact performance of the DRS.
Keywords: *Pharmacoepidemiology; confounders; comparative effectiveness*

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Oncology drug HTA Recommendations: Canadian versus UK experiences

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Objective: To compare the recommendations of INESSS (Institut National d'Excellence en Santé et Services Sociaux) and Canada's national process, alongside the National Institute for Health and Care Excellence (NICE) in the United Kingdom with respect to their recommendations record and the influence of clinical and cost effectiveness evidence to the recommendation.
Methods: Recommendations were identified from January 2002 to June 2013, and were limited to metastatic/advanced settings from five disease sites (lung, breast, colon, kidney, blood). Descriptive analyses examined the frequency of positive recommendation, and factors related to positive recommendations. Only publicly available information posted on the agency website was used.
Results: There was a wide variation in the rate of positive recommendations, ranging from 48% for NICE to 95% for Canada's national process. Inter-agency agreement was low, with full agreement for only 6 of the 14 drugs commonly reviewed by all three agencies. Evidence of a survival gain was not necessary for a positive recommendation; progression-free survival was acceptable. Different approaches were taken when addressing unacceptable cost-effectiveness. NICE was most likely to yield a negative recommendation on these grounds, while Canada's national process was most likely to yield a positive recommendation with a required pricing arrangement.
Conclusions: The primary reason for the observed divergence between agency recommendations appeared to be the availability of mechanisms in each jurisdiction to address cost-effectiveness issues. Consequently, recommendations may not correspond directly to subsequent funding decisions and actual patient access. This may be a concern, given the high international profile of HTA agencies.
Keywords: *Health technology assessment; oncology; reimbursement decision-making*

17

Use of multiple exposure measures in order to examine the potential mechanism of action by which statins could cause diabetes

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Funding Source: This study was financed by a CIHR grant. JRG is recipient of CIHR doctoral scholarship and a Pfizer post-doctoral scholarship.

Introduction: Observational studies often focus on the association between the exposure to a drug and the occurrence of a specific side-effect. However, many situations arise where the mechanism of action by which the study drug could cause the outcome are unknown. Testing multiple exposure measure (EM) within observational studies could help in identifying the most plausible mechanism of action. We tested this hypothesis within an observational study focusing on the link between statin exposure and the risk of diabetes.
Methods: We obtained a cohort of 404,129 diabetes-free incident users of a statin drug from the Régie de l'assurance maladie du Québec and assessed diabetes status within 2-years follow-up. We tested 3 EM within 3 distinct nested case-control studies, EM 1) high vs low-potency statin at baseline, EM 2) standardised statin dose (SSD) at the index date and EM 3) cumulative SSD at the index date. The optimal EM was selected based upon each model's AIC. Conditional logistic regressions were used to calculate each model's AIC.
Results: Both EM 1 and EM 3 identified that a higher statin dose increased the risk of diabetes while EM 2 found no association. Models' AIC identified EM 3 as the best EM for this association.
Conclusion: Our results hint that statins could cause diabetes due to a cumulative toxic effect on the patient.
Keywords: *Observational studies; diabetes; methods*

18
Clinical management and burden of prostate cancer: a Markov Monte Carlo model
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Background: Prostate cancer (PCa) is the most common non-skin cancer among men in developed countries. Several novel treatments have been adopted by healthcare systems to manage PCa. Observational/randomized trials on effectiveness often evaluated fewer treatments over limited follow-up. A contemporary decision analytic model was necessary to address these limitations by synthesizing the evidence on novel treatments thereby forecasting short and long-term clinical outcomes.
Objectives: The objectives of this study were to develop and validate a Markov Monte Carlo model for the contemporary clinical management of PCa; and to assess the clinical burden of the disease from diagnosis to end-of-life.
Methods: A decision model was developed to simulate the management of PCa from diagnosis to end-of-life. Health states modeled were: risk at diagnosis, active surveillance (AS), initial treatments (radical prostatectomy or radiation therapy), PCa recurrence, PCa recurrence free, metastatic castrate resistant prostate cancer (mCRPC), and death (cause specific/other causes). Treatment trajectories were based on state transition probabilities derived from the literature. Validation/sensitivity analyses assessed the accuracy and robustness of model predicted outcomes.
Results: Validation demonstrated good agreement between model predicted outcomes and observed outcomes. Over the lifetime simulated period 20.5% died from PCa and 79.5% died from other causes. Over lifetime for low-, intermediate-, high- risk groups the PCa and overall death rates were 3.1%, 17.5%, 41.6% and 96.9%, 82.5%, 58.4%; respectively.
Conclusion: The model predicted rates were corroborated by observed rates in the literature. This model could be used to assess healthcare resource use and costs associated with PCa treatments.
Keywords: *Prostate cancer; markov model; survival*

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Cost-effectiveness of screening hepatitis C in Canada
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Funding Source: None

Purpose: The prevalence of chronic hepatitis C (CHC) infection among Canadian is estimated to be between 0.3%-0.9%, among which 10-20% develop advanced liver disease by 30 years of infection. Targeted screening seems to be a plausible strategy. In collaboration with Public Health Agency of Canada, the objective of this study is to estimate the health and economic effects of CHC screening strategies.
Method: We used a state-transition model to examine the cost-effectiveness of three screening strategies: (1) "No screening"; (2) "Screen-and-treat with pegylated-interferon-plus-ribavirin (PR)" and (3) "Screen-and-treat with direct-acting-antiviral-agents (DAA)" for 25-64 year-old individuals. Our model includes health

states related to fibrosis stages, clinical diagnosis, treatment and clinical states. Model data were obtained from the published literature. We used a payer perspective, a lifetime time horizon and a 5% discount rate.

Result: For every 10,000 persons screened, screen-and-treat with PR would prevent 7 decompensated cirrhosis, 4 hepatocellular carcinoma and 11 HCV-related deaths over the lifetime of the cohort. Screening was associated with an increase of 0.0042-0.0052 QALYs and cost (C$145-C$187) per person, translating to an ICER of C$34,622/QALY-C$43,637/QALY gained compared with "No screening", which depends on different antiviral therapies received. Univariate and probabilistic sensitivity analyses suggest that the "Screen-and-treat" strategy would likely be cost-effective.

Conclusion: Our analysis suggested that a one-time hepatitis C screening program for individuals between 25 and 64 years of age would likely be cost-effective. Identification of silent CHC infection with the offer of treatment when appropriate can extend the lives of Canadian at reasonable cost.

Keywords: *Cost-effectiveness; hepatitis C; screening*

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First two years of health system resources and costs following a stage defined breast cancer diagnosis: a population based approach

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Funding Source: Ontario Institute for Cancer Research

Objective: To determine the publicly funded health care costs associated with breast cancer (BC) by stage of disease in the first two years following diagnosis.

Methods: Incident cases of female invasive BC (ICD-9 174.x) diagnosed between 2005 and 2009 were extracted from the provincial cancer registry and linked by their encrypted health card number to administrative datasets. The type and usage of health care services used were stratified by disease stage over the first two years. BC cases were matched to controls (women without cancer). Overall average costs (2008$CAN) and costs per resource were compared to a control group from a public payer perspective. The attributable cost for the two-year time horizon was determined.

Results: There were 39,655 BC cases and 190,520 controls with the average age as 61.1 years old and 60.9 years old, respectively. The majority of cases were Stage I (34.4%) and Stage II (31.8%). Eight percent of the entire cohort died within the first two years of diagnosis. The overall mean cost per BC case in the first two years following diagnosis was $41,686. The mean cost increased by stage: Stage I ($29,938), Stage II ($46,893), Stage III ($65,369) and IV ($66,627). When compared to controls, the net cost for BC cases was $31,732. Cost drivers were cancer clinic visits, physician billing and inpatient hospitalizations.

Conclusions: Costs increased by stage of disease. Cost drivers were identified and a net cost was calculated. This data will allow for planning and decision making around limited healthcare resources.

Keywords: *Healthcare resources; costs; cancer*

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Feasibility of routinely administrating the EQ-5D health utility instrument to cancer patients

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Objectives: To better inform policy decisions, collecting health utility information from cancer patients regularly through routine administration of the EQ-5D instrument would be beneficial. Currently, cancer patients in Ontario routinely complete symptom assessment surveys. We sought to assess their willingness to also complete the EQ-5D.

Approach: 618 adult cancer survivors across all non-CNS solid and hematologic cancer sites at the Princess Margaret Cancer Centre completed a survey of socio-demographic questions, the EQ-5D instrument, and a series of questions regarding willingness to complete/burden associated with completing the EQ-

5D. Results were analyzed using descriptive statistics and multivariate logistic regression.
Results: The mean (SD) health utility score was 0.81 (0.15). Amongst those surveyed, 88% reported that the EQ-5D was easy to complete, 92% took less than 5 minutes, 89% were satisfied with its length and 86% were satisfied with the types of questions asked. Importantly, 92% reported that they would complete the EQ-5D, even if it were used solely for research purposes and 73% agreed with the notion of completing it regularly at their clinic visits (not more than once per month). Patients with lower EQ-5D scores (p=0.0006), non-Caucasians (p=0.0024; 60% willing), and those that do not speak English at home (p=0.02; 53% willing) were less willing. In our model, age, gender, socioeconomic status, curability of tumor, disease site and performance status did not affect willingness.
Conclusion: Routine collection of EQ-5D in the cancer clinic is feasible, but a potential bias is the underrepresentation of ethnic minorities and patients with lower EQ-5D scores.
Keywords*: Health utility; EQ-5D; cancer*

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Socioeconomic status and risk of hemorrhage during warfarin therapy for atrial fibrillation: a population-based study

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Background: In patients prescribed warfarin therapy for atrial fibrillation, higher socioeconomic status is associated with superior anticoagulant control. However, the extent to which this influences the risk of hemorrhage is unknown.
Methods: We conducted a population-based study of patients aged 66 years or older with atrial fibrillation who commenced treatment with warfarin between April 1, 1997 and March, 31 2012. We ascertained socioeconomic status using neighbourhood level income quintiles. We followed patients for up to five years of continuous warfarin therapy, censoring on the first of drug discontinuation, mortality, or the end of the study period. We used Cox proportional hazards models to identify the association between income and hospitalization for hemorrhage. In a secondary analysis, we examined the association between income and fatal hemorrhage.
Results: Among 166,742 patients with atrial fibrillation who commenced treatment with warfarin, 16,371 (9.8%) were hospitalized for hemorrhage. After extensive multivariable adjustment, we observed an association between risk of hemorrhage and socioeconomic status, with those in the lowest income quintile facing an increased risk relative to those in the highest quintile (adjusted hazard ratio [HR] 1.17; 95% CI 1.12 to 1.23). We also observed an association between socioeconomic status and fatal hemorrhage, with an increased risk of death in those in the lowest income quintile relative to those in the highest quintile (adjusted HR 1.27; 95% CI 1.10 to 1.47).
Conclusions: In patients who commence warfarin therapy for atrial fibrillation, lower socioeconomic status is a risk factor for hemorrhage and mortality from hemorrhage.
Keywords: *Warfarin; socioeconomic status; hemorrhage*

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Order and good governance? Reporting on governance by research organizations

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Background: Governance is defined as the statutes and decisions that designate power, guide actions, and verify performance. Good governance within a large organization promotes excellence in performance and operations. In research, strategies dedicated to governance ensure scientific and ethical quality. The objective of this study was to rate publicly available governance statements for large organizations involved in or highly relevant to national or international eHealth research on drug safety and effectiveness.
Methods: Using five accepted principles of governance (legitimacy and voice, direction,

performance, accountability, and fairness), we rated the quality of governance reported by organizations. Selection began with organizations already involved in large-scale eHealth research (national or international networks using large datasets) followed by snowball sampling. Two reviewers obtained all publicly available documents related to governance and operations from websites or representatives from organizations.
Results: Governance reporting by 27 organizations from Canada, the United States and other countries were reviewed. Three (11.1%) organizations were rated highly, defined as addressing the majority of elements within each of the five principles. Six additional (22.2%) organizations met four of the five principles. Legitimacy and voice and accountability were most frequently addressed with 18 (66.7%) organizations meeting the evaluation criteria for each principle. Fairness (data access policies and code of ethics) was the most poorly addressed with only 8 (29.6%) organizations meeting this criteria.
Conclusion: Although actual governance practices might be better than policies reported in publicly available documents, our initial sampling of major organizations suggests insufficient attention to governance principles.
Keywords: *Governance; eHealth; drug safety and effectiveness*

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Which interventions may enhance medication adherence among seniors with cognitive impairment - a systematic literature review.

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Introduction: A growing number of Canadian seniors with cognitive impairment may have a considerably decreased ability to correctly use essential medications. Few systematic reviews on interventions to improve medication adherence have focussed on seniors with cognitive impairment, Alzheimer disease (AD) or dementia.
Objectives: To synthesize literature on interventions to enhance medication adherence among seniors with cognitive impairment, AD or dementia.
Methods: The review was based on the Cochrane handbook for systematic reviews of interventions and NICE guidance for quality assessment of individual studies. The review was conducted for all relevant scientific databases (e.g. PubMed, EMBASE, Cochrane Library, etc.). Grey literature was specifically searched as well. Keywords from the controlled vocabulary and free text were combined to identify all relevant publications. Study identification, data extraction and quality assessment of studies were conducted by two re viewers. Disagreements were resolved by discussion and consultation with a third team member.
Results: Nine studies could be included, but six were of low quality. Eight out of nine studies used an objective adherence measure, but they did not assess the effect of adherence on clinical outcomes. Seven showed significantly improved adherence. Seven studies used memory reminding or educational strategies, and three used simplification of dosing regimens.
Conclusion: There are few high quality intervention studies aimed at improving medication adherence among seniors with cognitive impairment, AD or dementia. Barriers and facilitators for adherence in this population may have to be identified first.
Keywords: *Adherence; cognitive impairment; systematic reviews*

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Estimate the clinical and economic impact of urologists' adherence to the follow-up guidelines after radical or partial nephrectomy for localized and locally advanced renal cell carcinoma in Canada

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Introduction: Surgical resection (radical or partial nephrectomy) remains the most effective therapy for clinically localized renal cell carcinoma RCC. Surveillance protocols after surgical resection varies depending on the risk of recurrence or development of metastasis.
Objective: To estimate the clinical and economic impact of urologists' adherence to the Canadian Urology Association (CUA) guidelines related to the follow-up after radical or partial nephrectomy in Canada as approved in 2009.
Methods: The study cohort was based on the Canadian Kidney Cancer Information System (CKCis) including seven Canadian provinces. Our cohort includes patients

having had radical or partial nephrectomy between January 2011 and January 2014. Kaplan-Meier method was used to evaluate the recurrence rate by urologists' adherence to the CUA follow-up guidelines. Cox proportional hazard model was used to evaluate association between time to recurrence and adherence level adjusted for pathological stage.
Results: A cohort of 1,030 patients with an average age of 61 years old has been selected. The mean follow-up was 12 months. During the follow-up, 34.7% of patients have had a number of abdominal CT or ultrasound tests as indicated by the CUA guidelines, whereas 58.9% of patients have had more tests and 6.5% less tests, respectively. Two-year recurrence rate was 27% in patients with more abdominal CT or ultrasound than recommended by guidelines, and 20% in the others (p-value < 0.0001). When adjusted for pathological stage, a hazard ratio of 3.1 (95%CI: 2.1-4.6) was estimated for patients with more abdominal CT or ultrasound than recommended by guidelines compared to the others.
Conclusions: The results suggest that clinicians have performed a more intense surveillance in patients with poor clinical outcomes.
Keywords: *Adherence to clinical guidelines; renal cell carcinoma; clinical and economic impact of urologists' adherence*

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Is oncology drug funding in Quebec different from the rest of Canada?

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Funding Source: Hoffmann-La Roche

Background: The pan-Canadian Oncology Drug Review (pCODR) assesses the clinical efficacy and cost-effectiveness of cancer drugs and provides funding recommendations to guide provincial funding decisions. Since Quebec does not participate in the pCODR process, it has an independent recommendation body, the Institut national d'excellence en santé et en services sociaux (INESSS).
Objectives: The objective of this analysis was to identify similarities and differences between these two oncology drug HTA bodies.
Methods: The pCODR database and INESSS website were searched to identify drugs reviewed by both bodies. Drug funding decisions were obtained through provincial formularies. pCODR/INESSS reviews and provincial drug listings were compared.
Results: A total of 29 drugs have been evaluated by both pCODR and INESSS (data cut-off June 2, 2014). The positive recommendation rate (list or list with cost criteria) for pCODR-reviewed drugs was 82%, and 76% for INESSS. 100% of these positive pCODR recommendations have been funded in at least two provinces/territories or are under pan-Canadian Pricing Alliance (PCPA) negotiations, while only 55% of positive INESSS recommendations have been funded in Quebec. Ontario has listed the most drugs, while Quebec has declined to fund the most drugs.
Conclusions: National HTA bodies such as pCODR are expected to lead to greater consistency and equity throughout the country. However, drug funding reviews and decisions in Quebec continue to operate independently from pan-Canadian initiatives. This analysis demonstrates a widening disparity between Quebec and the rest of Canada in both drug reviews and funding decisions for oncology products.
Keywords: *Cancer drug reimbursement; pCODR; INESSS*

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The health care cost of spinal cord injury in an Ontario cohort

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Background: Spinal cord injury (SCI) is associated with increased health care utilization. Individuals with SCI had more re-hospitalizations, physician visits and home care services. A consequence of higher health care utilization is increased costs. In Ontario the cost of SCI is above $100,000 per person per year. What remains unknown are the net costs specific to SCI as well as the lifetime costs for individuals with SCI. The objective of this study is to determine the total net lifetime cost of SCI from the perspective of the Ontario Ministry of Health and Long-term Care using phase-based costing methodology.
Methods: Using administrative data, individuals with SCI were identified from hospital inpatient discharge abstracts between 2005 and 2011. Resource utilization was collected post-SCI from various health care

settings. This cohort was then matched with individuals without SCI for various baseline demographic characteristics using propensity score matching. Cost phases for the SCI cohort were established by exploring cost patterns in the post-SCI and pre-death periods. Lifetime costs were calculated by mapping cost per phase to a survival curve of the SCI and non-SCI cohort.

Results: From preliminary results, it appears that the initial hospitalization is the cost driver post-SCI for the first two months followed by inpatient rehabilitation up to the first year. Similar to prior studies in other diseases, there appears to be three distinct phases: a post-SCI phase, stable phase and a pre-death phase. Costs per phase, total estimated lifetime costs and net lifetime costs and more will be presented.

Keywords: *Spinal cord injury; cost of illness; administrative data*

Poster Presentations
Sunday, November 2, 2014

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Reimbursement patterns for Enbrel® (etanercept) as senior patients transition from private to public drug plan insurance

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Funding Source: Amgen Canada Inc.

Objective: To understand whether a gap in Enbrel® (etanercept) reimbursement coverage exists when a patient transitions from private to public drug plan insurance upon becoming seniors.

Method: A retrospective cohort study using medication transaction data (IMS Brogan Lifelink® database) from Ontario and Quebec pharmacies was conducted. Patients were eligible if they were at least 64 years of age, and their last private and first public transaction for Enbrel® occurred between January 1st 2010 and March 31st 2013. The gap in coverage was determined by comparing the estimated date on which supplies purchased on the index date ended (start of gap) to the date of the first public script (end of gap), and calculating the difference (in days) between the two dates relative to days' supply.

Results: 150 patients were included in the study. Patients were split evenly between genders with 2/3 from Ontario. 64% had experienced a gap in coverage when transitioning between private and public payers. The remaining 36% had either no gap, or an overlap in dispensed prescriptions. 50% experienced reimbursement gaps lasting 6 days or more, while 25% of patients had gaps lasting 26 days or more. 27% of patients experienced a gap in reimbursement that would be considered a meaningful delay in Enbrel® treatment (> 21 days). There were no statistical differences in median gap on the basis of gender, indication, or physician specialty.

Conclusion: A clinically significant number of patients experienced a meaningful gap in reimbursement of Enbrel® which can result in suboptimal clinical outcomes.

Keywords: *Reimbursement; rheumatoid arthritis; etanercept*

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Development of an educational tool for an interprofessional intervention to reduce medication load for long term care residents with advanced dementia: OPTIMAMED

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Background: Seniors with advanced dementia residing in nursing homes (NH) often receive a large number of medications. With disease progression care goals shift from curative or preventive care to comfort care, and medications need to be reviewed, adjusted or discontinued, because of reduced life-expectancy or changes in the harm-benefit ratio. Research is lacking on which previously indicated medications may no more benefit these seniors and on interventions to optimise medication appropriateness.

Objectives: To develop an inter-professional intervention comprising continuous education (CE) and a tailored tool to optimise medication use among NH residents with advanced dementia.

Methods: Based on a scoping literature review on medications appropriate for NH residents with advanced dementia, lists of always, sometimes, rarely or never appropriate medications and elements of successful interventions were identified. A 15-member inter professional Delphi panel was convened. Delphi results and further collaboration with NH health professionals helped to develop a tailored tool. Results from a survey on health care professionals' needs for CE were used to enrich the CE session.

Results: The new 9-pages tool distinguishes three categories of medications: generally appropriate,

sometimes appropriate and exceptionally appropriate. This tool is the core of an inter-professional CE session and intervention.
Conclusions: The French language tool is currently being tested within a pilot study comprising six inter-professional and interactive CE sessions (physicians, pharmacists and nurses) in three Quebec NH.
Keywords: *Medication discontinuation; advanced dementia; interprofessional education*

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An indirect treatment comparison and cost-effectiveness analysis comparing FOLFIRINOX to nab-paclitaxel + gemcitabine for first-line treatment of patients with metastatic pancreatic cancer

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Background/Objective: An indirect treatment comparison (ITC) was performed to facilitate a Canadian cost-effectiveness analysis (CEA) of FOLFIRINOX versus nab-Paclitaxel plus gemcitabine (NabP+G), given head-to-head clinical data of these two treatments were unavailable.
Methods: The ITC was feasible given that both the FOLFIRINOX and NabP+G phase III trials had gemcitabine as a comparator. In the ACCORD 11 study, FOLFIRINOX significantly prolonged median overall survival (OS) by >4.3 months compared with gemcitabine (11.1 vs 6.8 months, Hazard ratio (HR)=0.57; P<0.001), while in the MPACT trial NabP+G provided 1.8 additional months over gemcitabine (8.5 vs 6.7 months, HR=0.72; P<0.001). In the ITC, HRs were calculated for FOLFIRINOX versus NabP+G for OS and PFS, and relative risks (RRs) were calculated for adverse events (AEs). The CEA incorporated the ITC OS, PFS and AE results into a three health state ("Progression-Free", "Progressed", and "Dead") Markov model. Published utility data and Canadian costs were applied.
Results/Conclusion: The ITC results comparing FOLFIRINOX with NabP+G for OS and PFS were HR 0.792 (95% CI, 0.597 to 1.05) and HR 0.681 (95% CI, 0.509 to 0.911) respectively. Most AEs were not statistically significantly different between treatments. The results of the CEA indicate that FOLFIRINOX is cost-effective when compared with NabP+G (ICER: $7,830/QALY). Due to longer treatment, and improved OS and PFS, there were slightly higher costs for FOLFIRINOX over a lifetime horizon when compared with NabP+G. The basecase and probabilistic sensitivity analyses demonstrate that FOLFIRINOX has a >90% probability of being cost-effective at a willingness-to-pay threshold of $50,000
Keywords: *Cost-effectiveness analysis; FOLFIRINOX; nab-Paclitaxel; metastatic pancreatic cancer*

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The impact of the abolition of Quebec's innovative drug protection plan (BAP15)

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Background: Government spending is coming under increased scrutiny, with calls to reduce debt loads. Quebec's Health Minister addressed this issue by abolishing the 15 year rule (BAP15) in 2013, which covered the cost of brand drugs for 15 years once added to the Quebec Formulary, despite patent expiry, data protection and generic entry to the market. Savings due to this policy change were expected to be approximately $150 million the first year and continue to save such an amount in subsequent years, affecting 60 brand drugs. The objective of this study was to evaluate the actual overall financial impact of this policy change in Quebec.
Methods: The list of medicines affected was defined and respective public and private pharmacy unit claims were extracted from PharmaStat. Costs of each unit were attributed accordingly, in function of claim date and drug strength. A forecast of brand and generic units sold was carried out for 3 years following the abolition of the BAP15, using a 12-month moving average.
Results: The abolition of the BAP15 produced savings of $74.2 million in the first year. It would continue to generate savings of $73.9 million, $72.2 million and $72.4 million for the years 2014, 2015 and 2016, respectively.
Conclusions: The abolition of the BAP15 generated short-term savings for the Quebec government; however, actual savings did not reach 50% of the estimates set forth in 2012. In turn, brand medicines declined significantly in sales and market shares. This impact could reflect declining investments within the pharmaceutical sector.

Keywords: *BAP15; Quebec; PharmaStat*

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Changes in opioid utilization and prescribing after delisting of long-acting oxycodone from a provincial drug plan

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Background: Ontario has the highest rate of prescription narcotic use in Canada. From 1991 to 2007, prescriptions for oxycodone-containing products rose by 850% in Ontario. Studies suggest that increased rates of opioid prescribing and use of higher doses, particularly long-acting (LA) oxycodone, contributes significantly to morbidity and unintentional opioid-related mortality. Under the Ontario Drug Benefit Program, LA oxycodone was delisted as a Limited Use benefit in February 2012 with the introduction of the new OxyNEO formulation. Prior recipients received automatic coverage of OxyNEO for one year. New patients were considered on a case-by-case basis under the Exceptional Access Program (EAP). Following the grandparenting period, all recipients required EAP approval for OxyNEO coverage. The high strength tablets (60mg and 80mg) are not reimbursed, and communications sent to prescribers encouraged them to refer to best practice guidelines for the safe and effective use of opioids in chronic non-cancer pain. Since the listing change, the number of LA oxycodone recipients has decreased from 31,000 to approximately 6,000; however, high dose prescribing of LA oxycodone and overall opioid utilization amongst ODB-eligible Ontarians has essentially remained unchanged. The largest increase in opioid use has been in hydromorphone utilization. Also, the average doses prescribed for LA oxycodone were more than double that of other LA opioids. The monitoring of opioid utilization is ongoing and a formulary class review of all opioids is underway. A prescription monitoring program has been implemented and other Ministry initiatives to support the appropriate use of prescription narcotics in Ontario are under development.

Keywords: *Opioids; oxycodone; reimbursement; formulary*

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Impact of expanded pharmacy services in British Columbia

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Background: Health legislation now allows pharmacists to provide additional health services to patients, including medication reviews, immunizations and prescription adaptations. There are new concerns rising about how the current pharmacy working environment effectively supports these changes.
Objectives: To explore the effect of expanded pharmacy service provision in British Columbia on pharmacists' working conditions and perceived safety of patient care.
Methods: An online survey was developed and distributed to all BC College of Pharmacists registrants by email. Responses were collected from October 1st - November 10th, 2013. The survey consisted of questions on pharmacists' demographics, practice setting, and perception of working conditions. Analyses included summary statistics and ANOVA, where applicable.
Results: 1,241/5,300 (23%) of pharmacists responded, 78% worked in the community pharmacy setting (58% chain, 19% independent). Overall, 46% of respondents reported not having enough time at work for breaks or lunch, and 45% reported not being satisfied with the amount of time they have to do their jobs. The majority agreed there were adequate pharmacist's staff but not enough technicians to support safe and effective patient care. 10 to 42% of respondents reported having to meet monthly quotas for certain expanded pharmacy services. Satisfaction with working conditions differed significantly by pharmacists' practice setting ($p<0.001$), provision of expanded services ($p<0.01$) and requirement of monthly quotas ($p<0.001$).
Conclusion: Pharmacists working in chain community pharmacies who are required to meet monthly quotas for expanded services report a substantial negative impact on their working conditions and perceived safety of patient care.

Keywords: *Pharmacy services; impact of legislation; reimbursement*

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Gender gap for LDL-C goal attainment amongst patients with diabetes: a systematic review

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Background: Studies demonstrated women with dyslipidemia are more likely than men to have a LDL-C above treatment goals.
Objective: To systematically explore the gender gap for LDL-C goal attainment using HgbA1c goals as indicator for adequacy of diabetes management.
Methods: This review focused on studies reported LDL-C and HgbA1c goal attainment in patients with diabetes. Studies were identified from an initial PubMed and EMBASE search using several combinations of the MESH terms. The search was limited to the clinical studies on adult human beings in English-language publications. Relevant studies were further extracted from the references of the studies already identified.
Results: 26 studies were identified that reported both LCL-C and HgbA1c goal achievement by gender for the cohort of patients with diabetes. Glycemic control as reported for HgbA1c goal achievement was comparable between women and men. Odds Ratios did not demonstrate any significant differences between men and women for HgbA1c goal achievement in the total cohort [Odds Ratio: 1.05; 95% confidence interval: 0.90 to 1.10; (P-value > 0.05)]. However, for the same cohort of patient with diabetes, LDL-C goal attainment illustrated a significant gap (10%) by gender and women had significantly higher levels of LDL-C on average (P = 0.001).
Conclusion: Women mostly had comparable, or even better, outcomes than men for HgbA1c goal attainment, however, women demonstrated significantly lower LDL-C goal achievement. This calls for further study to determine causes of possible gender disparities to tailor interventions for each risk factor to address the impact of gender differences.
Keywords: *Gender gap; diabetes; therapeutics; goal attainment*

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Challenges in pharmacotherapeutics education for diabetes in real-world clinical settings: views from family medicine and internal medicine residents

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Background: Pharmacotherapy for diabetes in real-world clinical settings is very complex and it is posing a challenge for residents in training.
Objective: To explore the views of residents in family medicine compared to internal medicine programs regarding educational challenges for pharmacotherapy in diabetes management in different clinical inpatient and outpatient settings.
Methods: The questionnaire and the letter of invitation were developed. The survey received approval of IRB at Queen's University. Then the survey was uploaded to "SurveyMonkey" system. The data was analyzed using Chi-square.
Results: Totally, 215 residents participated and completed the survey, 127 residents from family medicine and 88 residents from internal medicine. A significant number of residents (61% of family medicine and 62% of internal medicine, p-value = 0.30) viewed combination pharmacotherapy for diabetes management as the most important educational challenge. Among all classes of medication for blood glucose management the education on the use of newer class of medication such as GLP1 agonists, DPP4 inhibitors and SGLT2 inhibitors was recognized as a priority by 74% of family medicine and 79% of internal medicine residents (p-value = 0.10). Chronic Kidney Disease (CKD) as a comorbidity was viewed as an education challenge for pharmacotherapy in patient with diabetes by 69% and 72% of family medicine and internal medicine residents, respectively (p-value = 0.35).
Conclusion: This survey illustrated the both family medicine and internal medicine residents had similar views for pharmacotherapeutics educational challenges and priorities in diabetes management despite different educational environments regarding inpatient and outpatient settings.
Keywords: *Residency; education; diabetes; pharmacotherapy*

POSTER PRESENTATIONS
Monday, November 3, 2014

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Cost-effectiveness analysis of neoadjuvant pertuzumab and trastuzumab therapy for locally advanced, inflammatory, or early HER2+ breast cancer in Canada

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Background: The recent NeoSphere trial demonstrated that the addition of pertuzumab (P) to trastuzumab (H) and docetaxel (T) for the neoadjuvant treatment of HER2+ early breast cancer (eBC) resulted in a significant improvement in pathological complete response (pCR). Furthermore, the TRYPHAENA trial supported the benefit of neoadjuvant dual anti-HER2 therapy (P + H). Survival data for pertuzumab-treated patients are not yet available; however, other trials have demonstrated a correlation between pCR and improved event-free survival (EFS) and overall survival (OS) in HER2+ eBC.
Methods: A cost-utility analysis was conducted using a three health state ("progression-free", "progressed", and "dead") Markov model. Total pCR (ypT0/is ypN0) data from NeoSphere and TRYPHAENA were used to inform two separate analyses. Published EFS and OS data partitioned for patients achieving/not achieving pCR were used in combination with the percent of complete responders in the pertuzumab trials to estimate survival. Published utility estimates and Canadian costs were applied.
Results: Both analyses found that the addition of pertuzumab resulted in increased life-years and quality-adjusted life-years (QALYs). The incremental cost per QALY ranged from CAD25,000 (NeoSphere analysis) to CAD46,000 (TRYPHAENA analysis). Sensitivity analyses further support the use of pertuzumab. At a threshold of CAD100,000, the addition of pertuzumab was cost effective in nearly all scenarios (93% NeoSphere; 79% TRYPHAENA).
Conclusions: Given the improvement in clinical efficacy and a favourable cost per QALY, the addition of pertuzumab in the neoadjuvant setting represents an attractive treatment option for HER2+ eBC patients.
Keywords: *Cost-effectiveness analysis; pertuzumab; neoadjuvant breast cancer*

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Atomoxetine – utilization patterns in Canada

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Background: The use of ADHD medications, including atomoxetine has been increasing among children, adolescents and adults but little is known about its usage pattern over time and treatment adherence among distinct age groups in Canada.
Objective: To characterize utilization patterns of atomoxetine in terms of individual patient level data in Canada.
Methods: This retrospective study utilises anonymized longitudinal patient level data from IMS Brogan and the National Prescription Drug Utilization System (NPDUIS) and provides descriptive statistics to characterise drug utilization patterns. These utilization trends were analyzed with respect to age, gender, and concomitant medications. Adherence patters were measured by the medication possession ratio (MPR). NPDUIS data will be analyzed as it becomes available.
Results: Preliminary IMS data indicates that the average annual prescription volume of atomoxetine remained stable at 316,188 from 2009 to 2013. Children aged 6-18 years accounted for most of the prescriptions. Prescription volumes declined during the summer months. In 2013, over 20% of children aged 13-18 years had at least one gap of more than 30 days between the end of one prescription and the start of the next, and 25-35% of this age group had an MPR of under 80%.
Conclusions: Preliminary analysis shows that atomoxetine usage has remained stable over the last few years. Children aged 6-18 years account for most of the dispensed prescriptions, and they are most likely to go on a drug holiday during the summer months. Treatment duration, dosage, and concurrent use of ADHD and non-ADHD drugs will be further investigated.
Keywords: *Drug utilization; ADHD; atomoxetine*

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Using electronic medical records as real world evidence to understand the impact of flu vaccinations on patient health

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Funding Source: IMS Brogan provided the time, access to data, and materials needed for this research.

Background: The power of large scale electronic medical records (EMR) can be used as Real World Evidence (RWE) to better understand anonymized patient diagnoses, treatments and outcomes. Longitudinal EMR data (IMS Evidence 360, Canada) was used to better understand the impact of annual Flu Vaccines on patient illness in Ontario. Public debate between scientific and lay experts on the safety and efficacy of vaccine programs has led to patient ambivalence, and concern on the part of public health agencies. Longitudinal analyses of patients within a flu season were performed to understand the impact of approved vaccines on the volume of sick notes written. This was done for three patient cohorts across six seasons (2007/8-2012/13). The analysis focused on three diagnosis driven cohorts; patients with influenza, patients with diabetes and influenza, and patients with diabetes without influenza. Unvaccinated patients with influenza (vs vaccinated) had 2.8-5.7 times the volume of sick notes. Unvaccinated diabetes patients with influenza had 1.1-2.3 times the volume of sick notes. There was no significant difference between vaccinated and unvaccinated diabetes patients without influenza. Furthermore there was no significant difference in sick notes between vaccinated diabetes patients who developed the flu versus those that did not. Although these RWE results conservatively demonstrate the value of flu vaccinations in minimizing the volume of sick notes needed by influenza patients, the same technique can be used by governments, pharmaceutical manufacturers, medical researchers, and other healthcare professionals, to better understand the links between diagnoses, treatment and outcomes across many disease states.

Keywords: *Influenza vaccination; real world evidence; electronic medical records*

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Harmonization of health technology assessment and regulatory approval: a bridge over the chasm

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Objectives: Despite growing medical innovation, the diffusion of health technologies into the healthcare system has often proven problematic. In part, this stems from the separate processes of regulatory and reimbursement evaluation. This mixed-method study identified and assessed known initiatives that aim to better harmonize regulatory approval and health-technology assessment (HTA)-based reimbursement.

Methods: A systematic literature review was conducted to identify empirical cases of HTA-regulatory harmonization, capturing literature up to June 10, 2013. Semi-structured interviews with key international stakeholders from a broad range of perspectives were also conducted to supplement the literature review. The interviews elicited an organization's or individual's experiences with harmonization.

Results: A number of cases were identified in Canada and in other jurisdictions internationally. These initiatives included early tri-partite dialogue, alignment of evidence need, pre-market evaluation, parallel licensing and adaptive licensing. Approaches to harmonize can be categorized into those: i) focused on content (i.e. reducing uncertainty in the evidentiary requirements, translating evidence to reconcile regulatory and payer perspective); and/or, ii) focused on processes (i.e. aligning the timeframes or logistical elements in the review process). Recurring barriers and facilitators to harmonization fell into the following themes: healthy stakeholder relationships; well-intention; clearly defined governance and leadership; and available organizational infrastructure.

Conclusion: Considerable overlap exists between HTA and regulatory approval, and harmonization is both possible and feasible. Greater coordination can benefit all levels of the healthcare system and bring forth the necessary evidence to guide both agencies' decision-making needs. However, it may also have several drawbacks that require further investigation.

Keywords: *Government regulation; health technology assessment; policy-making*

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Expanding pharmacists' immunization authority in Ontario: a jurisdictional and scoping review

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Background: Ontario pharmacists have been a key component in the delivery of publicly-funded influenza vaccinations. In order to further protect Ontario residents from vaccine-preventable disease, and to promote optimal use of pharmacy-based services, there is potential for broadening the immunization authority of Ontario pharmacists. Which vaccines would be most

effectively available within a pharmacy setting in Ontario?
Methods: A jurisdictional review was conducted to determine which vaccines pharmacists are authorized to deliver in Canada, the United States, UK, Australia, and New Zealand, as well as required training or certification. Legislation was manually searched and key informants contacted. A scoping review of peer-reviewed literature was also performed to determine what data exists to provide insight into pharmacists as immunizers of non-influenza vaccines.
Results: Jurisdictional review: Pharmacists' authority to deliver non-influenza vaccines varies across provinces, states, and countries. In some jurisdictions pharmacists may deliver a broad range of vaccines, whereas in others pharmacists have no immunization authority. Ontario is currently situated within a group of provinces and states that only authorize influenza vaccination. All jurisdictions with pharmacist authority to immunize require some form of training or certification. Scoping review: 161 articles were identified. Early analyses indicate an emphasis on vaccine accessibility, patient perspectives, and pharmacists providing or promoting non-influenza immunization as a component of general health care. There is a major gap in terms of evaluation of the effectiveness of pharmacist-managed non-influenza vaccination programs.
Conclusions: *In progress*.
Keywords: *Immunization; pharmacist; review*

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Costs of employees with treatment-resistant depression based on a Canadian private claims database

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Introduction: Approximately 10-20% of individuals with Major Depressive Disorder (MDD) fail to respond to antidepressant monotherapy. These individuals with treatment resistant depression (TRD) have been found to be frequent users of healthcare services, thus incurring significantly greater costs than those without TRD.
Objective: To investigate the cost of Treatment-Resistant Depression from a private payer perspective in Canada.
Methods: An employer-sponsored benefits plan database (2011/2012) was used to define a cohort of Non-TRD and TRD claimants. TRD claimants are defined as those on their third antidepressant monotherapy; or combination antidepressant therapy; or antidepressant augmented with lithium, thyroid hormone or an antipsychotic medication. The cost of prescription medication utilization, short-term disability (STD), and long-term disability (LTD) benefits for employees was calculated (2011 and 2012 $CAN) for both Non-TRD and TRD groups. Descriptive statistics were used to characterize the cohort of claimants and employees, as well as resources and costs for employees.
Results: There were 55,324 and 61,028 employee claimants in 2011 and 2012, respectively. 717(1.3%) and 798(1.3%) were TRD claimants; 4,744(8.6%) and 5,137(8.4%) were Non-TRD claimants in 2011 and 2012, respectively. In 2011, the medication costs for treating depression was $774 per TRD employee claimant compared to $303 per Non-TRD claimant. STD costs were $6,263 for TRD (n=79) and $5,855 for Non-TRD (n=276). LTD costs were $13,598 for TRD (n=80) and $12,272 for Non-TRD (n=119). In 2012, the medication costs for treating depression per TRD employee claimant was $794 compared to $293 for Non-TRD claimants. STD costs were $7,832 for TRD (n=86) and $4,001 for Non-TRD (n=248). LTD costs were $13,927 for TRD (n=89) and $12,901 for Non-TRD (n=121).
Conclusions: Claimants identified with TRD had higher medication, STD and LTD costs than those with Non-TRD. Limitations include lack of diagnostic information for claimants and small sample sizes for STD and LTD subgroups.

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Incorporating dosages increase the relevance of network meta-analysis for decision-makers: a case example using data from a systematic review of serotonin (5-HT3) receptor antagonists in patients undergoing surgery

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Background: Network meta-analysis (NMA) is a useful tool for decision-makers (including patients,

healthcare providers, and policy-makers) and is the only feasible approach to formally compare the safety and effectiveness of all available treatment comparisons. However, some agents are administered at different doses and these differences are often not accounted for in NMA. This may lead to the results being less informative to decision-makers.
Objective: To explore optimal methods for estimating the relative efficacy of therapeutics provided at different doses in NMA.
Methods: We conducted a systematic review for the Drug Safety and Effectiveness Network on serotonin (5-HT3) receptor antagonists in patients undergoing surgery. Studies were identified through searching MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials, trial registries, conference proceedings, and reference lists. Screening of literature search results, data abstraction, and risk-of-bias was conducted by two reviewers, independently. Random-effects NMA were employed by: 1) treating each dose as a separate treatment, and 2) separating each dose within a treatment. We assumed a common within-treatment variance across all treatments to borrow strength by integrating evidence from the other treatments, as it is often the case that a treatment has only 1-2 different dosages.
Results: We included 455 studies and 89,608 patients after screening 7,610 citations and 1,016 full-text articles. The pros and cons of the two approaches will be discussed and appropriate analysis strategy will be provided.
Conclusions: Incorporating doses into NMA provides additional insight on heterogeneity in safety and effectiveness of treatments and is more informative for decision-makers
Keywords: *Systematic review; network meta-analysis; policy*

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Single-arm clinical trials and a lack of statistically significant overall survival are not an absolute barrier to a positive pCODR recommendation for an oncology product
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Objectives: Overall survival (OS) data for cancer products is an important endpoint to payers. This study examined the proportion of positive reimbursement recommendations by the pan-Canadian Oncology Drug Review (pCODR) for products without either a randomized clinical trial and/or statistically significant overall survival, and the proportion of negative recommendations that noted a lack of overall survival data as a contributing factor.
Methods: Reimbursement recommendations publicly accessible at www.pcodr.ca and reimbursementdecisions.com were reviewed for the period 13 July 2011 - 28 April 2014.
Results: During this time period, 32 submissions covering 38 indications were reviewed by pCODR; 28 received positive guidance. Two of ten indications that received a negative recommendation had statistically significant overall- and progression-free survival data. Four (14%) positive recommendations were based on single-arm clinical trials. The remaining 24 positive recommendations were based on randomized controlled trials (RCTs) with OS as an endpoint. Nine of these 24 indications had statistically significant OS data and 15 either did not have statistically significant OS data. More than half (60%) of the 15 indications with non-significant OS trial data allowed cross-over in the trial (n=9) thereby potentially confounding the clinical benefit of the active therapy.
Conclusions: This study highlights that positive pCODR recommendations may be made in the absence of a clear OS benefit, provided strong PFS and or additional endpoint data exist. This reflects recognition of the challenges with obtaining OS data for many oncology products and the importance of unmet need in reimbursement decisions.
Keywords: *Oncology; overall survival; reimbursement*

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Measuring private payer changes: trends in market access restrictions using real world data
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Funding Source: None

Background: Over the last two decades, Health Technology Assessments (HTA) have increasingly influenced the Canadian public payer environment in guiding drug reimbursement decisions and in influencing market access restrictions strategies on drugs. Private payers/Insurers have also been promoting and/or implementing cost containment measures that may be more or less influenced by HTA. Understanding private payer's restriction trends is essential to define opportunities to improve patient access to novel medications. The objective of this study is to examine private payer trends in plan restrictions using real world claims data.

Methods: Transactional claim rejections data from various private payer drug plans were pooled from the 2010 to 2013 period. The claim rejections were then cleaned and examined based on their rejection type, geographical location, therapeutic classes and claim date.
Results: The pooled claim rejections data contained 408,069 patients with more than 2.3 million claim rejections over the 4 years period. The claim rejection type distribution changed over the study period. The analysis also showed that the rejection type distribution also varied according to geographical location and therapeutic classes. The top 5 therapeutic classes subject to claim rejections were antihypertensives, antidiabetics, laxatives, erectile dysfunction and dermatological.
Conclusion: The current findings illustrate that the Canadian private payer market is a heterogeneous environment and is evolving. Private payer plan restrictions may also target other therapeutic classes beyond lifestyle drugs. We conclude that patterns in rejected claims can be used to provide valuable insights on private payer restriction trends over time.
Keywords: *Private payer; policy; trends; claim rejection; real world data; data mining; market access; evaluation; private payer restriction; Canada; reimbursement; real world study*

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Majority of oncology products receive a positive recommendation in Canada conditional on improved cost-effectiveness

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Funding Source: None

Objectives: Identifying decision patterns of health technology assessments can offer valuable insights into the factors that may influence reimbursement. This study examined oncology reimbursement recommendations made by the pan-Canadian Oncology Drug Review (pCODR) and determined the implications of these recommendations.
Methods: Final pCODR recommendations were identified from 13 July 2011 to 9 June 2014. Only publicly available information accessible at www.pcodr.ca and reimbursementdecisions.com were reviewed.
Results: During this time period, 40 indications were reviewed by pCODR; 30 received positive guidance while 10 received negative guidance. Twenty-one of the thirty (70%) indications that received a positive recommendation were recommended conditional on the cost-effectiveness being improved to an acceptable level. There were no observable relationships between tumor type and recommendation. Six positive recommendations (20%) were recommended without listing criteria or conditions, while the remaining three were recommended in a more restricted patient population. More than half (60%) of the negative recommendations were due to insufficient or unclear clinical benefit and economic analysis. The remaining four negative recommendations were based on a lack of clear clinical benefit. Interestingly, negative recommendations based solely on poor economic analysis were absent.
Conclusions: The majority of pCODR recommendations were positive conditional on improved cost-effectiveness, with the probability of a positive recommendation increasing with unmet need and strong clinical data. All negative recommendations included concerns regarding insufficient or unclear clinical benefit. This study highlights the value placed on unmet need and clinical data, as well as the need for a reimbursement strategy that incorporates price and cost-effectiveness considerations.
Keywords: *Canadian oncology drug review; oncology; reimbursement decisions*

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Value of pharmaceuticals- a multi-criteria approach

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Funding Source: The two workshops were supported by grants from Janssen, Pfizer, Astellas, Roche and Merck

Background: Coverage decisions for a new drug revolve around the balance between perceived value and price. But what is the value of a new drug? Traditionally, the assessment of such value has largely revolved around the estimation of cost-effectiveness (C/E). However, very few will argue that the C/E ratio presents a fulsome picture of 'value'. Multi-criteria decision analysis has been advocated as an alternative to cost-effectiveness analysis and it has been argued that it better reflects real world decision making. The

purpose of this paper is to report on a project that aimed to develop a framework to operationalize a multi-criteria decision analysis approach for incorporating societal values as they pertain to the value of drugs. Two workshops were held, one in Toronto on November 17th, 2013 in conjunction with the CAPT annual conference, and one on April 6th, 2014 in Ottawa, as part of the annual CADTH Symposium.

Results: Results are grouped into three themes: 'overarching context ideas' (thoughts and ideas that justify and shape the value framework in the sense that they define its role), 'guiding principles' (the values and process features that participants felt must be reflected in the value framework) and,' criteria' (the considerations that determine the value of the proposed drug and operationalize the guiding principles). There are currently ten criteria: Comparative effectiveness, Adoption feasibility, Risks of adverse events, Patient autonomy, Societal benefit, Equity, Strength of evidence, Incidence/prevalence/severity of condition, Innovation, Disease prevention/ health promotion. Feedback will determine the final shape of the framework proposed.

Keywords: *Coverage; multi-criteria; value*

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Medication copayment for seniors impacts prevalent but not incident users of chronic medications

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Background: In 2007, the Saskatchewan government implemented the Seniors' Drug Plan Benefit (SDP) that limited out-of-pocket payment to $15 per prescription for eligible individuals 65 years of age and older, for drugs listed on the Saskatchewan Formulary. We aimed to determine the impact of this policy on commonly used chronic medications: anti-hypertensives, cholesterol-lowering agents, oral hypoglycemic agents, and antidepressants.

Methods: Pharmacy claims data were used to calculate the monthly number of chronic medications dispensed between 2005 and 2009. An interrupted time-series analysis was used to test for differences in age-and sex standardized rates pre- and post-program. Overall, incident, and prevalent rates were examined.

Results: The number of prescriptions dispensed for the chronic medication classes increased by 5% (95% CI: 1-10%) overall following implementation of the SDP. Increases were observed for prevalent (5% (95% CI, 1 to10%) but not incident users (1%; 95% CI: -8 – 11). The SDP did not influence utilization of diabetes medications for either prevalent (0%; 95% CI: -6 – 5) or incident users (-14%; 95% CI: -36 – 7%). Antihypertensives were associated with significant increases amongst both incident and prevalent users.

Conclusions: Reduced copayment among Saskatchewan seniors did not result in a consistent increase in drug use across all chronic medication classes or types of users.

Keywords: *Medication utilization; out-of-pocket payment; copayment; reimbursement; policy*

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A Canadian cost impact analysis comparing maintenance therapy with bortezomib versus lenalidomide in multiple myeloma patients ineligible for stem cell transplant

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Funding Source: Research was supported by Janssen Inc.

Background/Objectives: Approximately 7,000 Canadians have multiple myeloma (MM). Management of stem cell transplant (SCT) ineligible MM patients is complex and varied. Maintenance therapies (MTs) after various induction regimens have been shown to improve response rate and progression-free survival. We sought to compare Canadian costs between two common approaches to MT, either bortezomib or lenalidomide, in MM patients ineligible for SCT.

Methods: The total annual drug cost of the two MT options were calculated and compared. Costs were based on 1.3mg/m^2 of bortezomib on days 1, 4, 8, 11 every three months, plus 50mg of prednisone every other day, or 10mg of lenalidomide on days 1 through 21 of each 28-day cycle. In addition to the acquisition costs of each MT, administration costs (e.g., nurse and pharmacist workload) were included for bortezomib, and pharmacy costs (e.g., markup and dispensing fees) were included for prednisone. Additional analyses

considered the impact of several variables (e.g., management of adverse events, second primary malignancies, and alternate costing assumptions).
Results: The total annual costs of treatment per patient were $20,106 and $98,824 for bortezomib and lenalidomide, respectively. The incremental differences were robust to changes in inputs and assumptions (to be presented in poster).
Conclusions: The results suggest that substantial savings were associated with bortezomib MT when compared with lenalidomide MT. As drug costs represent an increasing proportion of public spending in Canada, it is important to consider both efficacy and cost of treatment. Further studies are required to determine the complete cost-benefit of available MTs.
Keywords: *Costing analysis; bortezomib; lenalidomide; maintenance therapy*

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A Canadian cost analysis comparing the use of bortezomib or lenalidomide as maintenance therapies in multiple myeloma patients eligible for autologous stem cell transplant

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Background/Objectives: Multiple myeloma (MM) is the second most prevalent blood cancer in Canada. In patients who have undergone autologous stem cell transplant (ASCT), post-transplant maintenance therapy (MT) has been associated with substantial prolongation of progression-free survival. We sought to compare potential cost differences between two MTs, bortezomib and lenalidomide, in MM patients who have undergone ASCT.
Methods: The total annual drug costs of the two MT options were calculated. Costs were based on 1.3 mg/m^2 of bortezomib every two weeks, or 10 mg of lenalidomide daily. The cost of administration including oncology nursing time and pharmacist workload was added to the acquisition cost of bortezomib. Unit and labour costs were obtained from public Canadian sources. Additional analyses were conducted to consider the impact of several variables including the management of adverse events, second primary malignancies and alternate costing assumptions.
Results: The total annual costs of treatment per patient were $32,560 and $131,765 for bortezomib and lenalidomide, respectively. The incremental differences were robust to changes in inputs and assumptions (to be presented in poster).
Conclusions: In the absence of clear comparative clinical efficacy, the choice of MT may be influenced by patient characteristics as well as patient and physician preference. Taken together, the results of this analysis suggest that when comparing MTs, bortezomib is much less costly than lenalidomide and therefore there are important cost differences that should also be considered.
Keywords: *Costing analysis; bortezomib; lenalidomide; maintenance therapy*

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Health care resource utilization in the management of chronic lymphocytic leukemia at an Ontario cancer centre

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Objectives: To collect health care resource utilization (HCRU) in the management of chronic lymphocytic leukemia (CLL) patients who have relapsed/refractory disease, and had at least one previous chemotherapy treatment.
Methods: A retrospective, longitudinal, cohort study design is being used involving three cancer centres in Ontario, Canada. A convenience sample of 90 CLL patients was selected with inclusion criteria of adult age at diagnosis, date of diagnosis between January 1, 2006 to 2012, relapsed/refractory disease that required at least one previous therapy, and minimum of one oncology visit. Demographics and HCRU data were collected with descriptive statistics to be presented. Costs are in 2013 Canadian dollars.
Results: 30 CLL patients were evaluated at the Juravinski Cancer Centre (Hamilton, Ontario). 22 were male, mean age at diagnosis was 65.2 years and 43% had genetic testing. Chemotherapy-wise, 73.3% of patients received fludarabine-based first-line treatment, 26.7% received chlorambucil as first-line treatment and 40% were given rituximab. 90% of patients who needed other medications utilized a mean number of

6.0 drugs. Half of the cohort visited the emergency department for a total of 19 times and experienced 25 adverse events. The total cost of diagnostic tests/procedures was $17,502, $28,895 for hospitalizations, and $49,794 for specialist visits.
Conclusions: Preliminary results from one cancer centre indicate substantial HCRU associated with CLL management. The authors plan to complete data extraction at the two remaining cancer centres in order to determine HCRU and cost results for the full cohort.
Keywords: *Healthcare resource utilization; costs; cancer*

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Voluntary warnings and the limits of good prescribing behaviour: the case for de-adoption of meperidine (Demerol©)
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Funding Source: University of Manitoba

Background: Meperidine (Demerol©) is an opioid analgesic that is rapidly metabolized to normeperidine, which is associated with neurotoxicity and seizures. ISMP Canada issued warnings and guidelines for meperidine in August 2004. We examined the impact of this warning by conducting a cross-sectional review of meperidine use in the community over the period of 2001 to 2010 by utilizing the Manitoba Pharmacare database. During this period, the number of distinct users of meperidine has dropped by 55%, the number of prescriptions by 42%, and of Defined Daily Dose (DDD) units by 27%. A segmented linear regression determined the DDD rate trend broke from being level to decreasing at a rate of 0.2 DDD's per quarter beginning in July of 2005 (shortly after the ISMP warning). However, for the remaining users, the amount of meperidine dispensed to each individual user has risen by 62%, and the amount per prescription has risen by 27%. Furthermore, the declines were not seen uniformly throughout the province and pockets of higher use continue. Perhaps we have reached the limit of voluntary prescribing guidance. As there is no proven benefit to using meperidine over other narcotic analgesics, but there are significant risks, it may be time to delist the use of this potentially toxic medication. Nova Scotia and NIHB have already delisted meperidine from their formularies, and Ontario has restricted meperidine as a limited use benefit.
Keywords: *Meperidine policy de-adoption*

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NNTnet: A metric for evaluating relative harms and benefits
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Funding Source: None

Background: When there are competing risks and benefits associated with a therapy the relative baseline probabilities for the opposing effects are critical in determining whether benefits outweigh the risks. Even with similar baseline risks, comparing a relative benefit and a relative risk (harm) does not allow for an accurate assessment of net outcome because symmetry in relative rates (RR) does not provide a balanced effect, i.e., a RR of 2.0 for causing death does NOT balance a RR of 0.5 for preventing death. This will be illustrated with an example. Simple subtraction of NNT (number needed to treat) does not provide a valid measurement either. Using the weighted (by utility or dysutility) inverse of the respective NNT provides a novel and valid approach to risk-benefit assessment. 1/NNTnet = (1/NNTbenefit)(1.0) – (1/NNTharm)(Wt). The presentation of this paper will illustrate the application of this method using risk-benefit examples from the literature.
Keywords: *NNT; net benefit; harm; risk-benefit*

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Cost-effectiveness of directly mailed FOBT kits in a hard to reach population in colorectal cancer screening
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Objectives: To conduct a cost-effectiveness analysis comparing only mail invitations to Ontario family physicians in order to screen for colorectal cancer (CRC) with invitations plus the addition of the guaiac fecal occult blood test (FOBT) kit.
Methods: From a provincial cancer agency perspective, 1,700 patients were assigned to the invitation only group and 2,350 patients were assigned to the invitation plus kit group. Resources were stratified into fixed costs (initial set-up costs, document development, programming for ongoing maintenance),

variable or recurrent costs (costs of the kit, administrative costs, physician visits) and staff costs (call centre support personnel and business analyst). Costs were 2013 Canadian dollars.

Results: The total cost of the invitation only group was $95,781 and invitation plus kit group was $146,747. The cost per patient was $56.34 and $62.45, respectively. Physician visits accounted for the majority of the cost (49.8%and 59.6%). 39% of all kits were unused or returned, and included as wastage. The univariate sensitivity analyses showed that reducing the cost of the kit from $7.00 to $3.00 resulted in a decrease in the cost per patient ($57.11 and $50.90) and overall costs ($134,211 and $86,536). Also, 50% kit wastage showed a slight increase in total costs ($148,294 and $96,993).

Conclusions: The cost of physician visits and kits were shown to be the cost drivers. Although total and cost per patient was higher in the invitation plus kit group, higher rates of kit completion and early detection of potential CRC cases would offset the overall cost.

Keywords: *Coloncheck; resources; costs*

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Coverage with evidence development: opportunities for improving access to new technologies in the Canadian environment

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Background: In Canada as in other countries, promising new technologies can be licensed for patient use on the basis of early clinical data or surrogate outcomes. Reimbursement decision makers are challenged to provide timely access to these treatments even though levels of certainty on clinical benefit and cost-effectiveness do not meet standard health technology assessment requirements. Coverage with evidence development (CED) is a conditional interim reimbursement scheme linked to research to reduce uncertainty and subsequently allow informed final reimbursement decision. A CED program can either allow all eligible patients access during the research period or may allow use only within the research study. In Canada, CED programs have been successfully used to evaluate medical devices and surgical procedures, and there is limited experience for pharmaceuticals although detailed information is not publically available. Based on an environment scan and literature search of CED initiatives internationally, we describe criteria for potential CED use, as well as key features of design and implementation such as stakeholder involvement, clear definition of governance and funding, appropriate data collection, evaluation and final reimbursement decision rules. Possible indications in which CED may be beneficial are rare or orphan diseases which have been allowed clinical licensing conditional on final trial data. Oncology products also commonly come to market with significant uncertainty in required evidence and CED could be considered. CED may no t be suitable for all situations and challenges include difficulty and cost of implementation as well as potential difficulty in agreeing to and implementing final reimbursement decisions.

Keywords: *Coverage with evidence development; CED; reimbursement*

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