ABSTRACTS

"HEALTHCARE COST, QUALITY, AND POLICY: DRIVING STAKEHOLDER INNOVATION IN PROCESS AND PRACTICE"

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CAPT ACTP

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HEALTHCARE COST, QUALITY, AND POLICY: DRIVING STAKEHOLDERS INNOVATION IN PROCESS AND PRACTICE
November 17-19, 2013
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ORAL PRESENTATIONS
Sunday, November 17, 2013
(Note: Presenting authors are underlined)

1

Psychotropic medication use and 10-year incident fracture risk in men and women ages 50 and older in the population-based Canadian Multicentre Osteoporosis Study (CaMoS)

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Background: Previous studies suggest that serotonin reuptake inhibitors (SSRIs) and/or serotonin/norepinephrine reuptake inhibitors (SNRIs) may be associated with falls and fractures. The objective of this work was to evaluate whether SSRI/SNRI use is associated with 10-year risk for incident fracture in a population-based community cohort.

Methods: We used 10-year follow-up CaMoS cohort data to compare fracture risk between participants, >50, exposed versus unexposed to SSRIs/SNRIs. Incident fragility fractures reported in the absence of major trauma were confirmed radiographically. Time-dependent variables were created to capture current use of SSRIs or SNRIs. Multivariable Cox proportional hazard regression was used to estimate the hazard ratio (HR) for fracture, adjusting for other medications (anxiolytics, other antidepressants, glucocorticoids, bisphosphonates, calcium and vitamin D supplements), and for potential confounders (age, sex, co-morbidity, history of falls, and bone mineral density [BMD] at baseline).

Results: Among 6,645 subjects, 192 (2.9%) were using SSRIs or/and SNRIs at baseline and 583 (14.1%) used them at some time during follow-up. SSRI/SNRI users were more likely than non-users to be women and, at baseline, had more comorbidity, and higher use of anxiolytics and other antidepressants. There were 978 incident fractures (43 in the current SSRI/SNRI users) in 52,625.5 person-years. Controlling for all aforementioned covariates, current SSRI/SNRI use was associated with fragility fractures (HR: 1.67; 95% confidence interval: 1.33-2.14).

Conclusions: Current use of SSRI/SNRI was associated with an important, almost 70%, increase of risk of incident fragility fractures, even after controlling for important potential confounders.

Keywords: *Psychotropic medication; fractures; time-to-event analyses*

2

The impact of recent generic drug price policies on pharmaceutical innovation: a theoretical rationale and proposal of a method supporting innovation in areas of unmet medical need

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Background: Innovation is a critical priority for the pharmaceutical industry. However, the use of fixed cost-effectiveness (ICER) thresholds for health technology assessment (HTA) may decrease incentives to innovate and affect future treatment options. This presentation highlights, using a case study, the impact of recent generic drug price policies on pharmaceutical innovation and proposes a new consideration for the cost-effectiveness analysis (CEA).

Rationale: There is a causal relationship between HTA and the market price of a drug; in jurisdictions where

HTA agencies apply fixed ICER thresholds as important reimbursement listing criteria, the incremental cost of a new drug is expected to be proportional to its incremental benefit over the comparator. However, the comparator price is subject to market forces and may change markedly affecting the CEA (e.g. where the comparator patent expired). Since recent generic price regulations (e.g. 18% of innovative prices in Alberta) increased the price gap between drugs' generic and patented versions, it is harder to achieve a sufficient level of incremental benefits in order to offset incremental prices of new treatments.

Results: This analysis demonstrates that with recent changes in generic prices in Canada, even promising drugs will have challenges to show attractive ICERs.

Conclusion: Traditional decision-making process should be adapted to reflect these changes. In therapeutic areas with unmet medical needs, the ICER calculation of a new drug could include the comparator's patented price rather than the generic price. By identifying the relevant disease areas, decision-makers could convey the importance of investing in these areas to manufacturers.

Keywords: *Health technology assessment; pharmaceutical innovation; cost-effectiveness analysis; drug price regulations*

3

A qualitative assessment of patients' beliefs about adherence to oral anti-diabetes drug treatment

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Background: Poor adherence to oral antidiabetes drug (OAD) treatment is a barrier at achieving clinical targets in type 2 diabetes. Little is known of patients' beliefs about OAD-taking yet this information is essential to develop efficient adherence enhancing interventions.

Methods: This qualitative study aims to elicit patients' beliefs about OAD-taking. Adult members of the local diabetics association who had been taking an OAD for >3 months were solicited to participate in one of six focus groups. Discussions were facilitated using a structured guide designed to gather beliefs related to important constructs of the Theory of Planned

Behaviour (TPB): behavioural beliefs (i.e. advantages/disadvantages to take OAD as prescribed), normative beliefs (i.e. important persons who agree/disagree with their OAD-taking as prescribed) and control beliefs (i.e. facilitating factors/barriers to adherence to OAD treatment). Two coders using the TPB as the theoretical framework analysed audiotaped discussions.

Results: Forty-five adults participated in the study. The salient advantages for OAD-taking as prescribed were to avoid long-term complications and to control glycaemia. Family members were perceived as influential. To carry the OAD at all times, to have the OAD at sight and having a routine were important facilitating factors. Being away from home, not owning the disease and not having confidence in the physician's prescription were major barriers to OAD treatment adherence.

Conclusion: This study elicited several beliefs regarding the OAD-taking behaviour. Knowledge of these beliefs is important for clinicians treating patients taking OAD and is also crucial to the development and evaluation of interventions.

Keywords: *Type 2 diabetes; medication adherence; patient's beliefs; qualitative study*

4

Current management and associated cost of metastatic castration-resistant prostate cancer in Canada

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Funding Source: None

Introduction: Prostate cancer (PCa) is the most common cancer and the 3rd leading cause of cancer mortality in Canadian men. Men dying of PCa do so after failing castration. The management of the metastatic castration-resistant prostate cancer (mCRPC) is complex and the associated drug treatments are costly.

Objectives: The objective of this study was to estimate the cost of drug treatments over the mCRPC period, in the context of the latest evidence-based approach.

Methods: Two Markov models with Monte-Carlo microsimulations were developed in order to simulate

the management of the disease and to estimate the cost of drug treatments in mCRPC, as per Quebec's public healthcare system, and the latest drug developments. The drug exposure and survival were based on clinical trial results and clinical practice guidelines found in literature review.

Results: The mean cost of mCRPC drug treatments over an average period of 27.5 months was estimated at $49,488 per patient. Over the mCRPC period, the luteinizing hormone releasing hormone agonists (LHRHa) prescribed to maintain castrate testosterone accounted for 20.6% of the total medication cost, whereas denosumab prescribed to decrease bone-related events accounted for 32.6%, respectively. When patients receive cabazitaxel in sequence after abiraterone and docetaxel, the mCRPC medications cost per patient per month increases by 67%.

Conclusion: Our study estimates the direct drug costs associated with mCRPC treatments in the Canadian health system. The total cost of medications for the treatment of each annual cohort of 4,100 mCRPC patients was estimated at $ 202.9 million.

Keywords: *Cost of metastatic castration-resistant prostate cancer, new treatments for advanced prostate cancer, management of advanced prostate cancer*

ORAL PRESENTATIONS
Monday, November 18, 2013

5

Glucocorticoid-induced osteoporosis management among seniors

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Funding Source: None

Background: Osteoporosis is a major public health concern that results in considerable fracture-related morbidity and shortened survival. Glucocorticoid (GC) therapy is the most common cause of secondary osteoporosis. Since 1996, Canadian practice guidelines have recommended that all patients starting chronic oral GC therapy ($\geq$ 3 months) receive bone mineral density (BMD) testing and/or osteoporosis pharmacotherapy. We sought to examine trends in GC-induced osteoporosis management over time.

Methods: We identified all chronic oral GC users ($\geq$ 2 oral GC dispensed and $\geq$450 mg prednisone equivalent over a 6-month period) aged 66 or more years in Ontario using healthcare utilization data, 1997-2011. Osteoporosis management (BMD test and/or osteoporosis pharmacotherapy) within 6 months of starting chronic oral GC therapy was examined by sex and year. Results were summarized using descriptive statistics.

Results: We identified 75,621 male (mean age=74.7, SD=6.2) and 97,966 female (mean age=75.2, SD=6.5) patients on chronic oral GC therapy between 1997 and 2011. Over eighty percent had exposure $\geq$675 mg in the 6-month window used to define chronic GC exposure. GC-induced osteoporosis management increased steadily from 7% (men) and 20% (women) in 1997, to a high of 21% (men) and 46% (women) in 2007, with little change from 2007 through to 2011.

Conclusions: Rates of GC-induced osteoporosis management improved significantly over time in both sexes yet remain low, particularly among men. This represents a missed opportunity for fracture prevention among patients requiring prolonged GC therapy.

Keywords: *Glucocorticoids; osteoporosis; management*

6

Time series methods applied in drug utilization research: a systematic review

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Background: Interrupted time series analysis is a quasi-experimental approach often used to estimate the effects of healthcare interventions. We sought to examine the use of time series methods in drug utilization research.

Methods: We completed a systematic search of MEDLINE to identify English-language articles that employed time series methods in drug utilization research. Studies that examined the impact of government/media advisories, new guidelines, or formulary changes on drug utilization were eligible. We tabulated the number of publications by year and summarized methods used in empirical applications. Descriptive statistics were used to report findings.

Results: Of 1454 articles identified, 72 studies were eligible: 3 methodological contributions and 69 empirical applications. Few (7%, n=5) empirical applications were published before 2000. Most empirical applications assessed formulary changes (59%, n=41), 32% examined government/media

advisories, and 9% examined guideline changes. Of the 66 articles reporting statistical methods, segmented regression (59%), autoregressive integrated moving average (ARIMA) models (21%), and linear regression (17%) were most commonly applied. Testing for autocorrelation was reported in 81% (n=56) of all studies, 41% reported accounting for seasonality, and 15% tested for stationarity. Few studies reported forecasting (36%, n=25) or used a comparison group (30%, n=21).

Conclusion: Most time series analyses in drug utilization research used segmented regression or ARIMA models. While it is recommended that analyses account for autocorrelation, seasonality, and stationarity, few studies report these considerations. As the application of time series analysis increases, it is important to develop standards of practice to properly assess intervention impacts on drug utilization.

Keywords: *Time series analysis; systematic review; drug utilization*

7

Methods for survival extrapolation within cost-effectiveness analyses that address concerns raised in pCODR reviews

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Introduction: The pan-Canadian Oncology Drug Review (pCODR) provides provinces and territories with recommendations on reimbursement for cancer drugs. A commonly concern noted in pCODR reviews is the assumption of treatment benefit on overall survival (OS) after progression (treatment discontinuation). To address this concern, reanalyses by the pCODR of the cost-effectiveness of submitted drugs often involves reducing the time horizon to reduce post-progression survival benefit of the study drug and/or directly limiting post-progression survival benefit of the study drug. This reflects a recurring preference in the Economic Guidance Reports for survival to be separately modeled pre- and post-progression. Our research summarizes the pCODR reviews that address this issue and illustrate the implication of extrapolation methods for OS using a generic oncology model. Methods for the modeling of OS using regression analysis as well as pre- and post-progression hazards ratios are illustrated. Overall, extrapolation of control group and study drug survival curves independently can lead to scenarios where OS is more favorable than would be expected from a trial.

Use of a shortened time horizon may be too conservative as it negates any long-term benefit of increased survival within the trial. Use of a constant hazard that can be varied pre- and post-progression provides a flexible option that address the concerns we noted in the pCODR reviews and should be considered in models submitted to pCODR.

Keywords: *pCODR; oncology; cost-effectiveness*

8

Use of product listing agreements by Canadian provincial drug benefit plans

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Background: Product Listing Agreements negotiated between drug manufacturers and health care insurers are increasingly common worldwide but not without drawbacks. Our objective was to document PLA use in Canadian provinces.

Methods: From all ten provinces, we obtained drug-specific data on funding status and PLA use for 25 drugs recently reviewed by the CDR and funded by at least one province as of May 2012. We tested for correlations between coverage and PLA use, and between CDR recommendations and PLA use.

Results: The number of drugs from our sample funded by each province ranged from three in PEI to 21 in Ontario. PLA use ranged from zero Quebec, PEI, and Newfoundland and Labrador to 20 in Ontario. Including Ontario, the correlation between the number of drugs funded by each province and the number of drugs with PLAs in use by each province was statistically significant (r = 0.57, p = 0.04); excluding Ontario, the correlation was not significant (r = 0.10, p = 0.40). At the product level, there was a stronger correlation between the number of provinces funding a drug and the number using PLAs among the subset of drugs with negative CDR recommendations (r=0.87, p<0.01) versus those with positive recommendations (r=0.52, p=0.03).

Conclusions: There is wide interprovincial variation in PLA use and evidence that PLAs may be used to fund drugs that are not otherwise cost-effective at list prices. If global pricing strategies are making PLAs necessary, governments should collaborate to improve equity, transparency, and effectiveness of across provinces.

Keywords: *Pharmaceutical policy; product listing agreements; Canada; provinces; survey*

ORAL PRESENTATIONS
Tuesday, November 19, 2013

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Development and validation of severity criteria for drug-related problems in chronic kidney disease patients

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Background: Chronic kidney disease (CKD) patients are reported to have a mean of 3.5 drug-related problems (DRPs) per patient. However, the information about DRPs severity remains scarce.
Objective: To develop and evaluate the psychometric properties of a set of criteria for the evaluation of DRPs' severity in CKD patients from a community pharmacy perspective.
Methods: A team of clinicians and researchers developed an initial list of criteria based on the type of interventions required to manage DRPs in community pharmacy. Thereafter, ten community pharmacists were consulted individually to complete and fully adapt the criteria to community pharmacy practice. Finally, a group of 12 experts rated in parallel the appropriateness of each criteria. Criteria with uncertain appropriateness were discussed and their final status was defined by consensus.
Results: Three levels of severity (mild, moderate and severe) were defined and each level was further categorized in two sub-levels. At each level, specific pharmaceutical interventions required to manage DRPs were listed. These include patient's education, information transmission to health-care providers, writing of a pharmaceutical opinion, specific patient's monitoring and follow-up, and patient's referral to their physician or to the emergency department.
Conclusion: The criteria are the results of a collaborative work involving community pharmacists as well as CKD experts. It is unique and specific to actual clinical practices in community pharmacy. Their reliability, validity and responsiveness are currently under evaluation. If satisfactory, these criteria will constitute a new tool for pharmacy practice research.
Keywords: *Severity; drug related problems; community pharmacy*

10

Population-level costs and resource utilization of homecare for persons with Alzheimer's disease

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Background: The aging population in Ontario is accompanied by an increased incidence and prevalence of Alzheimer's disease (AD). Given this trend, the use of publicly-funded homecare services among persons with AD is rising. This requires an appropriate allocation of resources; however, detailed information on the use and relative costs of homecare for AD is limited.
Methods: The AD cohort was defined through the Ontario Drug Benefit Program as persons aged 65 years and older who were prescribed 1 of 3 cholinesterase inhibitors (i.e., galantamine, rivastigmine, or donepezil) between January 1st, 2004 and December 31st, 2006. Homecare utilization by this population was measured up to August 31st, 2011. Costs were obtained in 2009 dollars from Community Care Access Centres.
Results: A cohort of 78,410 individuals with AD were identified, 66.1% of which accessed publicly-funded homecare services during January 1, 2004 - August 31, 2011. For the 51,804 individuals who used homecare, a total of 10,089,721 services were delivered at a cumulative cost of $646,221,833 over the entire accrual period. The mean cost per individual over the entire time period was $12,474. Homemaking/personal support (8,534,973 claims; $336,961,323) were the most commonly reported homecare activities, followed by nursing (740,511 claims; $201,364,434) and case management (323,010 claims; $67,653,085).
Conclusions: The reported values are descriptive; a comparison with an age and resource utilization-matched control cohort is in progress. This will yield a cost attributable to the AD cohort defined here, segmented by phase of care.
Keywords: *Population-based cohort study, homecare, cost, utilization, Alzheimer's disease*

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Appraisal of non-inferiority margins in assessing study quality: new oral anticoagulants as an example

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Background: Dabigatran, rivaraoxaban, and apixaban are new oral anticoagulants (NOAC) used for stroke prevention. Approval of each NOAC for patients with atrial fibrillation (AF) was based on a single non-inferiority trial versus warfarin. To assess the quality of the NOAC AF trials, we critically appraised the non-inferiority margins (NIM) used in these trials.

Methods: The NOAC trials were identified using a systematic literature review. The NIM were evaluated using the CONSORT statement for NI trial reporting.

Results: Three NI trials were identified; one for each NOAC. We discovered four major limitations to the NIM. First, the population in the meta-analysis upon which the NIM were based was stratified by stroke history, whereas the NIM in the NOAC trials used an un-stratified population. Second, the NIM was based on outdated clinical data, and a more current estimate of stroke risk would have produced a smaller NIM than that in the NOAC trials. Third, the outcome evaluated in the meta-analysis was stroke, while the primary outcome in the NOAC trials was a composite of stroke and systemic embolism. Finally, the average risk reduction (ARR) used in the NIM was a miscalculation, and use of the correct ARR value would have resulted in a smaller NIM. These four flaws yielded a wider than expected NIM and a bias in favour of demonstrating NI. This compromises the quality of the NOAC trials.

Conclusion: Our findings illustrate that critical appraisal of clinical and methodological criteria used to derive NIM in important when assessing study quality.

Keywords: *Non-inferiority trials; new oral anticoagulants; CONSORT*

12

Safety and effectiveness of dabigatran versus warfarin in economic evaluations: a systematic review

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Funding Source: Academic Health Sciences Organization AFP Innovation Fund grant

Background: Atrial Fibrillation (AF) is an arrhythmia associated with an increased risk of stroke and mortality. It is traditionally managed with warfarin, which requires regular blood test monitoring. Dabigatran, a new oral anticoagulant, is increasingly used for AF instead of warfarin. Whether its comparative efficacy and safety is sufficient to offset the increased drug cost is controversial.

Methods: A systematic review was conducted of economic evaluations published to April 2013 evaluating the cost-effectiveness of dabigatran versus warfarin for stroke prevention in AF. Databases searched included Ovid MEDLINE, EMBASE, the Cochrane Library and PubMed as well as grey literature. A qualitative synthesis was completed examining study design, country of origin, setting, data sources, cost effectiveness results (i.e. incremental cost effectiveness ratios (ICER),safety parameters (i.e. hemorrhage) and effectiveness (monitoring) influencing the cost-effectiveness of dabigatran compared with warfarin.

Results: Twenty economic evaluations from 11 countries were identified comparing dabigatran and warfarin. ICERs for dabigatran versus warfarin ranged from \$1,294 (2013 CAD) (€970) to \$252,282 (2013 CAD) (244,121 USD) per QALY. Key assumptions in the models varied, including warfarin monitoring frequency and costs, quality of INR control, costs of treating dabigatran-related hemorrhages without an antidote, and incorporation of baseline risk in relative rates of adverse events.

Conclusions: The cost-effectiveness of dabigatran versus warfarin varied widely due to differing assumptions in the models. Economic evaluations from other jurisdictions may not always directly apply to the Canadian health care setting. Variations in care patterns and other factors need to be considered when making policy decisions.

Keywords: *Dabigatran; systematic review; economic evaluation*

13

Comparative gastrointestinal safety of bisphosphonates: a network meta-analysis

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Background: Bisphosphonates are first-line treatment for osteoporosis. Gastrointestinal (GI) adverse events (AE) are cited as a primary reason for non-adherence.
Objective: To use published clinical trial data to assess the comparative GI safety of bisphosphonates.
Methods: We completed a systematic review of all trials that assessed bisphosphonate safety and/or efficacy in primary osteoporosis. Randomized, blinded, and controlled studies were eligible. The primary outcome was any GI-related AE. Subanalyses were completed for upper GI, serious GI, nausea, esophageal-related events, and discontinuation due to AE. A Bayesian based network meta-analysis was completed using WINBUGS and GeMTC for indirect comparisons.
Results: We identified 51 studies eligible for analysis. Zoledronic acid had the highest probability (91%) of causing the greatest number of any GI AE and greatest incidence of nausea (70%). Etidronate (70%) and zoledronic acid (28%) had the highest probability of the greatest attrition due to AE. Only risedronate and alendronate had data on both serious GI and esophageal related AE with no significant difference between drugs or compared to placebo.
Conclusion: Zoledronic acid had the highest probability of having the greatest number of GI AE. Our results question the assumption that annual zoledronic acid will translate into better adherence long-term. More research into real-world comparative safety of bisphosphonates is needed.
Keywords: *Safety; bisphosphonates; network meta-analysis*

14

Cost effectiveness of a systematic guidelines-based approach to the prevention and management of vascular disease in a primary care setting

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Background: The Comprehensive Vascular Disease Prevention and Management Initiative (CVDPMI) is a program that applies a systematic, guidelines-based approach to the prevention and management of vascular disease. This study examined the cost effectiveness of the CVDPMI compared to no program.
Methods: Framingham risk scores (FRS) were used to calculate the estimated life expectancy (LE) for each patient. An incremental cost per life year gained ratio was determined by dividing the difference in discounted mean costs by the difference in discounted life expectancy between the CVDPMI program and no program. A one-way sensitivity analysis and probabilistic sensitivity analysis using a non-parametric bootstrap method was conducted. The perspective for this analysis was the Ontario Ministry of Health. A 5.0% discounting rate was applied to both costs and health outcomes. For each patient, the cost of an event (myocardial infarction, stroke) was multiplied by the number of events per patient per year and averaged across each patient cohort.
Results: In the base case analysis, the cost per life year gained (LYG) ratio was $13,250. Given a maximum acceptable ceiling ratio of $50,000/LYG, the probability that CVDPMI is cost effective compared to no program is 65%. The results of a one-way sensitivity analysis demonstrated that the ratio was most sensitive to the cost of the CVDPMI. Cost effectiveness in Framingham risk subgroups was $6,519/LYG for high risk and $9,409/LYG for moderate risk patients.
Conclusions: CVDPMI is a cost effective approach to the prevention and management of coronary heart disease when compared to no program.
Keywords: *Primary care; cardiovascular disease; cost effectiveness*

15

Hospitalization for hemorrhage among warfarin recipients prescribed amiodarone

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Introduction: Amiodarone inhibits the hepatic metabolism of warfarin, potentiating its anticoagulant effect. However, the clinical consequences of this are not well established. Our objective in this study was to characterize the hospitalization risk for a hemorrhage associated with the initiation of amiodarone within a cohort of continuous warfarin users in Ontario. We conducted a population-based retrospective cohort study among residents aged 66 years or older receiving warfarin. Among patients with at least 6 months of continuous warfarin therapy, we identified those who were newly prescribed amiodarone and an equal number who were not, matching on age, sex, year of cohort entry and a high-dimensional propensity score. The primary outcome was hospitalization for hemorrhage within 30 days of amiodarone initiation. Between July 1, 1994 and March 31, 2009, we identified 60,497 patients with at least 6 months of continuous warfarin therapy, of whom 11,665 (19%) commenced amiodarone. For 7,124 (61%) of these, we identified a matched control subject who did not receive amiodarone. Overall, 56 (0.8%) amiodarone recipients and 23 (0.3%) control patients were hospitalized for hemorrhage within 30 days of initiating amiodarone (adjusted hazard ratio 2.45; 95% confidence interval, 1.49 to 4.02). In total, 7 of 56 (12.5%) patients hospitalized for a hemorrhage after starting amiodarone died in hospital. In conclusion, initiation of amiodarone among older patients receiving warfarin is associated with a more than twofold increase in the risk of hospitalization for hemorrhage, with a relatively high fatality rate. Physicians should closely monitor patients who initiate amiodarone while receiving warfarin.
Keywords: *Warfarin; amiodarone; drug interaction*

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Creation of a reference set of the health preference values in oncology: a pilot study using an electronic data collection system

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Background: Individuals at cancer centres across Ontario are answering questions related to patient reported outcomes using an Interactive Symptom Assessment and Collection (ISAAC) kiosk.
Objectives: To determine whether the existing ISAAC infrastructure would allow for the collection of health preference values (and ultimately establish a reference set of health preference values in oncology). And to determine the proportion of individuals who complete the health preference questionnaire from those who are approached to participate.
Methods: Adult oncology patients were recruited from the Odette Cancer Centre (Toronto, Canada). Individuals who completed an ISAAC assessment were approached to also complete the EuroQuol-5 Dimensions (EQ-5D) on an iPad.
Results: 229 individuals were approached to participate in the study and 155 (67.7%) consented to participate. Of the consented cohort, 139 (89.7%) completed the EQ-5D. The majority were female (71.4%) and the mean age was 60.0 ± 13.2 years. The most common diagnosis was breast cancer (35.6%), followed by other cancer (23.3%) and then head/neck cancer (8.2%). The mean EQ-5D score was 0.80 ± 0.19 indicating a high-level health preference (with 1 equating as perfect health). **Conclusions:** The existing ISAAC infrastructure is amenable to collecting health preference data in an adult oncology population and more than two thirds of individuals consented to participate when approached. Collection of health preference values will allow for linkages to patient reported outcome data as well as the generation of an oncology population health preference database.
Keywords: *Quality of life; cancer; technology*

POSTER PRESENTATIONS
Sunday, November 17, 2013

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Systematic review of cost-of-illness studies in chronic ulcer population

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Introduction: In Canada, chronic ulcer prevalence rates range from 2.5% for diabetic foot ulcer (DFU) and leg ulcer (LU) in the acute setting to 30% for pressure ulcer (PU) in long-term care settings. Chronic ulcers can also prolong hospital stays. As a result, the economic burden of chronic ulcers is substantial. A literature review of chronic ulcer cost of illness studies was conducted to review the costing methods used and present the costs reported.

Methods: Medline, EMbase and CINAHL were searched for chronic ulcer cost of illness studies from January 2000 to February 2013. Cost and chronic ulcer search term algorithms were based on literature. Economic evaluations and intervention costing studies were excluded. A critical evaluation of study methods was conducted. Total, mean and median cost per chronic ulcer case was adjusted to 2012 Canadian dollar.

Results: 31 articles out of the 1427 identified were included for synthesis. 27 studies used the acute care hospital perspective; 27 followed a cohort of individuals with chronic ulcer; 4 modelled costs. Most studies (n=20) were non-comparative. Four studies included indirect costs. Mean cost range from $3,700 for LU to $31,200 for PU. Total costs per year were estimated to be as high as $1.5 million for DFU in Sweden, $33 million for LU in Italy and $4.2 billion for PU in the state of New York.

Conclusions: Chronic ulcers represent a substantial economic burden.

Keywords: *Diabetic foot ulcer; decubitus ulcer; costs*

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The health care resource utilization of recently spinal cord injured: preliminary results

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Background: Spinal cord injury (SCI) is a severely debilitating event that requires substantial health care resources. A study of direct health care costs of traumatic spinal cord injury in Alberta resulted in up to $121,600 in the first year after injury and $5,400 in the years after (Dryden2005). What remains uncertain is how these costs and health care utilizations patterns differ in an Ontario population. The primary aim of this study is to characterize the use of provincially funded health care services and identify the costs in the SCI population in Ontario over a 6-year timeframe.

Methods: An incident cohort was collected of individuals hospitalized for traumatic spinal cord injury between April 1, 2005 and March 31, 2010 and followed up until March 31, 2012 or death. Health care resource utilization during this period was collected from several health care settings. Data that will be collected include resource utilization information, costing information as well as patient demographic variables. Resource utilization will be reported using summary statistics. Costs will be calculated for this cohort and matched with a non-SCI cohort.

Results: Data extraction is currently ongoing and as a result only preliminary health care utilization data will be presented. The primary investigator hopes to present a summary of the health care resources consumed by SCI individuals and utilization patterns over time.

Conclusions: To be determined.

Keywords: *Spinal cord injury; costs; health care resources*

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Implementation and evaluation of pharmacy services through a practice-based research network (PBRN)

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Background: In recent years, pharmacists are more engaged in health education and disease prevention and assume a more active role in the management of chronic diseases. Research is essential to evaluate the relevance and impact of these new practices. The participation of primary-care pharmacists in such investigations is essential but has proven to be challenging. A common network for pharmacists, researchers and decision makers engaged in pharmacy-practice research could facilitate pharmacist's involvement in research. The objective of this study is to develop a PBRN and evaluate the feasibility of conducting pharmacy-practice research through this network.

Methods: The research team, supported by an advisory committee, will develop the PBRN. The research team will meet members of the advisory committee at least twice a year for two years to orient and facilitate the development and conduct of each component of the network.

Results: The PBRN will include five components: A web-based training program in pharmacy-practice research; A discussion forum where pharmacists, researchers and decision makers may exchange; A listserv, a bulletin board and a library to receive/post communications about research projects and share clinical tools; A quality improvement program to assess and improve pharmaceutical care related to anticoagulant therapy monitoring by community pharmacists (first demonstration project); and An economic evaluation program of enhanced medication-related services and expanded patient care services (second demonstration project).

Conclusions: This is a simple and innovative concept for primary-care pharmacists in Quebec who attempt to enable the development, evaluation and implementation of innovative pharmacy practice.

Keywords: *Network; community pharmacy; pilot project*

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Consistencies in cancer therapy reimbursement recommendations made in Canada, Australia, Sweden, and United Kingdom

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Background: Our aim was to compare recommendations made by the pan-Canadian Oncology Drug Review (pCODR) since its launch to other health technology assessment (HTA) agencies.

Methods: Publicly accessible recommendations were reviewed: Canada (pCODR, www.pcodr.ca), Australia (Pharmaceutical Benefits Advisory Committee (PBAC), www.pbs.gov.au), Sweden (Dental and Pharmaceutical Benefits Agency (TLV), www.tlv.se) and UK (National Institute for Health and Care Excellence (NICE), www.nice.org.uk).

Results: pCODR had six product reviews in common with PBAC, three with TLV, and nine with NICE. Overall, pCODR unlike the other agencies, was most likely to provide a positive recommendation, albeit, conditional on improvement of cost-effectiveness ratios. In general, negative recommendations made by pCODR based on clinical concerns were often mirrored by the other HTA agencies. Similarly, findings by pCODR of positive clinical benefit but with concerns over cost-effectiveness were often reciprocated by the other agencies in conditional positive recommendations or by negative recommendations due to cost-effectiveness.

Conclusions: The recommendations by pCODR, PBAC, TLV and NICE reflected significant agreement regarding overall clinical and economic benefit. Although discordance in recommendations between agencies was noted, these likely reflected process and funding differences rather than a difference in the perceived product value. pCODR differs from other agencies in its clear distinction between evidence review and funding negotiations. As such, pCODR can positively recommend a product with acceptable clinical value conditional on improved cost-effectiveness without specifying the degree of price reduction needed or negotiating such discounts. This creates an environment that favours early global launch in Canada without delays for price negotiation.

Keywords: *Pan-Canadian oncology drug review; oncology reimbursement decisions; health technology assessment*

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Cost-sharing for health care services: an examination of pharmaceutical reimbursement policies in Ontario

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Funding Source: None

Background: In most provinces in Canada many health services outside of the Canada Health Act have some element of cost-sharing, co-payments or service limits. These policies can have significant impacts on patients and their families related to both chronic and acute illnesses. Previous published research has shown significant financial burdens for homecare, devices and pharmaceuticals in diseases like cancer. One of the policy questions that arise as a consequence of these burdens is: Can we restructure, or redistribute government funding in a way that minimizes these burdens to the most vulnerable populations? (typically those under 65 and in the lower income quartile).
Methods: An examination of the current Ontario policies related to pharmaceutical reimbursement was undertaken, with the intent of formulating alternate policies that might better address patient level burden, most specifically in the vulnerable populations.
Results: Current policies result in significant costs for patients and their families related to either high co-pays for non-reimbursed pharmaceuticals, or full payment when insurance both public and private is not available. This evaluation presents alternate policies including first-dollar coverage based on modified means testing as an alternate strategy. Cost neutrality is obtained via offsets through higher co-payments in other populations to ensure no increase to existing funding envelopes.
Conclusions: Alternate funding models may help re-distribute funding to the most vulnerable populations and thereby minimize the additional suffering a financial burden adds to a disease treatment.
Keywords: *Reimbursement; policy;drugs*

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Economic evaluation of collagenase Clostridium histolyticum injection for the treatment of Dupuytren's contracture in Canada

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Background: Dupuytren's contracture (DC) is characterized by formation of alternative to limited fasciectomy (LF) surgery, the current mainstay treatment in Canada.
Methods: CCH (up to 3 injections per joint) and LF were compared in a cost-minimization analysis from Canadian public healthcare payer and societal perspectives in patients with up to three contracted metacarpophalangeal (20°–100°) or proximal interphalangeal (20°–80°) joints. Using a Markov model with a 5-year horizon, CCH effectiveness (contracture reduction to $\leq 5°$) was modeled by number of injections based on two phase III trials and recurrence was modeled using 3-year follow-up data. LF effectiveness and recurrence were assumed equivalent to CCH after up to three injections. Costs included were direct treatment costs, costs of complications and workdays lost (societal perspective). Sensitivity analyses varied, among other parameters, type and frequency of second-line treatment, definition of treatment success, and unit costs.
Results: Total direct costs were estimated at $1,212 per CCH injection and $3,122 to $3,264 (depending on perspective) per LF; respective indirect costs were $170 and $2,557. Over the 5-year horizon, CCH saved, depending on patient population (1 vs up to 3 joints), $3,333 to $3,426 per patient from the societal and, $588 to $1,022 from the public healthcare payer perspective. CCH remained cost-saving in all but one sensitivity analysis.
Conclusion: CCH is a cost-saving alternative to surgery in patients with DC.
Keywords: *Dupuytren's contracture; cost-minimization; collagenase Clostridium histolyticum; limited fasciectomy*

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The impact of ProFiL program on the progression of chronic kidney disease (CKD) and its risk factors: an interim analysis

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Background: A clinical trial is ongoing to evaluate ProFiL, a training-and-communication network program in nephrology for community pharmacists. The objective of this analysis is to evaluate the relevance of increasing its sample size to evaluate the impact of ProFiL on the progression of CKD (glomerular filtration rate (GFR)) and CKD risk factors.
Methods: In a one year multicentric, open, cluster-randomized controlled trial, moderate to severe CKD patients from two predialysis clinics and their community pharmacy were assigned to ProFiL or the usual care group (UC). Clinical variables were collected at baseline and after one year.
Results: 82 community pharmacists and 168 patients have completed the study. Greater reduction in systolic blood pressure was observed among ProFiL patients (-9.8 mmHg; 95%CI: -15.8; -3.7). The change in GFR and other risk factors were similar in ProfiL and UC groups (GFR: -2.8 mL/min/1.73m2 (95%CI: -6.0 to 0.4); LDL-cholesterol: 0.0 mmol/L (-0.2 to 0.2); and hemoglobin A1C (-0.2% (-0.6% to 0.1%)). Among patients with diabetes (n=100), an adjusted incremental reduction in A1C was observed in the ProFiL group (-0.4% (-0.9% to -0.1%)). A total, of 162 diabetic patients would be required to detect a significant difference with 80% power. No between-group difference in the change in LDL-cholesterol was observed among dyslipidemia patients.
Conclusion: A total of 454 patients, including 253 diabetic patients, have been recruited in the trial. The study will have sufficient statistical power to detect a beneficial effect of ProFiL on the management of hypertension and glycaemia among diabetic patients.
Keywords: *Chronic kidney disease; training program; risk factors*

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The impact of ProFiL program on the community pharmacists' knowledge and competencies and the quality of pharmacotherapy of their chronic kidney disease (CKD) patients: an interim analysis

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Background: Evaluate the impact of ProFiL, a training-and-communication network program in nephrology, on pharmacists' knowledge and clinical competencies, clinical practices and the quality of medication use of their CKD patients.
Methods: Patients in predialysis clinics of two hospitals and their community pharmacies were randomized to ProFiL or usual care (UC) group. Pharmacists' knowledge and competencies were assessed at baseline and after one year. The quality of pharmacotherapy and clinical practices were evaluated during the year before and after patient's recruitment using the PAIR criteria.
Results: An incremental improvement in the knowledge (5.6% (95%CI: 0.08% to 11.1%)), clinical competencies (10.8% (95%CI: 5.5% to 16.1%)) and global (9.0% (95%CI: 3.4% to 14.4%)) scores were observed among ProFiL pharmacists (n=55) as compared to the UC pharmacists (n=27). After a year, the mean number of drug-related problems (DRPs) per patient went from 3.2 to 1.7 DRPs/patient in the ProFiL group (n=117) compared to 2.6 to 2.1 DRPs/patient in UC patients (n=51), with an incremental overall reduction of 1.1 DRPs/patient (95%CI:0.4 to 1.8) in the ProFiL group; particularly for DRPs related to dosage adjustment in CKD (0.3 DRP/patient (95% CI: 0.02 to 0.5)) and non-optimal adherence to medication (0.5 DRP/patient (95% CI: 0.2 to 0.9)). More opinions and refusals were written for ProFiL patients (0.4 versus 0.1 opinion/patient).
Conclusion: ProFiL improves the long-term knowledge and clinical competency of community

pharmacists as well as their clinical practices and the quality of pharmacotherapy of their patients.

Keywords: *Chronic kidney disease; training program; knowledge and competency*

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AGIR: A self-management program for osteoarthritis patients and primary care clinicians supported by A Group of Interdisciplinary Regional team of clinicians

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Funding Source: IRSC

Context: Multimodal treatment of osteoarthritis by a multidisciplinary team of clinicians is recommended. A primary care program, supported by a regional team of clinicians, targeting patients and clinicians, was developed. A pilot study is on-going to assess the feasibility of conducting a large randomized controlled trial.

Objectives: Describe the characteristics of participating patients and clinicians, and the knowledge, attitudes and beliefs (KAB) of clinicians.

Method: A total of 20 physicians and 15 nurses working in 7 groups of family medicine (GFM), 35 community pharmacists, 12 physiotherapists from the private sectors, and 132 osteoarthritis patients with moderate to severe pain since at least six months were recruited. Patient's characteristics were measured by a self-administered questionnaire and a phone interview. KAB of clinicians were measured using the Know-Pain 50.

Results: Recruitment was completed within five months. Participation rates of patients and clinicians were equal to 88 % and 59 %, respectively. Most patients were women (77 %). Their mean age was 67 years (SD: 10; range: 41–88). They had pain since 11.3 years on the average (SD: 10.6) and reported a mean pain intensity score of 6.3 (SD: 1.9) in the past week. The mean score of depression and anxiety was 5.6 (SD: 3.7) and 8.0 (SD: 4.0) respectively. The mean KAB score of clinicians was equal to 61% (SD: 8%; range: 43-79%).

Conclusion: Considering the characteristics of patients and the level of KAB of clinicians, there is a need for AGIR Program in primary care.

Keywords: *Osteoarthritis; primary care; education*

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Socio-economic status and non-adherence to anti-hypertensive medications: a systematic review and meta-analysis

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Context: Conventional wisdom suggests low socio-economic status (SES) is a robust predictor of medication non-adherence.

Objective: To describe and quantify the association between SES and non-adherence to anti-hypertensive (AHT) medications.

Data Sources: Medline, Embase, International Pharmaceutical Abstracts, the Cochrane Library, Scopus, PsycINFO, Sociological Abstracts, ProQuest Dissertations & Theses, Web of Science, and OAIster were searched from inception date to February 2012.

Study Selection: Studies examining non-adherence to AHT medications measured by electronic prescription databases where explanatory factors were examined.

Data extraction and synthesis: Two authors recorded the use of SES measures (i.e., any material or social variable) and their influence on the occurrence of AHT non-adherence.

Results: Fifty-six studies with 4,780,293 subjects were included. Overall, 32 studies (57%) reported an SES

measure, and of them, only 7 (13%) identified more than one SES measure. Income or income-related measures (such as prescription-drug benefits or co-payments) were used in most studies (27/32, 84%). Meta-analysis of the influence of SES could be quantified in 40 cohorts reported in 30 studies. Over all, the pooled adjusted risk estimate for non-adherence according to SES (high versus low) was 0.89, 95% CI 0.87 to 0.92; I2=95%, p<0.001. Similar patterns were observed in all subgroups examined.

Conclusion: Published studies do not support a substantial association between low SES and non-adherence to AHT medications. However, important limitations in the assessment of SES can be identified in virtually all studies. Future studies are required to ascertain if a stronger association is observed when SES if determined by comprehensive measures.

Keywords: *Hypertension; antihypertensive drugs; quality of care and outcomes; public health*

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Antimalarial drug use during pregnancy and the risk of low birth weight (LBW): a systematic review

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Background: Untreated malaria increases the risk of low birth weight (LBW) during pregnancy but little is known on whether antimalarial use is associated with an increased risk of LBW.

Objective: This review aims to investigate the risk of LBW associated with antimalarial use during gestation.

Methods: We systematically searched PubMed, Embase, the Cochrane Infectious Group, and the reference lists of all relevant articles published in English or French from 1966 through 2012 for studies that reported associations between LBW and gestational exposure to antimalarials. Only comparative studies such as clinical trials and cohort studies were considered.

Results: Among the 39 studies that met inclusion criteria, 30 (77%) were randomized and non-randomized clinical trials and 9 (23%) were prospective and retrospective cohort studies. When compared to placebo, sulfadoxine combined with pyrimethamine use during pregnancy was shown to

significantly decrease the risk of LBW (RR = 0.26; 95% CI =0.14-0.47; RR = 0.35; 95% CI =0.22-0.56; RR = 0.35; 95% CI =0.2-0.59 RR = 0.5; 95% CI =0.27-0.94; 4 studies). When compared to no exposure, quinine (RR= 1,4 ; 95% CI = 1,1–1,9; 1 study), and mefloquine (RR= 1,7 ; 95% CI = 1,1 –1,8; 1 study) significantly increase the risk of LBW. chloroquine significantly increases the risk of LBW (RR = 5.39; 95% CI =1.22-23.85; RR = 2.79; 95% CI =1.32-5.96; RR = 1.4; 95% CI =1.03-1.9 ; 3 studies)

Conclusions: Although many antimalarial use during pregnancy increase the risk of LBW, indication bias could not be ruled out.

Keywords: *Safety; antimalarials; pregnancy*

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Validation of the telephone-administered Age and Stage Questionnaire and the Revised Pre-screening Denver Questionnaire: results from the OTIS

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Introduction: The Ages and Stages Questionnaire (ASQ) and Revised Pre-screening Denver Questionnaire (R-PDQ) assess children development. However, their telephone administration has not yet been done. The OTIS Antidepressants in Pregnancy Study cohort was used. Women were recruited through

nine North American Teratogen Information Services and at the CHU Ste-Justine outpatient obstetrical clinic (Montreal). To be included, women had to be >18 years old, <15 weeks pregnant, and not using known teratogens. Both questionnaires were self and telephone-administered to mothers at 12-months postpartum. The ASQ includes five domains (communication, gross motor, fine motor, problem-solving and personal-social). The R-PDQ tests gross and fine motor, personal-social and language skills. Socio-demographic variables were collected through telephone interviews. Concordance between the telephone and self-administration of both questionnaires were assessed with Intraclass Correlation Coefficients (ICC) with 95% Confidence Intervals (CI). Overall, 61 and 56 women filled the ASQ and R-PDQ, respectively. Concordance between the self and telephone-administered ASQ was substantial for the communication scale (ICC=0.76;95%CI (0.63;0.84)), almost perfect for the gross motor scale (ICC=0.83;95%CI (0.73;0.90), and moderate for the fine motor, problem-solving and personal-social scales (ICC=0.44;95%CI (0.21;0.62); ICC=0.43;95%CI (0.19;0.61); ICC=0.52;95%CI (0.31;0.68); respectively).Regarding the R-PDQ, the following concordance estimates were found: gross motor scale (ICC= 0.90;95%CI (0.83;0.94)), language (ICC=0.58;95%CI (0.38;0.72), personal-social scales (ICC=0.27;95%CI (0.07;0.49). The agreement was perfect for the fine motor scale. The telephone administration of the ASQ is a valid method of assessing children development. However, only the R-PDQ gross and fine motor and language scales give valid measures when administered over the telephone.
Keywords: *Telephone-validation children development*

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Long-term oral anticoagulant management associated with Routine Medical Care (RMC) in patients with Non-Valvular Atrial Fibrillation (NVAF) in Canada

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Objective: Resource utilization associated with Oral Anticoagulant Management (ROAM) is a prospective cohort study conducted across 9 Canadian provinces whose objective is to describe the process and quality of care, resource utilization (RU), and utility scores associated with long-term oral anticoagulant (warfarin) therapy in patients with NVAF.

Methods: Eligible, consenting patients are followed for 48 weeks and complete a weekly study diary providing data on international normalized ratio (INR) test dates and values, RU associated with warfarin monitoring, and all physician visits, procedures and hospitalizations. INR test values and source documentation are also collected from the participating physicians. Utility scores, representing the patient's health state, measured using the EuroQol-5D (EQ-5D) instrument are collected every 4 weeks.

Results: 482 patients who completed the study from April 2008 to April 2012 and had physician provided INR results were included in this preliminary analysis. Physicians reported a total of 6,705 INR tests over the study duration (mean±SD: 15.3 ±8.3 tests per patient) while patients recorded 7,260 tests being completed in their diaries over the same time period (16.8±9.5 tests per patient).

Conclusions: This is the first prospective cohort study of NVAF patients on long-term warfarin therapy being monitored primarily through RMC in Canada. Total number of INR tests is higher than previously reported for RMC, which may suggest a self-selection bias for better quality physician-patient combinations. Analysis of utility scores showed generally high scores for this community dwelling population, stable over the duration of the study.

Keywords: *Resource utilization; atrial fibrillation*

30

Estimation of outpatient versus inpatient adverse drug reactions (ADRS) reporting using ecology of medical care data

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Funding Source: None

Background: Adverse Drug Reactions (ADRs) occur in both inpatient and outpatient settings. However, in general established reporting systems for inpatient settings are different than outpatient settings.

Objective: To estimate expected ADRs reporting for outpatient settings versus inpatient settings using ecology of medical care data.

Method: Medical literature databases (Ovid, PubMed, and EMBASE) were searched for period 01/01/2000 and 01/01/2010. Data for ADRs per 100 admissions for both inpatient and outpatient settings was obtained from literature. Also, ecology of medical care data was obtained from various research studies. Using observed

data, an analysis was conducted to estimate expected outcomes.

Results: The observed average ADRs reported per 100 admissions was 6.3 (9.2) [Mean (SD)] for inpatient and 16.2 (12.2) for outpatient settings (P = 0.09). Ecology of medical care data demonstrated an average of 241 (57) visits for outpatient versus 10 (3) visits for inpatient settings as a monthly prevalence in a community (P = 0.02). The expected numbers for inpatient and outpatient ADRs reporting per 100 admissions, using ecology of medical care data, were estimated to be 6.3 (9.2) and 347 (261), respectively (P = 0.01)

Conclusion: This study demonstrated that using ecology of medical care data, the expected ADRs reporting from outpatient setting should be much higher than observed values. However, this can signify that more serious ADRs have been reported for both inpatient and outpatient settings and milder ADRs that mostly led to outpatient visits do not enter into the process of ADRs reporting.

Keywords: *Adverse drug reactions reporting ecology of medical care*

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Cost-effectiveness analysis of apixaban compared to warfarin for stroke prevention in atrial fibrillation (SPAF) in Canada

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Funding Source: Bristol-Myers Squibb Canada and Pfizer Canada

Objective: To determine the cost per quality adjusted life year (QALY) for apixaban compared to warfarin when used for stroke prevention in patients with atrial fibrillation (SPAF).

Methods: Using a Markov model, this analysis was conducted from the perspective of a Canadian third party payer relating to provincial ministries of health with a lifetime time horizon. The target population included patients with atrial fibrillation at risk of having a stroke and suitable for Vitamin K antagonists (VKA). Health outcomes were expressed in terms of the number of cardiovascular, bleeding, and death events. These were based on the results of the ARISTOTLE clinical study that compared apixaban with warfarin for SPAF. Patients were assigned utilities according to their health states. Costs (2012 CAD) and health outcomes were discounted at an annual rate of 5.0%. An incremental cost per QALY was calculated and sensitivity analyses were conducted.

Results: This model estimated that apixaban may prevent 18 strokes (ischemic or hemorrhagic, first or recurrent), 29 major bleeds (excludes hemorrhagic strokes) and 20 cardiovascular-related deaths in 1,000 patients over lifetime when compared to warfarin. On average, patients treated with apixaban accumulated 7.094 discounted QALYs. Apixaban had a greater overall cost ($2,175) but generated more QALYs (0.215) than warfarin, thus an incremental cost-utility ratio of $10,093 per QALY in the base case analysis. At a value of $50,000/QALY, apixaban was the optimal treatment in 93% of 2,000 replications.

Conclusions: This pharmacoeconomic evaluation supports the use of apixaban as a cost-effective first-line treatment for SPAF.

Keywords: *Cost-effectiveness; atrial fibrillation*

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Preliminary results of the impact of the use of pillbox on the stabilization of the INR among patients initiating warfarin treatment from a prospective cohort

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Funding Source: Canadian Institute of Health Research (CIHR) Center of Excellence in Personalized Medicine (CepMed)

Background: Many studies confirmed that the adherence to warfarin, a widely prescribed oral anticoagulant with a narrow therapeutic index, helps to achieve a stabilization of the INR. However, little data is available on the impact of the use of a pillbox.

Objectives: To evaluate the association between the use of a pillbox in patients initiating warfarin therapy and the stabilization of the INR. Methods: This study was based on an ongoing multicentric prospective cohort of patients initiating warfarin where demographic, clinical and lifestyle data were collected at cohort entry and each 3 months up to a year. We evaluated a subgroup of 265 patients who began the treatment between May 1st, 2010 and Oct. 1st, 2011. Our outcomes were the % of time in therapeutic range

(TTR), time to achieve stabilization and adherence. A multivariate linear model was used.

Results: 45.6%, 54.8%, 61.3% and 64.2% of patients used a pillbox at 3, 6, 9 and 12 months respectively. No significant association was found between the use of a pillbox and TTR, the time to achieve stabilization and adherence at each period of follow-up (p>0.05). Using a pillbox prepared by the pharmacist was negatively associated with the TTR (-0.122; 95%CI; -0.24 - -0.08) during the first 3 months.

Conclusion: Preliminary results suggest that using a pillbox is not associated with an improved stabilization of the INR. However, using a pillbox prepared by a pharmacist may have negative impact on the TTR. Additional analysis including comedication and genetics factors are ongoing.

Keywords: *Warfarin; pillbox; INR; TTR; adherence*

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Validity of self-reported regimen of dose by patient initiating warfarin treatment from a prospective cohort

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Introduction: Warfarin is a widely prescribed oral anticoagulant with a narrow therapeutic index. In observational studies, errors in measurement of the dose of warfarin can lead to a major misclassification bias.

Aims: To evaluate the validity of the dose of warfarin as reported by the patient when compared to the prescribed dose during monitoring visits.

Methods: Based on an ongoing prospective cohort, the study was limited to a subgroup of 219 patients who initiated warfarin between May 1, 2010 and Oct. 31, 2011 at the Montreal Heart Institute. Demographic, clinical and lifestyle data are collected at cohort entry and each three months during a year. We compared the reported and the prescribed weekly dose of warfarin with a t-test, Pearson correlation and a Kruskal-Wallis analysis for each period of follow-up.

Results: Mean age was 69.0 ñ 12.2, 61.2% were men and 73.5% had atrial fibrillation as a primary indication. Overall, there was no significant difference between the means of reported and prescribed warfarin weekly dose (p=0.544, Pearson coefficient=0.969). There was also no significant difference between the distributions of the mean of paired differences at each follow-up (p=0.868).

Conclusion: The weekly dose of warfarin as reported by patients in a prospective cohort study correlates well with the prescribed dose. Furthermore, the effect was similar whether measured in new-onset users of warfarin and up to 12 months of use. We conclude that patient-reported warfarin dose is a valid proxy for the conduct of observational studies of clinical and safety outcomes.

Keywords: *Warfarin; exposure; validity; self-reported; prescribed dose*

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Cost-effectiveness of insulin glargine versus sitagliptin in insulin naïve patients with type 2 diabetes mellitus

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Background: In the EASIE (Evaluation of insulin glargine versus Sitagliptin in Insulin-naive patients) trial, insulin glargine demonstrated a significant reduction in HbA1c compared to sitagliptin in type 2 diabetics who are inadequately controlled with metformin). The objective of this study was to assess the cost-effectiveness of insulin glargine compared to sitagliptin in type 2 diabetes patients from the perspective of the Canadian publicly funded health care system.

Methods: The IMS CORE Diabetes Model, a standard Markov structure and Monte Carlo simulation model was used. The model used a lifetime horizon in order to capture the long-term complications associated with type 2 diabetes. The efficacy of insulin glargine and sitagliptin in terms of HbA1c reduction, and corresponding rates of hypoglycemia were obtained from the EASIE trial. Health utility and cost data was obtained from recently published Canadian publications. Univariate and probabilistic sensitivity analyses were conducted.

Results: In the lifetime base case analysis, treatment with insulin glargine resulted in cost savings of $1,306 (CDN$) and a gain of 0.089 QALYs per patient. A

probabilistic sensitivity analysis demonstrated the robustness of the base case analysis, with 88% probability of insulin glargine being dominant (i.e. cost savings and more QALYs)

Conclusions: Insulin glargine is a clinically superior and cost-effective alternative to sitagliptin for type 2 diabetics who are inadequately controlled with metformin.

Keywords: *Diabetes; pharmacoeconomic; glargine*

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Transfusion-related costs before and after treatment with azacitidine in higher-risk myelodysplastic syndrome

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Background: This study's objective is to determine the transfusion resources utilized and cost of red blood cell (RBC) transfusions before and after azacitidine (AZA) treatment in patients with myelodysplastic syndrome (MDS).

Methods: In a retrospective review, 51 patients with MDS treated with AZA were followed from 6 months prior up to 18 months after AZA initiation. Clinical response and RBC transfusion requirements were obtained from blood banks and our prospective MDS database. Health resources utilized included transfusions and hospitalizations. A transfusion cost of $1,272.59 (2012 CAD$) per unit RBC was applied to transfusion resources utilized, based on an activity-based costing model in the literature.

Results: 51 patients received a median 11.0 cycles of AZA (IQR 6.5-16.8). Before AZA, 60.8% of patients were transfusion-dependent (TD), of whom 61.3% became transfusion-independent. In the six months before AZA, 31 patients (60.7%) received at least one transfusion (median 5.0 units, IQR 0.0-18.0). After AZA initiation, between 0-6 months, 42 patients (82.3%) were transfused (median 7.0 units, IQR 1.5-17.5); between 7-12 months, 26/45 patients transfused (57.7%) (median 2.0 units, IQR 0.0-14.0); and between 13-18 months, 14/31 patients transfused (45.1%) (median 0.0 units, IQR 0.0-11.5). The cost per patient

of RBC transfusions was $14,048.40 over the six months before AZA, and $13,898.68, $10,406.98, and $8,743.92 (1.1%; 25.9%; 37.7% reduction) at 6, 12, and 18 months after AZA initiation, respectively.

Conclusions: Treatment with azacitidine is associated with a reduction in RBC transfusion requirements and transfusion-related costs, particularly in patients who remain on therapy greater than 12 months.

Keywords: *Myelodysplastic syndrome; azacitidine; transfusion; red blood cells; cost*

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Targeting postprandial glucose (PPG) with the addition of a rapid acting meal time insulin is more efficient to lower A1C after 12 weeks than optimization of basal insulin in patients with type 2 diabetes (T2D)

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Background: We compared optimization of basal insulin to the introduction of rapid acting meal time insulin in the management of T2D.

Methods: We selected T2D patients treated with basal insulin at baseline that were part of START and INSIGHT studies. Patients were either optimized with insulin glargine (Gla, n=296) or received at breakfast, addition of insulin glulisine (Glu, n=226) for 12 weeks. Main meal was defined as the meal with the greatest glucose excursion between pre and post-meal glycaemia (calculated based on a 7-point glucose profile). Contribution of PPG to hyperglycemia was assessed. Values were adjusted for A1C, sex, gender and duration of diabetes at baseline.

Results: Baseline characteristics were similar between groups. At baseline, A1C level was lower in Glu patients (A1C (%): Gla=8.42; Glu=8.19, p=0.00242). After 12 weeks, patients receiving Glu had a more pronounced decrease in A1C level (change in A1C (%): Gla=-0.54; Glu=-0.80, p=0.0013) that resulted in lower final A1C levels (A1C (%): Gla=8.13; Glu=7.88, p0.0013). PPG at baseline was higher in Glu patients (PPG (%): Gla=50.78; Glu=74.07, p0.0001). Use of a meal time acting insulin resulted in a decrease of PPG in Glu patients (change in PPG (%): Gla=+19.07; Glu=-10.06, p0.0001). Final PPG was significantly lower in Glu patients after 12 weeks (PPG (%): Gla=70.03; Glu=63.33, p=0.0248).

Conclusion: In a representative population of T2D patients treated with OADs and basal insulin, targeting

breakfast for diabetes management appears more likely to succeed because more patients have breakfast as their main meal and PPG is significantly higher in patients with breakfast as their main meal.

Keywords: *Type 2 diabetes, basal insulin, meal time insulin*

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Targeting breakfast for type 2 diabetes (T2D) therapy appears more likely to succeed based on a subanalysis of START and INSIGHT Studies

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Funding Source: Sanofi

Background: We investigated the impact of the main meal on postprandial glucose (PPG) contribution in patients with T2D to increase the understanding of diabetes management.
Methods: T2D patients (n=1081) enrolled in START and INSIGHT studies were selected as part of sub-group analysis. Patients were separated based on 4 treatment protocols of 12 weeks: oral antidiabetic drugs (OADs) users optimized (n=168), OADs users switched to insulin glargine at bedtime (Gla, n=398), basal insulin users switched/optimized to Gla at bedtime (n=289) and Gla users received addition of insulin glulisine at breakfast (n=226). Main meal was defined as the meal with the greatest glucose excursion between pre and post-meal glycaemia (calculated based on a 7-point glucose profile). Contribution to hyperglycemia of PPG was assessed.
Results: The majority of users had breakfast as their main meal (47.2%) while the remaining patients had lunch (23.7%) or dinner (29.1%) as their main meal. Irrespectively of treatment regimen, people with breakfast as their main meal had a significantly greater PPG (54.87%, p0.05) than people having lunch (42.07%) or dinner (38.91%).Differences in PPG contribution were independent of age, gender, % of whites, BMI, A1C, doses of OADs and SU.
Conclusion: In a representative population of T2D patients treated with OADs and basal insulin, targeting breakfast for diabetes management appears more likely to succeed because 1) more patients have breakfast as their main meal as demonstrated by the am and 2hr 2) PPG is significantly higher in patients with breakfast as their main meal.

Keywords: *Type 2 diabetes; breakfast; postprandial glucose*

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Prescribing pattern of novel oral anticoagulants following regulatory approval for atrial fibrillation in Ontario, Canada

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Funding Source: Canadian Institutes of Health Research - Drug Safety and Effectiveness Network (Fall 2012 Operating Grant - Priority Announcement: Prospective Active Surveillance)

Background: Novel oral anticoagulants (NOACs) dabigatran, rivaroxaban and apixaban have been incorporated into various clinical guidelines since their approval for stroke prevention in atrial fibrillation (AF). However, patients in the general population often differ from participants of clinical trials. For NOACs, age is particularly interesting given the higher bleeding risk in older patients combined with lack of an antidote. We sought to determine utilization trends of oral anticoagulants in Ontario since the approval of NOACs for AF.
Methods: We conducted a descriptive study among Ontario residents aged 20 who filled prescriptions for an oral anticoagulant (warfarin, dabigatran, rivaroxaban) between October 2010 and September 2012. Monthly prescription volumes were obtained from IMS Brogan (Canadian CompuScript Audit). We calculated monthly prescriptions rates in five age categories: 20-39, 40-59, 60-64, 65-84 and 85.
Results: Over the 24-month period, 3,914,990 prescriptions for anticoagulants were dispensed, with monthly prescription rate of NOACs increasing from 16 to 336 prescriptions per 100,000 individuals. This was led by dabigatran, which by September 2012 represented 17.2% of all oral anticoagulants prescribed to adults aged 20. Warfarin prescriptions decreased during the study period, while 3.9% of prescriptions by September 2012 were for rivaroxaban. Dabigatran prescription rates were highest amongst individuals aged 85.
Conclusion: Within 2 years following their approval, NOACs have become rapidly integrated into Canadian medical practice. While patient outcomes and

healthcare utilization cannot be directly inferred from prescription trends, the growth in NOAC uptake in the elderly, a high-risk population, signals the urgent need to evaluate these outcomes.

Keywords: *Anticoagulants; atrial fibrillation; prescription trend.*

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Retrospective study of persistence and healthcare costs among opioid-dependent patients treated with buprenorphine/naloxone and methadone using a large US Medicaid database

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Background: Buprenorphine / naloxone (BUP/NAL) and methadone (MET) are used in the treatment of opioid dependence. Insurance claims data were analyzed to compare patient persistence and healthcare costs between BUP/NAL tablet formulation and MET.

Methods: A retrospective cohort analysis was performed using medical claim records extracted from the MarketScan Medicaid database. Two groups of matched patients with a diagnosis of opioid dependence or abuse treated with BUP/NAL or MET were selected. Treatment duration and healthcare costs were compared between groups, adjusting on baseline characteristics not taken as matching criteria. Costs were analyzed by time period (6 and 12 months after treatment initiation) and by treatment phase.

Results: The analysis included 381 pairs of matched patients and followed on average over 17.1 and 18.9 months for BUP/NAL and MET respectively. The groups had comparable demographic and health characteristics, but different insurance types with more patients in BUP/NAL group having capitation plan and coverage for prescription drugs. No significant difference in treatment persistence was detected. Cost analysis indicated that adjusted total costs were 15% lower in the BUP/NAL group (p=0.0416) in the 6 months after treatment initiation. Total non-pharmaceutical costs over 6 and 12 months after treatment initiation were statistically significantly lower in BUP/NAL group. Treatment with BUP/NAL resulted in 24% lower costs (p=0.01) relative to period before treatment.

Conclusion: While no difference in treatment duration was observed, cost analysis indicates that treatment with BUP/NAL may generate cost savings compared to treatment with MET.

Keywords: *Buprenorphine/naloxone; methadone; healthcare costs and persistence*

POSTER PRESENTATIONS
Monday, November 18, 2013

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Validation of a Canadian primary care electronic medical record database

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Background: Observational data derived from clinical practice is becoming increasingly important to answer questions that cannot be addressed in Randomized Clinical Trials. There is a need in Canada for more comprehensive clinical data such as smoking status, body weight and laboratory values. The objective of this study was to validate data from a primary care EMR system.

Methods: We analyzed consistency, completeness and comprehensiveness of de-identified patient data from 816 Primary Health Care Professionals 2009-2011. Overall demographic data were compared to Statistics Canada; the age and sex of patients with type 2 diabetes were compared to those in the Public Health Agency of Canada (PHAC) survey. Completeness was determined by visit for each variable.

Results: Records from 845,243 patients were analyzed, of these 255,274 were active (1 visit) during the study period. Data are available for demographics, vitals, smoking status, labs, medications, medical history, diagnosis (ICD-9), short term absences and referrals. Completeness ranged from 26% for pulse to 100% for age, sex, lab results, referrals and sick notes. Smoking status was reported in 68% of visits. The primary care population was slightly younger than the national average but there was no difference observed for sex. Similarly, demographics in patients with type 2 diabetes were consistent with PHAC; age was biased towards the younger population and sex was identical.

Conclusions: Validation of this primary care database indicated that it is highly comprehensive and representative of the Canadian population. It may serve as a valuable source for future observational studies.

Keywords: *Real world evidence, EMR; validation; observational data*

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Using anonymized longitudinal patient data to monitor the impact of reimbursement policies on patient compliance

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Introduction: Utilization data in provinces where public payer income-based reimbursement triggers are used tend to show a cyclical pattern in the volume of prescriptions dispensed. This suggests that uneven compliance may be an unintended consequence. This analysis focuses on BC where a longitudinal analysis of anonymized patient data (Lifelink LRx) for four patient cohorts based on different reimbursement payer share profiles were examined, to assess the impact of reimbursement on patient compliance over the course of a year. The analysis focused on the unit consumption pattern of continuing patients on four different diabetes medications (Metformin, Gliclazide, Sitagliptin, and Insulin Glargine), stratified by age (<66, 66+). High public patients consistently showed more year end consumption than high private or mixed patients, with cash patients having the most stable consumption over the course of the year. This effect was seen regardless of medication and age range. Fourth quarter consumption ranged from 27 to 33% of annual utilization. While prescription size did vary by payer, differences over time within payer were not consistent enough or large enough to explain the overall pattern observed above. The effect size does appear to be directly related to the prices of the medications involved, with year-end loading more pronounced with higher priced medications. Overall this suggests that compliance is maximized at the end of the year versus the start of the year for those dependent on public reimbursement using income based triggers. This technique can be used to assess almost any combination of medications, provinces, and reimbursement policy.

Keywords: *Reimbursement; compliance; longitudinal*

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Potential impact of days supply errors in pharmacy data on measurement of compliance with osteoporosis medications

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Background: Days supply (DS) values are commonly used to estimate drug exposure. We previously identified reporting errors in DS values for non-daily osteoporosis medications, particularly in long-term care (LTC). In this study we aimed to examine the potential impact of DS reporting errors on measurement of compliance with osteoporosis medications.
Methods: We identified oral bisphosphonate prescriptions dispensed in Ontario for seniors. DS values were examined by dosing regimen, and illogical values for non-daily regimens were flagged for data cleaning. DS values were cleaned using dose specific algorithms. Compliance with therapy was estimated using the proportion of days covered (PDC). Mean PDC and proportion with high compliance (PDC ≥80%) were compared using the observed and cleaned DS values. Results were examined separately for patients residing in LTC and community.
Results: A total of 356,134 eligible new users were identified, 25% in LTC. Among LTC users, mean PDC increased from 60% to 77% following data cleaning, and the proportion identified with high compliance (PDC ≥80%) increased from 48% to 79%. Fewer DS errors were noted in the community setting; mean PDC increased from 79% to 81%, and high compliance increased from 60% to 65% after data cleaning.
Conclusions: Results suggest that adherence to oral bisphosphonate therapy is underestimated in LTC. Careful attention to potential exposure misclassification is important. For example, differential misclassification may exaggerate the association between better compliance and drug effectiveness since oral bisphosphonate exposure is underestimated in LTC patients, who are also more likely to experience a fracture than community-dwelling patients.
Keywords: *Exposure misclassification; compliance; pharmacoepidemioloy; administrative data*

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The benefit of an automated step therapy program to manage diabetes medication use

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Background: Diabetes drug spend increased 8% in 2012, primarily driven by the increase in utilization due to disease progression, increase in prevalence, and higher cost per prescription due to new incretin therapies, specifically dipeptidyl peptidase-4 (DPP-4) inhibitors and glucagon-like-peptide 1 (GLP-1) agonists. This study examines how the Express Scripts Canada Step Therapy program encourages adherence to the Canadian Diabetes Association (CDA) Clinical Practice Guidelines (CPG) and estimates the savings through the use of lower-cost, therapeutically effective drugs prior to newer agents.

Methods: Retrospective diabetes claims data for all ESC plan members submitted in 2012 were collected. A Step Therapy simulation analysis was performed to quantify proportion of claimants who were prescribed with an incretin therapy as first line, and the potential savings if metformin was prescribed and utilized first-line as per the CPG.

Results: In 2012, incretin therapies made up 10.3% of the total diabetes drug claims and 27.8% of diabetes spend. Analysis found that 22.6% of diabetes patients used at least one incretin therapy, with 28.4% of new incretin claimants not in accordance with the CPG. This single Step Therapy edit would lead to a change in therapy resulting in a potential reduction of 6.8% of the total diabetes drug spend, comprising 0.3% in overall drug spend.

Conclusion: This study found that 28.4% of incretin patients were not compliant with CDA CPGs. A Step Therapy Program could decrease diabetes spend by 6.8% which translates into 0.3% of overall drug spend.

Keywords: *Step therapy; diabetes; incretin*

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Meta-analysis of the use of assisted reproductive technologies and the risk of multiple birth and major congenital malformations

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Funding Source: None

Background: Our meta-analysis summarizes the literature on ART risks in newborn, explains discrepancies between studies, and identifies the gaps in knowledge for future research.

Methods: We carried out a systematic review to identify published papers between 1966 and 2012 in Medline, Embase and Cochrane Central Register of Controlled Trials. We included observational studies and randomized clinical trials related to the risk of MCM or multiple birth conceived following ovarian stimulation (OS) alone, intrauterine insemination (IUI) and in-vitro fertilization (IVF) with related procedures compared to spontaneously conceived infants or infants conceived using other ART.

Results: We identified 2243 citations, 1806 citations were excluded after screening titles and abstracts leading to 238 eligible studies. Among them, 75% reported data on IVF, 16% on OS alone and 9% on IUI. Studies comparing infants conceived following OS alone and spontaneously conceived babies showed at least 40% increased risk of multiple birth. Studies suggested an increased risk of multiple birth when other fertility agents were used in addition to clomiphene citrate (CC). Half of the studies comparing infants conceived following OS alone to spontaneously conceived infants showed at least 7% increased risk of MCM. Studies comparing OS with or without other fertility agents with spontaneously conceived infants suggested an increased risk of certain neural tube defects and DandyWalker malformation.

Discussion: A limited number of observational studies focused on the risk of multiple birth and MCM following OS alone. Results suggest that overall OS without other ART increases the risk of multiple birth and MCM.

Keywords: *Medically assisted reproduction; birth defect; multiple birth*

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Cost-Effectiveness of a physician-nurse supplementary triage assistance team (MDRNSTAT) in an Ontario academic emergency department

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Background: Patient funding for Ontario academic emergency departments (ED) are historically calculated from annual patient-seen volume and acuity mix [Academic Funding Agreement (AFA)]. Since 2008, the Ontario government implemented a pay-for-performance (P4R) strategy to decrease ED length of stay (LOS). Financial incentives to the ED are rewarded after achieving physician initial assessment (PIA) time and EDLOS targets. Targets may be achieved through team-based solutions, but there is little evidence addressing their cost-effectiveness to decrease PIA and EDLOS.
Objectives: To evaluate the cost-effectiveness of physician-nurse supplementary triage assistance team (MDRNSTAT) on decreasing EDLOS, left-without-being-seen ED patients and achievement of P4R thresholds.
Methods: A cost-effectiveness evaluation of a single center randomized control trial of the MDRNSTAT (3,163 controls, 3,137 intervention) compared to nurse only triage in an ED was performed. Results were extrapolated to a 12-hour MDRNSTAT working every day for one year (2009). Costs were MDRNSTAT salaries. Revenue was calculated from P4R incentives and the AFA. Incremental cost-effectiveness ratio was determined as the ratio of MDRNSTAT cost per PIA or EDLOS minute or patient-seen gained. A univariate sensitivity analysis was performed.
Results: MDRNSTAT was associated with an added cost of $379.59 per additional patient-seen, which resulted in an additional $1.19 per PIA minute saved and added $1.07 per EDLOS minute. In the sensitivity analysis, if a 12-hour MDRNSTAT could achieve all P4R thresholds, incremental revenue would be gained (+127.52 per patient).
Conclusion: The MDRNSTAT was more costly than nurse-only triage but decreased EDLOS and increased patient throughput.
Keywords: *Economic evaluation; emergency department; provincial targets; triage team*

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Diffusion of methodological innovation in pharmacoepidemiology: high-dimensional propensity score co-authorship network analysis

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Background: The field of pharmacoepidemiology has experienced rapid scientific growth and methodological innovation. We sought to characterize the diffusion of the high-dimensional propensity score (hdPS) method since its innovation in 2009.
Methods: A systematic keyword (MEDLINE and EMBASE) and citation (Web of Science and Scopus) search was completed to identify all empirical applications of hdPS. Sociograms were generated from a co-authorship matrix to visualize the network and identify components and cut-points. A component is a group of authors connected directly or indirectly through co-authorship. Cut-points are authors whose removal would increase the number of components. First and last author affiliations were identified to ascribe institutional contribution to each paper and the entire network.
Results: We identified 23 papers by 84 distinct authors, 2009/07-2013/04 –all from North America, and one outside the field of pharmacoepidemiology. The network consisted of 3 components, 2 included only a single paper in the area of pediatrics. The main component included 21 (91%) papers from 72 (86%) authors. The primary institution credited for the hdPS network was the innovator (Brigham and Women's Hospital/Harvard Medical School; 50%), with two cut-points: 1. innovator to the University of Toronto (credited with 13% of the network), and 2. an early adopter at the University of British Columbia (credited with 15% of the network).
Conclusions: The hdPS has generated 23 empirical applications within 4 years; primarily from the innovator or recent affiliates of the innovator. We expect to see further growth in application of the hdPS, particularly in pediatric research.
Keywords: *High-dimensional propensity score; systematic review; co-authorship network analysis; methodological innovation*

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Time savings with trastuzumab subcutaneous (SC) injection vs. trastuzumab intravenous (IV) infusion: a time and motion study in 5 Canadian centres

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Funding Source: Study funded by F. Hoffman-La Roche Ltd.

Background: Trastuzumab (TRA) subcutaneous single-use injection device (SC SID) is an alternative to intravenous (IV) administration for the treatment of HER2+ early breast cancer. This study quantifies healthcare professional (HCP) time and patient chair time related to TRA SC SID vs. TRA IV processes to estimate potential time savings with a conversion from IV to SC SID.

Methods: A multi-centre, prospective, observational time-and-motion study was run alongside the PrefHer trial (a patient preference trial for route of administration of TRA, ClinicalTrials.gov id: NCT01401166) in Canada. Generic case report forms for IV, SC SID, and pharmacy management were tailored to reflect site practices. Trained observers recorded durations that HCPs were actively completing pre-specified tasks, and separately patient chair time. Mean IV vs. SC SID process time was calculated as the sum of the mean task times, and corresponding 95% confidence intervals.

Results: Mean reduction in HCP time per patient session was 18.7min (-47%) (IV: 39.4min vs. SC 20.7min) with 72% and 28% of savings achieved in the pharmacy and treatment room, respectively; range of time savings across centres: 11.8-25.1min. Per treatment course (18 sessions), estimated time reduction was 5.6hours (range across centres: 3.0-7.5hours). Reduction in mean chair time was 52.3min (-68%) (IV: 76.7min vs. SC 24.4min); range across centres: 44.0-67.4min.

Conclusion: Conversion from IV to SC SID TRA leads to substantial reductions in administration chair time as well as in active HCP time. Consequently, this provides a potential for systemic therapy suites to increase both patient treatment capacity and staff efficiency.

Keywords: *Time-and-motion; trastuzumab; subcutaneous*

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Establishing a database to prospectively track health technology assessments - a case study of the pan-Canadian Oncology Drug Review (pCODR)

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Introduction: One of the challenges faced by Health Technology Assessment (HTA) committees, such as the pan-Canadian Oncology Drug Review Expert Review Committee (pERC), is to ensure consistency and transparency of their deliberations. This is essential to build trust among stakeholders dependent on receiving high quality, well considered, evidence-based advice. pERC began making recommendations to the Canadian provinces and territories to guide their cancer drug funding decisions in October 2011. Shortly thereafter, several committee members formed a working group to create a database as a tool to help prospectively track consistency of decision-making. The variables chosen for the database were derived from pERC's publicly available Deliberative Framework, which describes all of the elements that should be considered during a review (e.g. overall clinical benefit, alignment with patient values, cost-effectiveness, and feasibility of adoption into the health system). A key rationale for this project is that an essential element of the ethical framework that guides pCODRs review process is consistency in decision-making. This database will assist pERC in measuring its own consistency, and identifying precedents so that policy makers and the public have confidence that the ethical framework is being applied. This presentation will outline the steps required to create a successful database that is user-friendly, can capture relevant information, and will generate capacity for potential research projects. This topic is relevant to health policy makers as it provides a practical example of an innovative quality improvement initiative that can strengthen the impact of HTA and evidence-informed decision-making.

Keywords: *Innovation; collaboration; stakeholder*

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Lessons learned from the dedicated oncology drug review process in Canada: 2013 update

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Funding Source: None

Background: The pan-Canadian Oncology Drug Review (pCODR) was established to provide provinces/territories with recommendations on reimbursement for cancer drugs. We analyzed these recommendations to identify trends.
Methods: Recommendations publicly accessible at www.pcodr.ca were reviewed since pCODRs operation: 13 July 2011 - 17 May 2013.
Results: Of the eleven positive recommendations, two suggested a more limited patient population than the one requested (Inlyta and Votrient). In eight cases (Afinitor –two indications, Halaven, Jakavi, Sutent, Treanda, Yervoy, Zelboraf), positive recommendations for the requested population were made conditional on improvement of cost-effectiveness ratios. Treanda received a positive recommendation for the requested population without conditions. Velcade received a positive recommendation for only one of the requested populations. Xalkori received a positive recommendation limited to second-line therapy and conditional on improved cost-effectiveness. Three negative recommendations were made due to: a) limitations in evidence from open-label, phase two trials (Xalkori); b) modest progression-free survival, lack of statistically significant overall survival, lack of quality of life data and poor cost-effectiveness (Votrient), and; c) unclear clinical benefit and an unacceptable cost-effectiveness model (Treanda). Many economic reviews included re-analyses (e.g., limiting product benefit post- progression, time horizon reductions, or changes to post-progression mortality risk) which had substantial impact on cost-effectiveness.
Conclusions: The positive conditional pCODR recommendations clearly support a continued provincial product listing agreement structure that includes rebates to lower cost-effectiveness. The economic re-analyses may raise doubts as to the value of the products which could weaken the negotiation position of manufacturers for subsequent provincial price listing agreements.
Keywords: *Pan-Canadian oncology drug review; oncology reimbursement decisions; health technology assessment*

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Interim results from the burden of bowel dysfunction in spinal cord injury study
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Background: There are approximately 40,000 Canadians living with spinal cord injury (SCI). Most individuals with SCI experience some type of bowel dysfunction (BD), which can contribute to a high burden in individuals and caregivers.
Methods: This study is a prospective, observational study with 80 adult participants being recruited at three SCI clinics in Ontario, Canada. Participants complete a total of nine questionnaires (baseline, three weekly and five monthly) over a 6-month time horizon. Information related to demographics, BD (e.g., neurogenic bowel dysfunction score), health preference (e.g., Health Utility Index (HUI) Mark 3) and resource utilization (e.g., physician, supplies, etc.) attributed to BD is being collected.
Results: Results from three clinics are being evaluated. To date, 45 participants have completed the questionnaires, the majority (60.00%) being male. Mean time since SCI was 20.2 ± 13.7 (2 –42) years. Twenty (44.4%) participants were employed. At baseline, the mean neurogenic BD score was 14.37 ± 6.05 (0 –31). At 6 months, the score was 12.9 ± 6.6 (2 –28). The mean HUI-3 score at baseline was 0.17 ± 0.31 (-0.37 –0.95). At 6 months the score was 0.19 ± 0.33 (-0.37 –1). The cohort visited their primary physician an average of 8.3 ñ8.6 (0 –33) times over 6 months. 52.21% of participants required caregiver assistance. 12.50% required a mean 1.21 ± 0.67 (0.3 –2) hours daily assistance with their bowel routine.
Conclusions: Results from the 45 SCI individuals with BD indicate a variety of health resources are being utilized over a 6-month period.
Keywords: *Spinal cord injury; bowel dysfunction; resource utilization*

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A comparison of resource utilization and costs in patients with pemphigus and pemphigoid 6 months before and 6 months after rituximab treatment

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Introduction: Pemphigus and pemphigoid are a rare group of potentially fatal diseases, causing blistering on mucosal and epidermal surfaces. Long-term systemic treatment with systemic corticosteroids and immunosuppressive agents including IVIg are usually required. Rituximab (RTX) is increasingly being used for autoimmune bullous dermatoses (AIBD). In Canada, RTX is not approved for AIBD. Given the potential cost associated with the use of RTX, there is a need to quantify the issues around accessing it for AIBD patients.

Methods: Resources (e.g., treatment, lab costs, procedures, access to healthcare providers) associated with 89 AIBD patients were collected and quantified 6 months prior and post RTX initiation. Unit costs (2013 $CAN) were applied to the resources. Overall cohort costs pre and post RTX, as well as cost per patient, were calculated. Cost drivers were identified.

Results: The overall cohort cost for 6 months pre-RTX was $3.7million (M), and 6 months post was $2.6M, (30.3% decrease). The main cost driver was IVIG. 6 months pre-RTX, 157 months of IVIG was used ($3.6M) compared to 71 months ($1.6M) 6 months post. The cost associated with access to healthcare resources significantly reduced from $46,715 vs. $22,978, and fewer visits to the dermatologist were required (377 vs. 256 visits). A decrease was also observed in the cost of specialist consultations required ($5,807 vs. $3,234) and other treatment/medication use ($64,548 vs. $48,045). The cost per patient decreased ($41,497 vs. $28,923).

Conclusion: Using RTX is effective in reducing the number of resources and costs associated with treatment of AIBD.

Keywords: *Pemphigus; rituximab; resource utilization*

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Utilization of economic evaluations and organizational impact analysis in formulary decision making; a survey of a local health integration network (LHIN) in Ontario

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Background: Pharmacy and therapeutics (P&T) committees have an important role to play in optimizing drug formulary listings through evidenced-based drug review processes of clinical and economic data. The objective of this survey was to examine the current formulary review processes across P&T committees within a Local Health Integration Network (LHIN).

Methods: A 2-part questionnaire was developed to capture information about the institutions' current drug review processes (Part 1) and gathered feedback from P&T committee members on drug review processes, quality of evidence, decision-making, and preferences for a coordinated review process (Part 2).

Results: At hospitals (N=10), the P&T committees reviewed at least 1-5 new drug formulary requests per year. Evidence related to economic evaluation and organizational impact analysis was requested by 60% and 40% of the hospitals, respectively. Only 4 (40%) of the hospitals stated that they sometimes (N=2) or often (N=2) completed economic evaluations as a part of their formulary review. Of the 28 P&T committee members, 9 (32%) indicated that sufficient expertise to review economic evidence was available. Most members agreed that a standardized drug formulary submission process and coordination with the Ontario Drug Benefit Formulary would be beneficial for efficiency (workload, cost) and to improve quality of reviews, but have concerns about equity and institution-specific needs.

Conclusions: Availability of health economic expertise for new drug formulary reviews by P&T committees in

the LHIN is limited. A centralized review process has both potential benefits and limitations.

Keywords: *Formulary review; health technology assessment; economic evaluation*

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Anticoagulation control with daily low dose vitamin K to reduce clinically adverse outcomes and INR variability: a systematic review and meta-analysis

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Introduction: We sought to systematically review available literature examining the effectiveness of low dose vitamin K supplementation for the reduction of clinically relevant adverse events due to vitamin K antagonist (VKA) use and for stabilization of international normalized ratio (INR). We searched MEDLINE, EMBASE, the Cochrane Library, International Pharmaceutical Abstracts (IPA), and the United States National Institute of Health clinical trials registry through February 2011 for randomized control trials of vitamin K supplementation versus placebo in patients receiving a VKA. We evaluated the outcomes of hemorrhage, thromboembolic events and percentage time in therapeutic range (TTR) of INR using the GRADE quality rating system. Of the 624 studies we identified and screened, three studies (626 patients) were included in the meta-analysis. Most of the patients had a satisfactory TTR at baseline. We found low-quality evidence-downgraded for imprecision and risk of bias (i.e., limitation in study design and/or execution)-of no effect of vitamin K use (100 to 200g) on hemorrhagic events (relative risk [RR] 3.2, 95% confidence interval [CI] 0.2–64.2) and thromboembolic events (RR 2.2, 95% CI 0.1–47.5) and a significant but clinically unimportant effect on TTR with an absolute

increase of 3.5% (95% CI 1.1–6.0). This meta-analysis, despite few studies and overall low quality, suggests no beneficial role of low dose (i.e. 100g to 200g) vitamin K supplementation on the reduction of clinically relevant adverse events in patients taking warfarin, despite a small improvement of the TTR. However, there are insufficient data from patients with unstable INR.

Keywords: *Vitamin K antagonist; vitamin K supplementation; systematic review*

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The early challenges of facilitating the transformation of interprofessional practices to prevent cardiovascular diseases in primary care

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Background: In primary care, cardiovascular disease prevention is less than optimal, especially among patients with multiple chronic conditions. An interprofessional program of interventions for cardiovascular prevention targeting multimorbid patients was developed. However, integrating interprofessional follow-up is challenging. Facilitation is a strategy that could help clinicians transforming interprofessional practices.

Methods: Case studies (embedded within a pragmatic, controlled, cluster-randomized, implementation trial) were performed to describe how two strategies, facilitation and passive diffusion, helped transforming interprofessional practices in primary care. Family Medicine Groups (FMGs) in Laval and Saint-Eustache (Québec, Canada) were recruited. In FMGs with

facilitation (n=6), an external facilitator supported Internal Facilitation Teams (IFTs) in implementing the program, each composed of at least one family physician, one case-management nurse, one community pharmacist and one nutritionist, kinesiologist or psychologist. In FMGs with passive diffusion (n=2), no external facilitator was provided. IFTs, facilitators, and nurses were interviewed.

Results: Primary care case-management nurses assessed patients' cardiovascular health, helped them elaborate a treatment plan using motivational interviewing, coordinated the appropriate use of health and community resources, and collaborated in advanced care with community pharmacists, nutritionists, kinesiologists and psychologists. Medical leadership, buy-in, and openness to interprofessional collaboration influenced implementation of those interventions in all FMGs. Overloaded nurse schedules, lack of management skills, and recent changes in clinical information systems are barriers to change. Facilitation helped connecting clinics with external health professionals and exploring new partnerships.

Conclusions: The current primary care context challenges the establishment of channels for interprofessional communication. Facilitation can help overcoming barriers to partnerships.

Keywords: *Facilitation; primary care; cardiovascular prevention*

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Impact of mandatory generic substitution policies on Canadian private payer drug plan costs and patients

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Background: The relationship between private payer reimbursement policies and utilization of pharmaceutical products within Canada is infrequently studied. Many private payers are implementing mandatory generic substitution policies without fully understanding how this policy may affect plan members. The objective is to quantify the number of patients and claims affected by a mandatory generic substitution policy within private payer drug plans.

Methods: Transactional claims data from various private payer drug plans with mandatory generic substitution policies were pooled and examined over a 12 month period. The number of patients and claims subject to these policies were examined relative to the overall claims pool.

Results: The pooled claims data contained 8,170 patients with 78,490 claims over the 12 month period. Only 2,895 claims (3.7%) were subject to the mandatory generic substitution policy. Drug cost reduction from this policy was approximately 2% of the total drug cost submitted to these private payer plans. The top 5 drug categories subject to this policy were oral contraceptives, proton pump inhibitors, cardiovascular drugs, narcotic pain drugs, CNS stimulants.

Conclusion: Mandatory generic substitution policies have a minimal impact on overall private payer drug plan costs due to the high rate of generic substitution in Canadian private payer drug plans. The costs associated with implementing this policy should be examined relative to the cost savings gained.

Keywords: *Private payer; mandatory generic substitution; policy*

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Using retrospective chart review methodology to characterize patients, treatment patterns and resource utilization in a cohort of patients with multicentric Castleman's disease

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Funding Source: Study funded by Janssen Global Services

Background: Multicentric Castleman Disease (MCD) is a rare lymphoproliferative disorder with no established therapy. Little is known about MCD usual care treatment patterns and associated outcomes. The design and execution of a retrospective chart review study of patients with MCD are described, highlighting methodological considerations for conducting chart review studies in this rare disease.

Methods: Multi-center, retrospective, chart review study of 59 MCD patients (61.0% male; mean age 53 years) conducted in 2 centers in the United States. All MCD cases between January 1, 2000 and December 31, 2009 were identified. Medical record data up to 6 months pre-diagnosis and up to 3 years post-diagnosis were abstracted by site study staff. Anonymized data were entered into an electronic data capture (EDC) system.

Results: Key challenges: 1) disease complexity and lack of published literature make it difficult to inform protocol and CRF development 2) limited number of participating treatment centers resulting in small study

population; 3) MCD diagnosis not well documented in medical chart 4) patients seen at the site for a one-time consultation or second opinion resulting in minimal and missing data from their medical chart; 5) EDC system must permit large volumes of clinical tests, exams and physicians visits data collection for patients with ongoing medical care, with a validation plan to ensure quality data.

Conclusions: Acquisition of clinical outcomes and treatment pattern data through retrospective chart review study in a rare disease population such as MCD requires early planning and innovative approach to overcome associated methodological challenges.

Keywords: *Multicentric Castleman's disease; chart review methodology; healthcare utilization*

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Costs and survival of patients with metastatic melanoma: evidence from the Ontario Cancer Registry and administrative databases

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Background: Malignant melanoma is the most aggressive and deadly form of skin cancer. In patients with distant metastasis, median survival is less than one year. In this study, we use administrative databases available from the Ontario Cancer Data Linkage Project (cd-link) to identify and examine a cohort of patients with metastatic melanoma.

Methods: We included patients in the cohort if they had no evidence of surgical resection and they had received chemotherapy during or after the year 2000. The presence of chemotherapy was used to indicate metastatic disease. This cohort was then linked to various Ontario health administrative databases (e.g., Ontario Cancer Registry, Ontario Health Insurance Plan (OHIP)) to estimate costs and survival for members of the cohort.

Results: From a total of 33,585 patients diagnosed with malignant melanoma in Ontario for the period 1991-2010, 553 qualified for our cohort. Their mean age was 57 years, and approximately 65% were male. Mean costs per patient for the period ranged from approximately $20,000 for hospitalizations to $5,000 for OHIP and drug claims. Survival was about 50%, 25%, and 15% at years one, five and ten, respectively.

Conclusions: This research explores the use of administrative databases and their ability to provide important real-world data on patients. The resulting information contributes to the totality of evidence available to inform health care decision making. In the context of metastatic melanoma, such data on standard care represent potentially valuable inputs in the assessment of the relative costs and effects of introducing novel treatments.

Keywords: *Cohort analysis; administrative databases; metastatic melanoma*

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Homecare utilization and costs in colorectal cancer

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Objective: To determine the utilization and costs of homecare services (HS) for a population of individuals with colorectal cancer (CRC).

Methods: New cases of CRC were extracted from the Ontario Cancer Registry (2005-2009) and linked to the HS administrative datasets. Controls were selected from the population who were not ever diagnosed with any type of cancer. The type and proportions of HS used were determined and stratified by disease stage. Net homecare utilization and costs for cases were determined. Regression analysis was used to examine factors associated with utilization and cost.

Results: There were 36,195 CRC cases (14.2% Stage I; 19.6% Stage II; 21.3% Stage III; 14.6% Stage IV; 30.3% Not Staged) and 175,358 controls Median age was 71 years for both cohorts and 68.1% of CRC cases used HS compared to 21.5% in controls. The number and cost of HS utilized increased by disease stage. There was a significantly higher number of HS utilized per patient-year in CRC cases compared to controls (27.45 vs. 9.16, p<0.01). Higher HS utilization resulted in a higher cost per patient-year ($2,180 vs. $493, $1,687 net cost to colorectal cancer p<0.01). The number of HS utilized (15.45 to 62.51 visits) and their associated costs ($1,170 to $5,541) increased as disease severity increased (Stage I to IV).

Interpretation: CRC cases utilized HS three-fold higher resulting in four-fold higher costs compared to a matched control group; $1,600 per patient per year of HS utilization costs were attributable to CRC.
Keywords: *Costing; cancer; administrative databases*

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Exploring homecare services for persons with Alzheimer's disease

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Background: Alzheimer's disease (AD) is the most common form of dementia among individuals aged 65 years and older. There is currently no cure for AD; the focus from a care perspective is therefore on supporting patients and their families at home. A recent shift in Ontario health policy has led to a substantial increase in funding for homecare; however, whether the services currently supplied are adequate is unclear. Profiles of service utilization and the needs of caregivers are required.
Methods: Recruitment of formal (i.e., nurses or personal support workers) and informal (i.e., family members) caregivers that provide care for an individual with AD at home is in progress. Data analysis is guided by the principles of grounded theory.
Results: Preliminary results from interviews with 20 informal caregivers reveal two themes: the need for respite care, and a desire for more information to assist decision-making. Some families attended community groups where two programs were simultaneously run, one for the care recipient, and another providing respite for caregivers. Those in the latter groups, typically led by someone knowledgeable on managing AD, felt better able to cope. Many found it difficult to obtain information on services available in the community. Interviews with nurses and personal support workers are ongoing.
Conclusions: Informal caregivers often mention a need for more respite care; an interesting revelation is the lack of information. Further analysis is expected to reveal other service gaps, providing opportunities to better equip and support caregivers.
Keywords: *Homecare; grounded theory; Alzheimer's disease*

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Drug utilization and safety evaluations: lessons learned from multi-national retrospective chart review case studies

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Background: Increasingly, to meet marketing authorization and risk management real-world data needs, regulators are requiring real-world prescription pattern data including off-label information. In the absence of suitable databases, chart review studies can result in robust datasets appropriate for evaluations of drug utilization and safety outcomes.
Methods: Design and operational parameters of 4 recent chart review studies of clinical outcomes and/or drug utilization and safety conducted in Canada, the United States, and Europe have been summarized. Opportunities, challenges and lessons learned are described.
Results: All studies were post authorization safety studies and all but one study was mandated by the FDA or EMA. The therapeutic areas varied by study and included renal, cardiovascular and intensive care populations. Sample size varied from 100 patients to more than 2000 patients and the number of countries and sites/prescribers varied from 1-5 and 12-375 respectively. Across studies, key challenges included determining eligibility criteria and study periods that permitted evaluations of recent care patterns while allowing sufficient follow-up time; design and local implementation of case identification and sampling frame methodologies; and safety reporting in the context of retrospective chart data. The studies evaluating inappropriate or off-label drug use required careful attention to protocol language to minimize response bias, as well as a carefully executed operational plan for the identification of prescribers and the collection of data from prescribers over time.
Conclusions: Methodological and operational challenges can be anticipated and overcome to achieve rigorous patient-level datasets to inform important drug utilization and safety related research questions.
Keywords: *Retrospective chart review; safety outcomes; drug utilization*

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Facilitation in primary care: roles supporting change implementation in clinical practices

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Background: Primary care faces serious challenges in the care of multimorbid patients with cardiovascular diseases, such as interprofessional collaboration optimization and healthcare providers' preventive practices improvement. More evidence-based results suggest the efficacy of facilitation for implementing changes in clinical practice. The objective of this study is to better understand the dynamics of facilitation roles undertaken by external facilitators (EFs) and internal facilitation teams (IFTs) to support the implementation of changes in primary care practices.

Methods: Qualitative evaluation (case studies) of an implementation process involving Family Medicine Groups (FMGs) in greater Laval (Quebec, Canada), embedded within a pragmatic, controlled, cluster-randomized trial, has been used. Over one year, EFs (n=2) hosted up to ten (10) meetings with three IFTs each (n=6), to help implement changes related with the Chronic Care Model. IFTs included at least one family physician, one case-manager nurse and community specialists (one pharmacist, plus one nutritionist, kinesiologist or psychologist). IFTs role was to translate knowledge and disseminate change to FMGs and external community specialists. Data was collected through focus group interviews (IFTs), individual interviews (EFs), and content analysis of facilitation documents.

Results: This study gives insight on which facilitation roles are shared between EFs and IFTs (ex.: create local ownership of change, help overcome resistance to change, networking). Facilitation is influenced by contextual factors (inner/outer settings) and facilitator characteristics (competencies, style preferences).

Conclusions: The way facilitation roles are shared and performed by EFs and IFTs affects the learning process of IFTs/FMGs. Facilitator characteristics and contextual factors affect facilitation.

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Physician experience with rituximab to treat pemphigus vulgaris in Canada: a questionnaire-based study

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Objectives: To examine the experience of physicians who treat patients with pemphigus vulgaris (PV) in Canada as well as the utilization and access of the drug rituximab (Rtx).

Methods: An online questionnaire was created in SurveyMonkey® to collect data from participants based on a convenience sample size of 10 English-speaking dermatologists. Consent was implied once the dermatologist completed the questionnaire. Non-identifying information for both dermatologists and PV patients was collected.

Results: The 10 participating dermatologists have been treating PV patients an average of 20.9 ± 10.7 $(5 - 45)$ years in which 28.8 ± 58.3 $(0 - 200)$ was the mean number in their practice. Experience with Rtx is based on an average of 4.1 ± 3.8 $(0 - 10)$ years and 13.1 ± 29.2 $(0 - 100)$ PV patients treated with Rtx. All participants answered that "failure of conventional therapy for at least six months" was the primary reason for using Rtx and that azathioprine, intravenous immunoglobulin and mycophenolate mofetil were the most popular treatments used to treat PV patients prior to Rtx. On average, it takes 3.2 ± 2.2 $(0 - 6)$ months for a remission to be induced after Rtx treatment and 90 percent of the dermatologists were concerned that infections would be an adverse event. Lastly, 6.3 ± 12.3 $(0 - 40)$ was the mean number of Rtx drug reimbursement letters that the dermatologists had written on behalf of PV patients in which 1.9 ± 2.5 $(0 - 6)$ letters were successful in securing Rtx drug reimbursements.

Conclusions: A recent survey of 10 Canadian dermatologists experienced with treating PV patients found that Rtx utilization is still new, disease remission is achieved within a short period of time, and the drug

reimbursement process remains a barrier based on the low number of letters written by the dermatologists.

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