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THE CANADIAN ASSOCIATION FOR POPULATION THERAPEUTICS ANNUAL CONFERENCE

"A Look to the Future: Medication Use, Safety and Effectiveness under Economic Uncertainty"

April 19-21, 2009
Montreal, Québec

CAPT ACTP

ABSTRACTS

THE CANADIAN ASSOCIATION FOR POPULATION THERAPEUTICS ANNUAL CONFERENCE

"A LOOK TO THE FUTURE: MEDICATION USE, SAFETY AND EFFECTIVENESS UNDER ECONOMIC UNCERTAINTY"

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ABSTRACTS

1 – ENCORE PRESENTATION

A cluster randomized controlled Trial to Evaluate an Ambulatory primary care Management program for patients with dyslipidemia: TEAM study

Lalonde L, Villeneuve J, Genest J, Blais L, Vanier MC, Lamarre D, Fredette M, Lussier MT, Perreault S, Hudon E, Berbiche D
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Antidepressant medication use during pregnancy and the risk of miscarriage

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Funding Source: FRSQ
Background: Depression is a common psychiatric disorder affecting up to 14 % of pregnant women. Antidepressants have been shown to be effective in depressive pregnant women but the extent to which antidepressants are increasing the risk of miscarriage is unknown. Objectives: To quantify the association between antidepressant use during pregnancy and the risk of miscarriage.
Methods: A nested case-control study was conducted within the Quebec Pregnancy Registry. Women were eligible for this study if they were; 1) between 15-45 years old on the first day of gestation and covered by the Quebec drug plan for at least 12 months before and during pregnancy. Cases were defined as pregnant women with a diagnosis or a procedure related to a miscarriage and index date was defined as calendar time at the time of the diagnosis or procedure, whichever came first. Ten controls per case were randomly selected within the remaining cohort and matched on cases index date. Women with a procedure related to planned abortions were excluded. Conditional logistic regression models were used to calculate odds ratio (OR) and 95% confidence intervals (95%CI), adjusting for potential confounders.
Results: 5124 cases and 51240 controls were included for analyses. Antidepressant use was associated with the risk of miscarriage (OR 1.68, 95%CI 1.38-2.06). Stratified analyses revealed that paroxetine (OR 1.75, 95%CI 1.31-2.34) and venlafaxine users (OR 2.10, 95%CI 1.34-3.30) had a higher risk of miscarriage than none users.
Conclusions: Gestational use of antidepressant medications, especially paroxetine and venlafaxine, significantly increased the risk of miscarriage.
Keywords: *Antidepressant, pregnancy, miscarriage*

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Case series as a tool for therapeutic risk management: a review of the literature

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Funding Source: None
Background: Case series of adverse drug effects are considered a cornerstone of drug safety surveillance, having led to most market withdrawals. However, their characteristics remain poorly examined to date. Objective: To describe the characteristics of drug-related case series published in the literature.
Methods: All articles published from 2003 to 2007 which focused on drug safety were identified. Medline keywords included "case series" "adverse drug reaction", "pharmacovigilance", "drug safety".

Results: A total of 173 articles met the search criteria. After screening abstracts, 88 (50.9%) were excluded because they were not case series or were not drug-related. Among those retained, 77 corresponded to series of at least two cases of similar characteristics, 4 arose from observational studies, 2 were an epidemiological design, 2 were from the Prescription Event Monitoring system. The median number of cases included in a series was 5 (range: 2 – 1,411). Adverse effects involved in rank order: skin, eye, allergic or hypersensitivity reactions, nervous and circulatory. The main drug classes ascribed as causal factors were: CNS, anti-infective, anti-cancer and immuno-modulating agents, alimentary tract and metabolism, and cardiovascular drugs.
Conclusions: This literature review confirms the considerable heterogeneity in the nature and characteristics of published case series on adverse drug effects. Since major consideration is given to case series for regulatory decisions, one may highlight the following methodological gaps: lack of harmonization in the recruitment period, sample size, and, for each case series, absence of data on the number of cases of adverse effects needed to warrant a regulatory intervention.
Keywords: *Case series, drug safety, therapeutic risk management*

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Cholinesterase inhibitors and hospitalization for bradycardia: a population-based study

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Funding Source: CIHR
Background: Cholinesterase inhibitors enhance the effects of acetylcholine and reports suggest they may precipitate bradycardia in some patients. We examined the association between use of cholinesterase inhibitors and hospitalization for bradycardia.
Methods: We examined the healthcare records of more than 1.4 million older adults using a case-time-control design, allowing each individual to serve as his or her own control. Case patients were residents of Ontario, Canada, aged 67 years or older hospitalized for bradycardia between January 1, 2003 and March 31, 2008. Control patients (3:1) were not hospitalized for bradycardia, and were matched to the corresponding case on age, sex, and a disease risk index. All patients had received cholinesterase inhibitor therapy in the 9 months preceding the index hospitalization.
Results: We identified 1009 community-dwelling older persons hospitalized for bradycardia within 9 months of using a cholinesterase inhibitor. Of these, 161 cases informed the matched analysis of discordant pairs. After adjusting for temporal changes in drug utilization, hospitalization for bradycardia was associated with recent initiation of a cholinesterase inhibitor (adjusted odds-ratio, 2.13, 95% confidence interval 1.29 to 3.51). Despite hospitalization for bradycardia, more than half of the patients (57%) who survived to discharge subsequently resumed cholinesterase inhibitor therapy.
Conclusions: Among older patients, initiation of cholinesterase inhibitor therapy is associated with a more than doubling of the risk of hospitalization for bradycardia, with some instances resulting in death. Resumption of therapy following discharge is common, suggesting that the cardiovascular toxicity of cholinesterase inhibitors is underappreciated by clinicians.
Keywords: *Cholinesterase inhibitors, bradycardia, adverse drug events*

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Comparison of sleep quality between benzodiazepine users and non users

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Background: Sleep disturbances are frequently reported by older adults, and benzodiazepines (BZD) are the drugs most often prescribed to treat these problems. Nearly 25% of older adults use BZD, with 83% of users experiencing sleep problems. Although duration of use should not exceed 3 months, previous studies conducted in a real-life setting reported longer durations. This study aimed at assessing the association between duration of BZD use and sleep quality in community-dwelling elderly age 65+.
Methods: A prospective cohort study (the Seniors Health Survey (ESA)), was conducted in a representative sample of community-dwelling elderly in Quebec (n=892). Sleep quality was assessed using the Pittsburgh Sleep Quality Index scale and a structural equation modeling strategy was used to assess the association with BZD use.
Results: Two groups were compared: sleep disturbed (n=466) and non-sleep disturbed (n=426) at onset of BZD use. Over a one-year follow-up, quality of sleep

among patients initially sleep-disturbed tended to improve (slope= -0.92). However, long-term BZD use tended to slow the improvement. In the group of initial non-sleep disturbed, sleep tended to deteriorate (slope=0.78). Long-term use of BZD led to an increase in the rate of deterioration.
Conclusions: Results show that the long-term use of BZD could be ineffective. A frequent follow-up by practitioners is recommended to evaluate the quality of sleep among long-term BZD users and optimize the benefits of these drugs.
Keywords: *Sleep quality, benzodiazepines, lisrel*

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Economic evaluation of rivaroxaban vs. enoxaparin in Canadian patients undergoing total hip replacement (THR) and total knee replacement (TKR)

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Background: To assess the cost-effectiveness of rivaroxaban versus subcutaneous enoxaparin for the prevention of venous thromboembolism (VTE) following THR or TKR from a Canadian provincial payer perspective.
Methods: A cost-utility model was developed. Analyses were conducted from the perspective of the provincial Ministry of Health over a 5 year time horizon. The efficacy and safety of rivaroxaban vs. enoxaparin were derived from the RECORD clinical trials. RECORD 1, which compared equal durations of prophylaxis with rivaroxaban and enoxaparin 40 mg od (5 weeks) was used for THR. RECORD3, which compared 2 weeks of prophylaxis with rivaroxaban to 2 week of prophylaxis with enoxaparin 40 mg od, was used for TKR. The risk of VTE events and post-thrombotic syndrome beyond the trial period was estimated using published data. Costs were derived from Canadian sources and expressed in 2007 Canadian Dollars (C$). Utility values were derived from published literature.
Results: When equal durations of rivaroxaban and enoxaparin are compared In THR, rivaroxaban dominates enoxaparin. That is, it is associated with greater benefit (0.0005 QALYS) and less cost (savings of $264) per patient. Similarly, in TKR, rivaroxaban dominated enoxaparin, achieving greater QALYs (0.0021) at a lower cost (savings of $107) per patient. In addition, when the higher price of enoxaparin 30mg bid was used instead of 40mg od ($12.38 vs. $8.20), rivaroxaban still dominated in THR and TKR.
Conclusions: Rivaroxaban is a cost-effective alternative to enoxaparin, providing greater benefit at a lower cost, for VTE prophylaxis in patients undergoing THR and TKR.
Keywords: *Rivaroxaban, cost-effectiveness analysis, orthopaedic surgery*

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ePrescribing: current state, perceived benefits and barriers

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Background: ePrescribing is often viewed as a 'breakthrough technology' for healthcare. Our objective in this study was to assess the current state of ePrescribing internationally and to identify key barriers and incentives to ePrescribing implementation as expressed by key stakeholders using Ontario as the sample jurisdiction.
Methods: A narrative literature review using MEDLINE 1996-present and Google was conducted. Stakeholders (n=30), representing eHealth and drug program leadership, federal and provincial governments, health technology assessment groups, academia, professional and patient associations and eHealth vendors were recruited to structured individual interviews which were audio-recorded. Analysis was qualitative.
Results: Canada lags behind other nations including the United States, in the reported use of ePrescribing, although reported use could not be independently validated. No-one has demonstrated the cost-effectiveness of ePrescribing for improving patient outcomes. All provinces and territories are at various stages of planning for ePrescribing implementation. Each stakeholder interviewee expressed faith in the potential benefits to patient safety, medication management and population research; few were aware of the lack of evidence of clinical benefit. Main barriers noted were costs and the lack of leadership provincially and nationally.
Conclusions: Despite a lack of supporting evidence, there are broadly held beliefs that ePrescribing can improve the quality of medication prescribing, dispensing and utilization but leadership and cost issues are seen to be impeding progress. A consensus

on a 'critical path' towards successful ePrescribing, incorporating and developing best evidence on each step, may be of benefit.

Keywords: *ePrescribing, qualitative research, stakeholder engagement*

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Factors associated with taking antihypertensives - a population-based cross-sectional study of hypertensive patients in the Canadian Community Health Survey

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Background: Hypertension affects 20% of Canadians and despite clear evidence for common antihypertensives, many remain untreated. We examined factors associated with taking antihypertensives in a population of Ontarians with hypertension, including prescription drug coverage and demographic, socioeconomic and health status characteristics.

Methods: Using the population-based, cross-sectional Canadian Community Health Survey (CCHS) Cycle 3.1, we evaluated respondents 30 years of age and older that reported having hypertension and whether they had prescription drug coverage. Multivariate logistic regression was used to determine the adjusted odds ratios (AOR) of factors associated with taking antihypertensives.

Results: Of 7,662 respondents, over half were female and over age 65. Over 80% of respondents lived in dwellings owned by a household member and reported having prescription drug coverage. In total, 90% of respondents took antihypertensives (91% of insured and 87% of uninsured). While there was no association between taking antihypertensives and having coverage (AOR 1.16 95% CI 0.96-1.39), seniors were more than four times as likely to take an antihypertensive than those under age 65 (AOR 4.38 95% CI 3.60-5.34) and 14 times more likely than those in their 30s (AOR 13.96 95% CI 10.64-18.32). Respondents with diabetes, heart disease or a history of stroke were two to three times more likely to take antihypertensives.

Conclusions: In hypertensive respondents, prescription drug coverage was not significantly associated with taking antihypertensives. However, older age and cardiovascular comorbidities significantly increased the likelihood, suggesting that attempts to improve access to care should be targeted at younger individuals and primary prevention.

Keywords: *Hypertension, insurance, quality of health care*

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Fracture risk from cardiovascular medications: a population-based analysis

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Background: Various classes of cardiovascular drugs have been associated with either decreased risk of fracture in older adults or the association has been equivocal. The aim of this study was to better define the magnitude of fracture risk with cardiovascular medications.

Methods: Population-based administrative databases were used to examine cardiovascular medication exposure and fractures in persons aged 50 years and older in Manitoba between 1996 and 2004. Persons with osteoporotic fractures (vertebral, wrist, or hip [n =15,792]) were compared with controls (3 controls for each case matched for age, sex, ethnicity, and comordibity [n = 47,289]). Medications examined included antianginals (beta blockers, organic nitrates, and calcium channel blockers), diuretics (thiazide, high ceiling and potassium-sparing), statins and anticoagulants. Conditional logistic regression analysis was used to calculate odds ratios with 95% CIs. Multivariate models were adjusted for demographic variables and confounding diagnoses and medications.

Results: Statins were associated with the lowest adjusted odds of osteoporotic fractures (adjusted odds ratio [OR] = 0.84; 95% confidence interval [CI], 0.78 – 0.90). Lower fracture risk was also associated with thiazide diuretics (OR = 0.84; 95% CI, 0.79 – 0.89) and beta blockers (OR 0.91, 95% CI, 0.86-0.97). The effects of other antianginal drugs, non-thiazide diuretics and anticoagulants on fracture risk were not significant.

Conclusions: This study provides further evidence of the relationship between fractures and the use of cardiovascular medications in an elderly population. Three classes of cardiovascular drugs seem to be protective against fractures: statins, thiazide diuretics and beta blockers. These findings are consistent with other summary reports in the literature.

Keywords: *Fracture, cardiovascular pharmcoepidemiology*

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Illegal use of prescription drugs prior to the implementation of a province-wide Pharmacy Network

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Background: The extent of prescription drug abuse in Canada is not clearly understood. The purpose of this study was to gain an understanding of the issue of prescription drug abuse and examine the expected impact of a province-wide Pharmacy Network in Newfoundland and Labrador. This study is a component of a larger study evaluating the impact of the Pharmacy Network on prescription drug abuse.
Methods: Forty-four professionals involved with prescription drug abuse were invited to participate in a focus group or interview. A series of open-ended questions guided the discussions. A questionnaire was administered to 500 pharmacists and 1032 physicians throughout the province, consisting of closed-ended, open-ended and Likert scale questions.
Results: Thirty-two individuals participated in a focus group or interview. Survey response rate was 46.9%. Findings indicated that benzodiazepines, oxycodone and codeine are the drugs in highest demand. Double-doctoring was thought to be the most common method of obtaining prescription drugs and participants felt that this is the area in which the Pharmacy Network will have the greatest impact. Potential negative consequences following the implementation of the Pharmacy Network include an increase in crime and greater demand on addiction services.
Conclusions: The Pharmacy Network is expected to reduce prescription drug abuse, though it is recognized that it is a multifaceted problem that cannot be fixed with a single intervention. Findings of the pre/post implementation study can be used to support public health decision-making to help address the issue of prescription drug abuse.
Keywords: *Prescription drug abuse, Pharmacy Network, qualitative study*

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Impact of missing data on potential confounders in perinatal pharmacoepidemiologic studies using administrative databases

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Background: Administrative databases are increasingly being used in perinatal pharmacoepidemiology. Although such studies have increased statistical power, they are prone to biases due to lack of information on potential confounders. Hence, the objective was to quantify the degree of bias introduced by the lack of data on smoking status and maternal pre-pregnancy weight in the association between gestational exposure to antidepressants and the risk of low birth weight (LBW) infants.
Methods: The Quebec Pregnancy Registry was used to sample a cohort of women who had delivered a liveborn singleton, and answered a self-administered questionnaire on lifestyles during pregnancy and family history. The association between antidepressant use during pregnancy and the risk of LBW was calculated unadjusting for smoking status and maternal pre-pregnancy weight using the Registry data. The association was further estimated adjusting for smoking and maternal pre-pregnancy weight using the questionnaire data. Percent bias in the Registry estimate was calculated using Schneeweiss' method.
Results: Overall, the unadjusted estimate (Registry data) for the association between antidepressant use during pregnancy and the risk of LBW was 1.16 (p>.05). Adjusting for smoking status resulted in an estimate of 0.99 (p>.05), and for maternal pre-pregnancy weight, 1.19 (p>.05). The percent bias introduced by the non-adjustment for smoking and maternal pre-pregnancy weight using only the Registry data was 13%, and did not change the direction of the effect.
Conclusions: Although data on potential confounders are often missing in perinatal pharmacoepidemiologic studies using administrative databases, the bias that results for the non-adjustment does not necessarily invalidate findings.
Keywords: *Quebec Pregnancy Registry, unmeasured confounders, bias*

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Macrolide-induced digoxin toxicity: a population-based study

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Background: Macrolide-induced digoxin toxicity is widely appreciated. However, macrolides inhibit P-glycoprotein to varying degrees, and there is relatively little data examining the risk of digoxin toxicity with the various macrolides.
Methods: We conducted a population-based nested case-control study using healthcare records of Ontarians aged 66 and older treated with digoxin between April 1, 1993 and March 31, 2008. Cases were those hospitalized for digoxin toxicity during follow-up, Up to 4 controls were matched to each case on age, gender, history of renal disease, and index date. Exposure to macrolide antibiotics in the 14 days prior to index date was determined for all patients.
Results: Of 327,142 individuals treated with digoxin, we identified 1659 cases with digoxin toxicity and 6,439 controls. Following extensive multivariate adjustment, the highest risk of digoxin toxicity occurred within 14 days of receiving a prescription for clarithromycin (Adjusted OR 13.4; 95% C.I. 7.1 to 25.2) and a much lower risk with erythromycin (AOR 3.9; 95% C.I. 1.8 to 8.5). We identified an increased risk of digoxin toxicity with azithromycin that did not reach statistical significance (AOR 2.7; 95% C.I. 0.8 to 9.1). We found no such risk with cefuroxime, which we included as a test of specificity.
Conclusions: In older patients taking digoxin, treatment with clarithromycin is associated with a more than 3-fold greater risk of digoxin toxicity than erythromycin. Although azithromycin is perceived as safe during treatment with digoxin, our data suggest that azithromycin can precipitate digoxin toxicity. Further research is needed to explore this possibility.
Keywords: *Drug interaction, digoxin, macrolide antibiotics*

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Oncology drugs in non-small cell lung cancer treatment: actual utilization versus treatment guidelines

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Background: Administrative databases from cancer agencies are invaluable in establishing actual utilization of oncology drugs. Using such a database, this study compares the most widely administered regimens in non-small cell lung cancer (NSCLC) therapy to treatment guideline recommendations.
Methods: This retrospective, longitudinal cohort study examined NSCLC patients who received chemotherapy in 2006/2007 in 12 Cancer Care Ontario (CCO) affiliated centers. Regimens were identified based on patients' utilization of oncology drugs. Patients were assumed to have progressed to further lines of therapy following a change in dispensed regimen or a significant break in therapy (more than 100 days). A total of 5,827 patients were included in the study; all received at least one line of therapy.
Results: The most commonly used first line regimens were: vinorelbine & cisplatin, gemcitabine & cisplatin and gemcitabine & carboplatin, dispensed to 39%, 11% and 10% of patients, respectively. These regimens tend to coincide with first line therapies recommended by CCO. A second line of therapy was dispensed to 38% of patients. Of those, 34% received 3-week or weekly docetaxel, 16% were dispensed vinorelbine and 9% were treated with vinorelbine & cisplatin. Only 9% of patients continued to a third line of therapy, with 51% of them receiving docetaxel. Regimens dispensed beyond first line tend to differ from CCO treatment guidelines.
Conclusions: Departures from guidelines in NSCLC treatment tend to increase as patients progress beyond first-line therapy. Oncologists can use discretion when treating patients to ensure they receive the safest and most effective care given their condition.
Keywords: *Retrospective longitudinal cohort study, non-small cell lung cancer, cancer care*

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Patient preferences towards the clinical adoption of pharmacogenomics: a discrete choice experiment and implications for health policy

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Background: Pharmacogenomics, the study of the effects of genetic differences between individuals in their responses to drugs in terms of their metabolism or action, is increasingly being translated into personalized medicine applications. However, the adoption and diffusion of personalized medicine applications has been slow. There has been relatively little empirical work evaluating how novel genomic diagnostic and drug combinations will be accepted and adopted by patients. The objective of this study was to quantitatively assess patient preferences for novel genomic diagnostics and targeted therapeutics, and identify the attributes considered important by patients

including willingness-to-pay for pharmacogenomics-based treatments.
Methods: We used conjoint analysis, a method that has roots in economics, to measure patient preferences for novel genomic diagnostics and assess the relative importance placed in different attributes. In congruence with discrete choice theory, attribute levels were assigned to represent the range of values or characteristics. Generation of scenarios based on the attributes and levels were created using SAS.
Results: The use of genomic diagnostics to facilitate personalized medicine has considerable support from patients; however, our data revealed that participants were concerned with a number of issues. Questions regarding willingness to pay revealed: patients would be more willing to pay out-of-pocket if the disease associated with pharmacogenomic testing for treatment was perceived to be high risk vs. a chronic condition that was perceived as lower risk.
Conclusions: As the personalized medicine approach is increasingly incorporated into health care, understanding patient preferences will become progressively more important for the development of appropriate health policies.
Keywords: *Personalized medicine, pharmacogenomics, discrete choice methods*

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The monetary value of a genetic test for muscular adverse events induced by statins

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Background: Statins have proven their effectiveness in the treatment of dyslipidemias. However, these molecules are associated with muscular side effects. Since these side- effects play an important role in the discontinuation of statin therapy it is of interest to develop a test that would identify a priori the patients who are likely to develop them. The determination of the monetary value of this test is an important component of the multidisciplinary team working on this project.
Methods: We used Discrete Event Simulation (DES) to study a cohort of 10 000 hypothetical patients newly started on statin therapy. This virtual population was cloned to have two identical cohorts of patients. One cohort received the test and an appropriate treatment and the other cohort did not have the test and received the actual standard treatment (a statin). Both cohorts evolved in a model with cardiovascular, side-effects, mortality and compliance risk with a follow up of 15 years. We then compared the costs and the consequences incurred by these two populations.
Results: The cohort with the test cost $124 more in medications, $170 less for the treatment of cardiovascular diseases and $134 more in the treatment of muscular side-effects. The total mean cost for the cohort without the test was $180 more than the cohort with the test.
Conclusions: These results suggest a value of $180 per test. However the incidence, hazard functions, costs and consequences of the side-effects will have to be determined by an ongoing prospective field study since they are not available in the literature.
Keywords: *Economic, genetic, statin*

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The unintended effects of prescription contraception: experiences of youth in northern British Columbia

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Background: The social space necessary to access contraceptives, (e.g., the look, feel, and location of health services), creates an unintended barrier to the effective use of birth control. This study evaluated the impact of gender, place and culture on the experiences of northern youth in accessing and using contraception.
Methods: Ethnographic fieldwork was employed in Fort St. James (population 2,000). During 8 weeks of participant observation, in-depth interviews were conducted with 23 female and 22 male English-speaking youth (ages 15 – 24) with varied socio-cultural and economic backgrounds and diverse contraceptive experiences, using a targeted sampling strategy. During the interview, youth mapped the routes they typically travelled in the community.
Results: Findings suggest that the process of prescribing contraceptives erects unintentional barriers to access and use. Youth described facing obstacles that included emotional discomfort with the physical setting of the clinic; the social stigma associated with the geographic location of the clinic; and a lack of a safe place and space to gain knowledge about contraception options, including the real and imagined side effects.
Conclusions: Although the Canadian Contraception Consensus Guidelines provide information for health-care providers regarding the provision of contraception-related services (e.g., prescribing hormonal birth control), this kind of approach has been criticized for an over-emphasis on more medicalized

views of sexual health and for not fully considering the unique needs of youth. Thus, our study focuses on identifying the ways in which social space creates an unintentional youth culture of resistance to contraception access and use.

Keywords: *Hormonal contraception, youth, ethnographic fieldwork*

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Validity of a model mapping quality of life scores to utility scores in lymphoma

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Background: Utility scores are a common measure of effectiveness in pharmacoeconomics. While clinical trials frequently collect quality of life (QoL), instruments to measure utility scores are often omitted. Recent studies have investigated models for deriving utility from QoL scores. The purpose of the analysis was to examine the validity of modelling utility scores in lymphoma.

Methods: EQ-5D elicited utility scores and FACT-G was collected from 184 consecutive lymphoma patients. The EQ-5D is a generic QoL instrument while the FACT-G is cancer specific with four domains (physical, social/family, emotional and functional well-being). Patients at all disease stages irrespective of treatment were eligible. A linear model was used to predict utility scores from the four FACT-G domain scores. Ten-fold cross-validation was used to assess fit.

Results: The mean age for patients 4.5 years. All four ±15.7 years. The mean time since diagnosis was 4.5±was 57.2 FACT-G summary scores were included in the final model ($p < 0.1$ for all independent variables). Adjusted R-squared for the model was 0.63. Mean (standard deviation) utility score for the actual and predicted were 0.81 (0.17) and 0.81 (0.11) respectively. Mean squared error was 0.02.

Conclusions: The analysis demonstrated a potential model for deriving utility from QoL scores. The predicted mean utility score was comparable to the actual utility score. However, the model tended to poorly predict lower utility scores since fewer patients with low utility scores were available in the current analysis.

Keywords: *Quality of life, utility score, regression*

POSTER PRESENTATIONS

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A stakeholder analysis of consumers' and pharmacists' willingness to accept and provide enhanced pharmacist services: a use of mixed methods to inform on policy implementation

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Funding Source: Faculty of Pharmacy Lesley Buggey Scholarship

Background: Pharmacists have been shown to improve appropriate medication use when given the opportunity. As a result, limited prescribing rights for pharmacists have been introduced. We examined these rights from consumer and pharmacist perspectives. Preference for pharmacists providing and consumers receiving refill prescriptions, emergency dispensations, over-the-counter (OTC) advice and complex regimen monitoring were determined; the effect of paying for these services was also examined.

Methods: A web-based survey was used to describe pharmacist and consumer willingness to provide/use these services. Influential facilitators and barriers were also identified. Contingent valuation methods using hypothetical purchase scenarios and conjoint analysis were used to do predict the provision/use of these services by pharmacists/ consumers when a price was assigned to the service.

Results: Respondents included 452 consumers (MB) and 601 pharmacists (BC, AB, MB, ON, PEI). 40% of pharmacists and consumers were ready to provide/receive pharmacists services within 1 month. Whereas 80% of pharmacists would provide refills, OTC advice and emergency prescriptions, fewer than 50% would provide medication management. Of consumers, 77% would use the refill service, 30% would seek OTC advice and use emergency dispensations; 12% of consumers would use monitoring services. Pharmacists and consumers assigned the highest utility to the pharmacy that provided the refill service at the lower price level ($15.00/10 min).

Conclusions: The results of this study indicate that there is a comparable readiness to provide new pharmacy services by pharmacists and willingness to accept these services by consumers, with the highest value placed on refill services at the pharmacy level.

Keywords*: Pharmacy, prescribing, behaviour*

19 – ENCORE PRESENTATION

Alignment to prophylaxis guidelines and occurrence of venous thromboembolism after total hip and knee replacement

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Burden of illness of venous thromboembolism following total hip and total knee replacement in Canada

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Background: The purpose of this study was to estimate the annual Canadian burden of VTE-related events following total hip and total knee replacement (THR and TKR). The burden was evaluated in total and for two subgroups: patients who received prophylaxis 1) in alignment and 2) not in alignment with the American College of Chest Physicians (ACCP) guidelines.
Methods: An incidence-based burden of illness (BOI) model was developed to predict the annual economic and clinical outcomes associated with VTE-related events following THR and TKR. Event rates and ACCP alignment were derived by linking a claims database from a large US health plan to the Premier database, which provides details of inpatient medication use. Costs were determined using the healthcare system perspective.
Results: The model predicts an annual total of 2,434 DVTs, 614 PEs, and 592 deaths in Canadian THR/TKR patients. Event rates were 1.9-fold higher for DVT (3.76% vs. 2.01%, p=0.003), and 8.5-fold higher for PE (1.19% vs. 0.14%, p=0.001) in the non-ACCP relative to the ACCP cohort. The annual economic BOI was estimated at $18,816,781. The cost per ACCP patient was lower than per non-ACCP patient at $213 and $252, respectively. Inpatient costs were almost 3-fold higher in the non-ACCP subgroup.
Conclusions: The Canadian burden associated with VTE-related events in THR/TKR patients is substantial. The increased rate of VTE events and higher per patient cost in the non-ACCP subgroup suggests that options to increase alignment with ACCP prophylaxis guidelines may help reduce the burden to the Canadian healthcare system.

Keywords: *Orthopaedic surgery, VTE prevention, burden of illness*

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Antihypertensive medication use during pregnancy and the risk of major congenital malformations or small-for-gestational-age newborns

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Funding Source: FRSQ

Background: Antihypertensives are among the most widely used medication during pregnancy. Nevertheless, it remains that data on their risks and benefits for the newborn are limited. Objectives: To quantify the association between antihypertensive use during pregnancy and the risk of major congenital malformation (MCM) or small-for-gestational age (SGA) newborn.
Methods: Two separate case-control studies were conducted within the Quebec Pregnancy Registry. In the first study, case was defined as MCM diagnosed during the first year of life and controls were selected from the same cohort with no MCM; index date was date of delivery. Exposure to antihypertensive was defined as filling a prescription for an antihypertensive during the 1st trimester. In the second study, case (SGA) was defined as newborn with a birth weight < 10th percentile for that gestational age and gender; controls were newborns between the 10th and 90th percentile. Exposure was defined as antihypertensive use either during the 2nd or 3rd trimester. Multivariate logistic regression models were used to estimate odds ratio (OR) and 95% confidence intervals (95%CI).
Results: Adjusting for confounders before and during pregnancy, antihypertensive use during the 1st trimester was not associated with the risk of MCM (OR 1.25, 95% CI 0.72-2.16) compared to non-use. However, antihypertensive use during the 2nd or 3rd trimester was associated with an increased risk of SGA (OR 1.53, 95% CI 1.17-1.99) compared to non-use.
Conclusions: This study adds evidence on the risk of antihypertensives use during pregnancy on the newborn with regards to SGA.
Keywords: *Antihypertensive, pregnancy, SGA*

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Benzodiazepine use during pregnancy and the risk of major congenital malformations

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Background: Previous studies have shown that the risk of major congenital malformations is increased among infants exposed to benzodiazepines in utero; other studies have not confirmed this association. We quantify the association between benzodiazepine use during the first trimester of pregnancy and the occurrence of major congenital malformations.

Methods: Within the Quebec Pregnancy Registry we identified a cohort of women who had delivered a live-born infant and had filled at least one prescription for a benzodiazepine in the year prior to gestation. We conducted a case-control analysis: cases were infants with any major congenital malformation, controls were infants with no malformation. Using logistic regression we quantified the association between exposure to benzodiazepines in the first trimester of pregnancy and the occurrence of major congenital malformations.

Results: Among the 3,159 women meeting eligibility criteria, 860 filled a prescription for a benzodiazepine in the first trimester of pregnancy. 10.1% of women who filled a prescription for a benzodiazepine during the first trimester of pregnancy and 9.7% of those who did not, gave birth to a baby with at least one major malformation. Adjusting for several potential confounders, the risk of any major congenital malformation associated with first trimester exposure to a benzodiazepine was OR = 0.99 (95% CI: 0.73-1.34).

Conclusions: This study was conducted in a group of women who had previously filled a prescription for a benzodiazepine, thereby controlling for maternal lifestyle and indication for use. These factors likely led to the previously observed associations between benzodiazepine exposure and congenital malformations.

Keywords: *Benzodiazepines, Quebec Pregnancy Registry, congenital malformations*

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Calcium-based phosphate binders lead to increased progression of vascular calcification in chronic kidney disease

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Background: Cardiovascular (CV) disease is the leading cause of death among patients with Chronic Kidney Disease (CKD). Vascular calcification (VC) is a common feature of CKD that predicts mortality and may contribute to future outcomes. CKD treatment guidelines recommend that calcium-based phosphate binders (CBBs) be restricted to doses of 1.5 g/day elemental calcium, however a previous study showed that this dose was associated with VC in CKD. Similarly, the use of calcium (<1.5 g/day) has been associated with poorer CV outcomes in other patient populations. The aim of this review was to compare the prevalence of VC among CKD patients treated with CBBs and sevelamer.

Methods: A literature search using Medline was conducted using the following terms: CBB, calcium carbonate, calcium acetate, non-CBB, sevelamer, lanthanum, VC, coronary and aorta. Studies reporting mean changes from baseline (%) in VC scores in CBB and sevelamer groups were used for data extraction.

Results: Increased progression of coronary calcification was observed in CBB groups as compared to sevelamer: 13.4% to 50.8% vs. -8.0% to 23.4% (n=6 studies). Sevelamer was associated with regression of aortic calcification compared to CBBs: -71.3% to -13.4% vs. 5.7% to 135% (n=3 studies). Average doses of calcium ranged from 1.39 to 2.3 g/day.

Conclusions: Although the doses of elemental calcium used in these studies approached those recommended by treatment guidelines, CBBs were associated with increased progression of VC, which is a predictor for mortality. More research on the impact of CBBs on VC and future outcomes is required.

Keywords*: Chronic kidney disease, calcium, vascular calcification*

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Clinical bio-equivalent doses versus milligram-equivalent doses of therapeutics for pharmacoeconomic models

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Background: Therapeutically equivalent drugs are chemically dissimilar but produce essentially the same therapeutic outcome and have similar toxicity profiles. Therapeutic equivalent doses usually reflect the starting dose of a drug in clinical practice (real world) and should be considered in economic evaluation. However, this important matter was not considered in

most economic evaluation of statins. Objective: To determine the effect of incorporating clinical bio-equivalent doses versus milligram-equivalent doses of therapeutics in pharmacoeconomic models.
Methods: The benefit of reducing LDL-C was incorporated into a model to calculate reduction in cardiovascular (cardiac and cerebrovascular) events and resulted economic outcomes. Data for LDL-C reduction from a head-to-head RCT [Am Heart J 2002;144:1044-51]; rosuvastatin (starting 5mg and 10mg) versus atorvastatin (starting 10mg) with up-titration doses; and distribution of cardiovascular risk for users [N = 100,000, duration 5 years] in Canadian population [Clin Invest Med 2007;30:E63-E69].
Results: The simulation illustrated that rosuvastatin (starting 5 mg), rosuvastatin (starting 10 mg), and atorvastatin (starting 10 mg) can prevent 9505, 10518 and 8702 cardiovascular events (non-fatal MI and stroke), respectively. Reduction in non-fatal MI and stroke can be translated to $252,300,392, $299,129,432 and $230,980,624 direct cost savings for the Canadian healthcare system. In this simulation, comparison between 5 mg rosuvastatin and 10 mg atorvastatin, which are bioequivalent doses, would be reasonable.
Conclusions: Economic evaluation of therapeutics can accurately support decision-making in resource allocation in healthcare if therapeutically equivalent doses are incorporated into the economic analysis to reflect the clinical comparability of therapeutics.
Keywords: *Pharmacoeconomics, methodology, statins*

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Essentials of incorporating escalating doses (up-titration) of therapeutics in pharmacoeconomic models

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Background: Escalating doses or up-titration reflects pharmacokinetics and pharmacodynamics of therapeutics, which are applicable to clinical protocols in practice setting. Objective: To demonstrate the effect of integrating the fixed doses versus escalating doses of statins in economic models.
Method: The benefit of reducing LDL-C was incorporated into a model to calculate reduction in cardiovascular (cardiac and cerebrovascular) events and resulted economic outcomes. Data for LDL-C reduction from a head-to-head RCT [Am Heart J 2002;144:1044-51]; rosuvastatin (starting 10mg) versus atorvastatin (starting 10mg) with fixed doses as well as up-titration doses; and distribution of cardiovascular risk for users [N = 100,000, duration 5 years] in Canadian population [Clin Invest Med 2007;30:E63-E69].
Results: The simulation illustrated that, if the assumption of fixed doses for rosuvastatin (5 mg) and atorvastatin (10 mg) were incorporated into the model, only 6177 and 5052 cardiovascular events (non-fatal MI and stroke) could be prevented, respectively. This reduction in non-fatal MI and stroke can be translated to $161,731,394 and $128,586,496 direct cost savings for the Canadian healthcare system (adherence to therapy was assumed to be at the level of RCT). Incorporation of fixed doses instead of up-titration of rosuvastatin and atorvastatin into the model underestimated the direct cost savings from statin therapy as much as $90,568,998 and $102,394,128, respectively.
Conclusion: Management of hyperlipidemia with statins in clinical practice requires up-titration of the drug to achieve pre-defined goals. This fundamental fact should be reflected in economic evaluation of statins.
Keywords: *Pharmacoeconomics, methodology, statins*

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Cost-effectiveness of antidepressants in the adult patient population of Quebec: persistence as an indicator of effectiveness

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Background: Although practice guidelines recommend that antidepressants (ADs) be used for at least 6 months, premature discontinuation is very frequent in a "real-life" setting. Previous studies have assessed the economical impact of non-persistence but differences across products remain inadequately explored. Objective: To compare treatment persistence and incremental cost-persistence ratios across products (excl. tricyclics) in the adult population covered by the public drug program of Quebec.
Methods: A retrospective cohort study was conducted in a random sample of 13,936 adults ages 18 - 64 who initiated an antidepressant treatment in 2003. Persistence was defined as treatment duration of at least 6 months. Economical impact was assessed over the first year of treatment through drug costs (antidepressants and all other drugs), medical services costs (psychiatric- or non-psychiatric), hospitalization costs, and total health care costs. Comparisons across

products were conducted using the incremental cost-persistence ratio (ICPR).
Results: Treatment non-persistence ranged from 60.4% (paroxetine) to 65.1% (citalopram). The product associated with the highest total health care costs was citalopram (CDN$2,653) and the lowest was venlafaxine (CND$2,168). Fluoxetine was associated with the lowest medical services costs (CND$473) and hospitalization costs (CND$702), and citalopram with the highest for both types of costs: CND$559 and CND$970, respectively. The ICPR for total health care costs ranged from CDN$119 (fluoxetine) to CDN$1,283 (paroxetine).
Conclusions: Total costs were similar across products except for citalopram, which was more costly. In our ICPR analyses, paroxetine, fluoxetine and venlafaxine appear to be the best choice compared to the other antidepressant alternatives.
Keywords: *Antidepressants, persistence, cost-effectiveness*

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Impact of frailty on risk management strategies in the elderly population: psychotropic medications as a case study

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Background: Psychotropic drugs are known to be extensively used in the elderly population. However, the majority of studies on the effects of these drugs have considered the elderly as whole, without attempts to distinguish between specific subpopulations. Such comparisons are warranted as they may impact directly on risk management plans and risk minimization strategies. Objective: This study aimed at comparing the use of psychotropic drugs (incl. benzodiazepines, antidepressants, antipsychotics) in two distinct elderly subpopulations of community-dwelling elderly: the demented and the non-demented.
Methods: Data originated from two observational cohort studies: 1) a cohort of elderly with Alzheimer's Disease (AD) assembled through the Quebec prescription claims database (n= 18,217); 2) the Seniors' Health Survey (ESA) conducted in a representative sample of Quebec community-dwelling elderly (n=2,800). Patterns of psychotropic drug use at baseline and over the first 12 month of follow-up were characterized through dosages and duration.
Results: At the time of cohort entry (same month as index date), Alzheimer's Disease patients used more frequently anxiolytics than community-dwelling elderly (26.27% and 18.3%, respectively) and more antidepressants (19.40% versus 11.0%). After one year of follow-up, 26% of Alzheimer's disease patients are taking antidepressants compared to 12.0% ok community-dwelling elderly. Patterns of use over the first year of follow-up will be presented.
Conclusions: The assessment of the needs for further risk minimization interventions should take into consideration the sub-populations of elderly who will use the drugs.
Keywords: *Risk management, antidepressants, benzodiazepines*

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Costs analysis of the prevention of severe preeclampsia/fetal restriction by dalteparin

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Funding Source: Canadian Foundation for Women's Health, Pharmacia & Upjohn Inc. and Pfizer Canada
Background: Preeclampsia (PE) and intrauterine growth retardation (IUGR) are major causes of maternal and perinatal morbidity and mortality, and consequently have important economic implications. We recently demonstrated that dalteparin, a low-molecular- weight heparin, is effective in preventing the recurrence of these complications in women without thrombophilia. However, dalteparin is an expensive drug. Our objective is to appraise the costs observed in this randomized study.
Methods: Outpatient and inpatient costs, such as the fees of Dalteparin, other drugs, home care program, fetal surveillance tests, delivery mode, maternal and neonatal hospitalisations, were collected in women from the main centre of the clinical randomized study (n=82). The incremental costs of severe PE/ IUGR and the use of dalteparin were calculated in an intention-to-treat basis. Costs are in 2002 Canadian dollars. ISRCTN78732833
Results: Dalteparin was associated with a lower rate of severe PE/IUGR (4.9% vs.24.4%). No serious side effects of the drug were observed. Each case of severe PE/IUGR increased maternal and perinatal costs by $1162 and $8709, respectively. The additional maternal and perinatal costs per woman receiving dalteparin were $970 and $85, respectively. The

incremental cost of preventing one case of severe PE/IUGR was $54.
Conclusions: In the setting of preventing severe complications of pregnancy, dalteparin, at prophylactic dose, is cost-effective.
Keywords: *Pregnancy, dalteparin, costs*

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Critical appraisal of the development and validation of adverse drug event indicators

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Background: Adverse drug events (ADEs) are a major threat to patient safety and result in considerable costs for healthcare systems; many are thought to be preventable. As a result, ADE indicators (signals that alert clinicians of the occurrence of an ADE) have been developed to attempt to identify potential ADEs before they occur. The objective of this study was to critically appraise development and validation methods of ADE indicators described in the literature.
Methods: Using a search strategy developed in collaboration with a research librarian, a literature review was conducted in MEDLINE, EMBASE, and Cochrane Library electronic databases from 1990 to January 2009 and a manual search of references from retrieved articles was performed. Studies were included if they addressed the development and validation of ADE indicators with broad applicability to medical practice.
Results: The majority of selected studies pertained to ADE indicator models targeting the general adult population in an inpatient setting. Most ADE indicators were developed based on findings from the literature and expert panel consensus, often with modifications based on local clinical experience. The most frequent form of validation was comparison against chart review as the diagnostic gold standard and calculation of positive predictive value only. Few studies reported calculations of sensitivity and specificity of indicators.
Conclusions: Few studies were able to provide a complete description of the validity of their ADE indicators. Higher quality methods of development and validation are required for these indicators to be useful diagnostic tools to prevent ADEs.
Keywords: *Adverse drug events, clinical indicators, review*

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Déterminants des variations géographiques de l'usage des médicaments d'asthme au Québec

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Background: Plusieurs études rapportent des variations géographiques dans la médication, mais celles-ci ne sont pas toujours expliquées. Objectif: Identifier les facteurs pouvant expliquer les différences géographiques dans l'utilisation des médicaments d'asthme en vue de mieux apprécier cette utilisation et contribuer à une médication optimale.
Méthodes: La prévalence d'usage, la moyenne standardisée de doses quotidiennes (DDD) par personne couverte et par usager ont été mesurées. À l'aide d'une analyse multiniveaux, les différences entre 73 aires géographiques dans 15 régions ont été appréciées, chez les personnes de 5-44 ans couvertes par le programme d'assurance-médicaments du Québec.
Résultats: La prévalence d'usage s'élevait à 5,7% en 2003 pour la province de Québec, variant de 3,8% à 8,4% selon les aires. L'intensité standardisée de la médication variait d'une aire à l'autre (81,8 à 171,8DDD par usager), avec en moyenne 130,1DDD (±15,7). Elle était de 1,8 à 6,1DDD par personne couverte. En général, ce sont la prévalence d'usage et le taux d'hospitalisation qui contribuent à expliquer les variations géographiques de l'intensité de la médication au Québec. Quant à la prévalence d'usage, elle est liée au milieu de résidence, au pourcentage de prestataires et au tabagisme.
Conclusion: L'approche d'analyse géographique utilisée permet d'identifier certains endroits qui semblent être sujets à des problèmes plus importants de prévalence et de prise en charge de l'asthme. Bien que non exhaustifs, les facteurs explicatifs identifiés dans notre analyse pourraient aider à orienter les actions en vue de la prise en charge de l'asthme. L'accès à des ressources médicales suffisantes et la prise en compte du milieu de vie paraissent nécessaires pour un meilleur contrôle de l'asthme.
Keywords: *Usage de médicaments, asthme, variations géographiques, régression multi-niveaux, analyse des petites aires*

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Small-area variations in asthma medication

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Background: The use of medication is a field subject to geographic variations that has not been widely researched. In the case of chronic diseases, it would be useful to understand the differences, not only in terms of prevalence but also in terms of medication. Purpose: To partition the regions of Quebec into pertinent geographic areas and to examine geographic differences in asthma medication among asthmatics using administrative data.
Methods: Ward's cluster method was used to establish relatively homogeneous geographic areas based on a distribution by age and deprivation. Data from RAMQ pharmaceutical service claims (2003) were used to assess the intensity, distribution and quality of asthma medications among users in each area.
Results: Seventy-three geographic areas were created. Antiasthmatics were used by 5.7% of the population in 2003, ranging from 3.8% to 8.4% depending on the region. Inhaled Short-acting B2 antagonists and inhaled corticosteroids were most frequently prescribed. Considering the average annual number of antiasthmatics per user, 122 DDD were executed (81 to 162 per district). In the majority of districts, there were fewer users and fewer DDD of ICS than ISABA.
Conclusions: Even though guidelines exist to regulate the medical management of asthma, we observed important variations in the intensity and quality of asthma medication at the heart of Quebec's asthma population.
Keywords: *Asthma, small-area analysis, medication use*

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Determining the minimal clinically important difference for important outcomes of statin therapy

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Background: The objectives of the study were to examine the method of selection for the delta that statin trials were designed to detect, and to establish a minimal clinically important difference with prescribing physicians. The MCID was defined as the smallest benefit of statin therapy that would result in physicians recommending it to their patients after considering potential harm and cost.
Methods: A systematic review of RCTs of statin therapy was conducted. Methods of selecting the delta were critically appraised. A self-administered questionnaire was faxed or mailed to 736 Hamilton physicians. Using specific scenarios, they provided a MCID for statins and vascular outcomes.
Results: Most studies (15/28) did not provide a justification for the size of the delta, nor indicate whether it represents the MCID. Results of the physician survey(n=176) showed that physicians would recommend statin therapy if it would at least reduce the relative risk of coronary death, non-fatal MI, stroke, coronary revascularization, and any major vascular event(composite of the four outcomes) by 31.6%(SD:19.6), 33.5%(SD:18.6), 31.7%(SD:20.5), 34.3%(SD:19.4) and 31.2%(SD:19.4) respectively. For patient scenarios involving a 30%, 13% and 5% baseline risk of developing a vascular event in five years, physicians would recommend treatment if it reduced that baseline risk by 31.4%(SD:19.8), 34.6%(SD:18.0), and 46.2%(SD:24.6).
Conclusions: Most statin trials seemed to be designed to produce a statistically significant result without taking into account its clinical importance. Better reporting guidelines may be required. We also have shown that it is possible to elicit a MCID across vascular outcomes, but with inter-physician variability.
Keywords: *Minimal clinically important difference, statin, physician opinion*

33 – ENCORE PRESENTATION

Disease-modifying anti-rheumatic drug (DMARD) exposures and serious infections in seniors with rheumatoid arthritis (RA): a nested case-control study

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34 – ENCORE PRESENTATION

Tuberculosis (TB) in a population-based cohort of seniors with rheumatoid arthritis (RA)

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35 – ENCORE PRESENTATION

Use of administrative data to determine the potential effects of a national consensus statement on optimal early rheumatoid arthritis (RA) treatment in persons >65

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36 – ENCORE PRESENTATION

Utilization of biologic response modifying drugs (BRMs) by Ontario rheumatology specialists

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Does the Canadian general public support an increase in annual taxes to provide access to an Alzheimer's disease medication?

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Background: To measure support for a program of unrestricted access to AD medications and identify determinants of support.
Methods: A national sample of 500 adult Canadians was randomly recruited to participate in a telephone interview. The sample was stratified by income. Participants were presented with a set of randomly-ordered scenarios describing a new, hypothetical AD medication. The efficacy of the medication was varied by scenario: the medication was alternately described as modifying the symptoms of cognitive decline or actually halting disease progression. The adverse effects profile was also varied in the scenarios: no adverse effects or a 30% chance of some adverse effects. For each scenario, participants were asked whether they supported an annual increase in personal income taxes to fund unrestricted access to the AD medication. Logistic regression was conducted to identify factors that might explain support for the tax increase.
Results: Support varied: symptom modification and 30% chance of adverse effects=49% (n=244); symptom modification, no adverse effects=58% (n=290); halt progression and 30% chance of adverse effects=54% (n=270); halt progression, no adverse effects=67% (n=333). Relative to the 'symptom treatment and 30% chance of adverse effects' scenario, the level of support was different ($p < 0.05$) for all except the 'halt progression and 30% chance of adverse effects' scenario ($p > 0.15$). No determinant (e.g., age, sex) could consistently explain support across all four scenarios.
Conclusions: Support for the tax increase varied by medication efficacy and adverse effects. Most support was registered for the optimal scenario (halt disease progression, no adverse effects).
Keywords: *Alzheimer's, medication, taxes*

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Drug-related problems in patients with vascular risks

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Background: Medications are often the first-line treatment for patients' vascular risks, but patients may experience medication management barriers and drug-related problems (DRPs) that interfere with the goals of their drug therapy. Our objective in this study was to examine medication use and types and frequency of DRPs reported by patients with vascular risks.
Methods: We analyzed baseline medication data of adult primary care patients participating in a randomized controlled trial, which had a primary goal to evaluate the effect of a shared Web-based vascular tracker intervention on improving vascular risk

management. The Brief Medication Questionnaire was administered via telephone interview and data on medication use and DRPs was collected and a descriptive analysis was conducted.

Results: A total of 1046 patients (mean (standard deviation [SD] age 70.3 (8.6) years) completed the questionnaire. Patients were taking a mean (SD) of 4.5 (2.6) prescribed medications and a mean (SD) of 2.2 (1.6) vascular medications. A majority of patients (59.4%) reported experiencing at least one DRP, and patients experienced a mean (SD) of 1.1 (1.2) DRPs. The most commonly reported DRPs and medication issues included medications causing side effects (24.9%), difficulty opening the medication container (23.1%), and difficulty reading the print on the medication container (10.9%).

Conclusions: A significant proportion of patients with vascular risks experience DRPs and issues with their medication treatment. Eliminating barriers to medication use and management will enable patients to receive the most benefit from their drug therapy.

Keywords: *Medication management, drug-related problems, cross-sectional analysis*

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Emergency department experiences of senior fallers: an operations research analysis

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Background: Among seniors, falls account for 10% of all Emergency Department (ED) presentations. Previous research on senior fallers ED experiences indicates that the time they spend in the ED often exceeds current standards. This study was designed to prospectively evaluate characteristics of elderly fallers' ED experience including: care received; flow through the ED; and wait times.

Methods: Recruitment took place between September 2007 and November 2008 at Vancouver General Hospital (VGH) ED, a tertiary care institution with >1300 fall related ED presentations by seniors annually. We recruited cognitively intact individuals aged 70+ who could read/speak English and whose primary reason for ED presentation was a fall. Information was collected on participant demographics, fall mechanism, and ED care.

Results: Data were collected on 100 fall related ED presentations. The average age of fallers was 82.5 (SD:6.3) years, 76 of whom were female. 36 fallers were hospitalized, and 67% of those had subsequent in-hospital surgeries. On average, fallers discharged to community waited 88 (SD:57) minutes to see an emergency physician and spent 283 (SD:151) minutes in the ED. For those admitted to hospital, the mean time spent in the ED was 861 minutes (SD:493), of which 60 minutes (SD:56) were spent waiting for an emergency physician assessment. The recommended wait time to see a physician and the total time in the ED were exceeded for 70 and 60 participants respectively.

Conclusion: Falls in seniors place significant burden on EDs, with over 1/3 of those who present require admission and 60% experiencing extended ED stays.

Keywords: *Seniors falls, emergency department, operations research*

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Exposure to anti-infective drugs during pregnancy and the risk of prematurity

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Background: Anti-infective drugs are indicated for the treatment of prevalent pregnancy complications such as genital-urinary tract infections, which are associated with a high incidence of prematurity, pelvic inflammatory disease and low birth weight infants. The objective of this study was to quantify the association between anti-infective exposure during pregnancy and the risk of prematurity according to trimester of exposure and indication for use.

Methods: We performed a case-control analysis within the Quebec Pregnancy Registry which was built from the linkage of three administrative databases (RAMQ, Med-Echo and ISQ). Women in the Registry were included in the study if they were continuously insured by the RAMQ drug plan for at least 12 months before and during pregnancy, and if they gave birth to live born singleton. The index date was the date of delivery. Prematurity was defined as a delivery occurring < 37th week of gestation; controls were defined as deliveries

occurring ≥37th weeks. Exposure to anti-infective drugs was categorized using the 2008 ATC classification index. Multivariable logistic regression models were constructed to conduct analysis.

Results: After adjustment for potential confounders, exposure to anti-infective drugs during the 1st trimester was positively associated with an increased risk of prematurity (OR=1.14 (1.03-1.3)). Anti-infective exposure during the 2nd or 3rd trimester was associated with a decreased risk of prematurity (OR=0.8 (0.65-0.98)).

Conclusions: Exposure to anti-infective drugs seems to protect against prematurity. More analyses are needed to investigate the independent impact of each anti-infective class.

Keywords: *Anti-infective drugs, prematurity, Quebec Pregnancy Registry*

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Exposure to herbal products during pregnancy and the risk of low birth weight

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Background: Previous studies showed that up to 55% of pregnant women use at least one herbal product (HP) during gestation. However, evidence on the safety of their use during pregnancy and their impact on pregnancy outcomes remain lacking. Objectives: To quantify the association between HP use, more specifically chamomile, flax, peppermint, and green tea use, during the last two trimesters of pregnancy [≥15 weeks of gestation] and the risk of low birth weight (LBW).

Methods: A questionnaire was mailed to 8505 women selected from the Quebec Pregnancy Registry created by the linkage of three administrative databases: RAMQ, Méd-Echo, and ISQ; 38.5% of women (n=3273) returned their questionnaire, and were included in the study. A case-control analysis was performed. A case was defined as a woman who delivered <2500g baby. A control was defined as a woman with a ≥2500g delivery. Multivariate logistic regression models were carried out to analyze data.

Results: 424 (13.32%) cases were identified. After adjusting for possible confounders, no statistically significant associations between LBW and the use of any HP [OR=1.16; 95%CI 0.23-5.72], flax [OR=1.19; 95%CI 0.24-5.93], chamomile [OR=0.28; 95%CI 0.05-1.44], peppermint [OR=0.15; 95%CI 0.008-3.08], or green tea [OR=3.02; 95%CI 0.55-16.63], during the last two trimesters of pregnancy were detected.

Conclusions: HP use, specifically flax, chamomile, peppermint, and green tea use during the last two trimesters of pregnancy did not significantly increase the risk of LBW. However, more studies are needed to confirm these results.

Keywords: *Herbal products, low birth weight, Quebec pregnancy registry*

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Fluoxetine use during pregnancy and the risk of major congenital malformations

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Background: Recent evidence showing that some types of SSRI use during pregnancy were increasing the risk of cardiovascular malformations has resulted in a decrease in the number of filled prescriptions for antidepressants. Given that fluoxetine is one the most widely used antidepressants, it is important to further quantify the risk of major congenital malformations when used during organogenesis. Objective: Quantify the association between first trimester exposure to fluoxetine and the risk of major congenital malformations.

Methods: A case-control analysis was performed within the cohort of pregnant women included in the Quebec Pregnancy Registry who filled the following eligibility criteria: women had to be 1) 15-45 years of age, 2) covered by the Quebec drug plan ≥12 months before and during pregnancy, 3) using only one type of antidepressant during the first trimester, and 4) have a live birth. Pregnant women exposed to paroxetine were excluded. Cases were defined as any major congenital malformations diagnosed in the first year of life; controls were defined as no malformations.

Results: Among the 861 women meeting inclusion criteria, 58 had given birth to a child with major congenital malformations (7%). Adjusting for possible confounders, exposure to fluoxetine (OR: 0.72, 95%CI: 0.24, 2.21) during the first trimester of pregnancy did not increase the risk of major congenital malformations compared to the use of non-SSRI antidepressants. In addition, no pattern of malformations was observed.

Conclusion: This study showed that fluoxetine exposure in the first trimester of gestation was not associated with the risk of major congenital malformation.

Keywords: *Quebec Pregnancy Registry, fluoxetine, major congenital malformations*

43 – WITHDRAWN

Forecasting the incidence and costs of DM in Canada with alternative population forecasts

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Background: The purpose of this model is to develop updated medium-term projections of the costs of DM in Canada. The goal of the model is to effectively present the potential economic challenges posed by DM to the Canadian economy. The focus is on demographic incidence projection models incorporating the most recent estimates of diabetes incidence and prevalence as well as estimates of direct and indirect health costs. The cost estimates are being derived from unpublished estimates from the recently updated 2000 estimates from the Economic Burden of Disease in Canada (EBIC)
Results: The results are expected to be highly impacted by the changes in the age/sex structure of the population. Changes in the intensity of drug therapy for specific age groups will be considered in scenario analysis in future studies. Drivers in model: The main drivers are the usual demographic drivers, incidence and incremental mortality assumptions as well as actual cost data associated with DM and other diseases with estimates for hospitalizations, physicians, drugs and indirect costs. The main driver of the forecasts is the age-sex-province population in Canada. There is some uncertainty about its future composition, given variability in fertility, death rates and immigration assumptions. This study uses a model to calculate the sensitivity of the forecasts to different demographic assumptions incorporated in the 13 projection scenarios released by Statistics Canada.
Keywords: *Modeling, incidence, costs*

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Gestational exposure to antidepressants and the risk of miscarriage: a review

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Background: Although the relationship between antidepressant use during pregnancy and its complications has been widely investigated, very few studies have attempted to evaluate the impact of antidepressant use during pregnancy on the risk of miscarriage. We present an overview of the evidence relating to the association between antidepressant use during gestation and the risk of miscarriage.
Methods: We systematically searched PubMed and the reference lists of all relevant articles, including reviews, published in English and in French from 1975 through 2008 for studies that examined the association between adverse pregnancy outcomes and gestational exposure to antidepressants with data on miscarriages. Only etiologic studies were considered.
Results: We found 12 studies that met inclusion criteria. The majority of these were prospective cohort studies on tricyclics or SSRI use during pregnancy. Overall, in unadjusted analyses, fluoxetine (OR = 2.2; 95% CI = 1.2 – 4.1) and bupropion (OR = 4.1; 95% CI = 1.5 – 11.1) were associated with the risk of miscarriage. However, in adjusted analyses, only paroxetine (OR = 1.7; 95% CI = 1.3 – 2.3) and venlafaxine (OR = 2.1; 95% CI = 1.3 – 3.3) were associated with the risk of miscarriage.
Conclusions: This review suggests that gestational exposure to antidepressants, especially paroxetine and venlafaxine, could lead to miscarriage.
Keywords: *Antidepressant, miscarriage, review*

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Growth hormone for treating Turner syndrome in Canada: structuring evidence into the EVIDEM multi-criteria decision analysis framework to support decision making

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Background: Treatment of Turner syndrome (TS) with growth hormone (GH) is complex and all factors need to be considered if we wish to optimize health for children with this disease. EVIDEM is a multi-criteria decision analysis (MCDA) framework allowing deconstruction of the components of decision and facilitating access to evidence. The objective of this study was to explore complex decision using this framework.
Methods: Using previously described methodology and instruments, an EVIDEM Record was developed

for GH for the treatment of TS in Canada. Data from the public domain was collected, synthesized, assessed for quality and the validated by experts. A web-based prototype of the Record was developed.
Results: The EVIDEM record provided structured access to the available data prepared in a synthesized format for TS, its epidemiology and efficacy, safety and quality of life evidence for GH treatment. Economic evidence in the Canadian context included cost-effectiveness and impact on drug and healthcare spending. There were data limitations that affected the relevance to decision making and validity of clinical and economic evidence. Ethical and health system-related issues were also identified. An interactive web 2.0 environment provided access to an electronic record that facilitated knowledge transfer. The value of GH and benefits of the framework will be assessed by a panel of representative stakeholders.
Conclusion: The EVIDEM framework provides a practical tool for those who need to make policy or clinical decisions regarding the use of GH in treatment of TS.
Keywords: *Multi-criteria decision analysis, Turner syndrome, growth hormone*

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How does the Canadian general public view moderate Alzheimer's disease? Determination of health utility scores

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Background: 1) To elicit health utility scores for moderate Alzheimer's disease (AD) using the Canadian general public; 2) to compare utility scores for Canadians' self-assessed health status with utility scores for health status defined as moderate AD; 3) to measure awareness of AD; and 4) to determine factors that influence utility scores.
Methods: Five-hundred Canadians were chosen randomly to participate in a telephone interview. The EQ-5D was administered to measure utility for respondents' current health status (i.e., no AD). After describing moderate AD, respondents were asked to answer the EQ-5D again, this time imagining they had moderate AD. AD awareness was measured with the Alzheimer's Disease Knowledge Test (ADKT). Respondents were also asked about socio-demographics and whether they knew someone with AD. OLS regressions were conducted to identify determinants of EQ-5D utility scores.
Results: The mean age of respondents was 51 years, 61% were female, and 42% knew someone with AD. Mean ADKT score was 3.4 (SD: 1.1) out of 5 (higher scores indicate better knowledge of AD). Respondents' mean EQ-5D score for their current health status was 0.857 (SD: 0.15). Mean EQ-5D score for a hypothetical, moderate AD health status was 0.638 (SD: .20). Only age was significant in the determination of the utility score under the assumption of moderate AD. Gender, knowledge of someone with AD, or AD awareness scores had no impact.
Conclusions: When measured by the EQ-5D, Canadians would expect to assign a lower utility to their health status when they have moderate AD.
Keywords: *Alzheimer's disease, HRQoL*

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The burden of obesity in adults living in Ontario

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Background: To present an overview of the burden of obesity in adults by using the richness of a Canadian population health survey linked to Ontario administrative databases.
Methods: The records of all Ontarians who participated in the Canadian Community Health Survey (CCHS), cycle 1.1 (2000/2001) and provided consent to data linkage with administrative databases were linked to the Ontario Health Insurance Program (OHIP) claims database and the Discharge Abstract Database (DAD) In-Patient and Day Procedure database. Prevalence of obesity in this adult population was documented using the body mass index (BMI) calculated by Statistics Canada for adults aged 20-64 years of age. Socio-demographics (e.g. age, gender, education), medical characteristics (e.g. comorbidities), health related quality of life (Health Utility Index 3), self-reported health and one-year physician and hospitalization costs were described per BMI category (i.e. underweight, normal weight, overweight and obese). A Generalized Linear Model (GLM) was used to identify determinants of costs.
Results: More than 50% percent of adult participants were either overweight or obese in 2000/2001. When classified by BMI categories, obese individuals were more likely to be older, males, have more comorbidities, a lower quality of life and higher one-year medical costs. Age, gender, being inactive and smoker increased significantly the total costs. Compared to normal weight adults, being underweight or obese were also positive predictors of costs. Health-related quality of life, income or being overweight had no impact on costs.

Conclusions: These results suggest that the burden of obesity in Ontario is considerable.
Keywords: *Obesity, costs, HRQoL*

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Impact of adalimumab (HUMIRA®) on work productivity in patients with psoriatic arthritis: results from ACCLAIM

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Background: ACCLAIM is an open-label, Phase IIIb study of Canadian patients with active psoriatic arthritis (PsA) who had not responded to DMARD therapy and who were treated with adalimumab 40 mg by subcutaneous injection every other week for 12 weeks. We assessed the impact of adalimumab treatment on work limitations and productivity in PsA patients.
Methods: The Work Limitations Questionnaire (WLQ), a 25-item, self-administered questionnaire, measures the disease impact on productivity of employed patients, specifically: difficulty in time-related demands (Time), physical impairment (Physical), cognitive function and interpersonal interactions (Mental), and ability to successfully meet task demands (Output). The WLQ Productivity Loss Score summarizes the limitations in performing job tasks. The mean change in WLQ from baseline to 12 weeks was assessed in the entire group and relevant subgroups defined by baseline characteristics (age, sex, DMARDs use, disease duration).
Results: 127 patients enrolled and completed the study (mean age=49; male=54.3%). All 99 employed patients (78%) completed the WLQ. Mean (SD) significant changes in all scales were observed between baseline and Week12: Physical, –14.5 (31.5); Time, –12.6 (27.3); Work Productivity, –2.3 (5.1), (all $p<0.001$); Mental, –4.4 (22.1; $p=0.060$); and Output, –8.1 (25.4; $p=0.003$). Significant changes were also observed for the majority of subgroups analyzed.
Conclusions: This stratified analysis further describes the impact of adalimumab on work productivity, considering potential confounding variables. Treatment benefits were observed across relevant patient subgroups in the ACCLAIM study. Adalimumab was associated with significant improvements in work productivity, as measured by the WLQ in employed PsA patients.
Keywords: *Psoriatic arthritis, Work Limitations Questionnaire (WLQ)*

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Reliability and validity of the Work Limitations Questionnaire in patients with psoriatic arthritis: results from ACCLAIM

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Background: The Work Limitations Questionnaire (WLQ) is a 25-item, self-administered instrument measuring the disease impact on productivity of employed patients. The objective was to assess the reliability and validity of the WLQ in psoriatic arthritis (PsA) patients and describe adalimumab impact on presenteeism.
Methods: Data were obtained from ACCLAIM, a Canadian, prospective, open-label cohort study of 127 PsA patients treated for 12 weeks with adalimumab. Internal consistency of the 4 WLQ scales, measured by Cronbach's alpha, was used to assess reliability. Overall construct validity was assessed by a correlation matrix of change in WLQ scales over the 12-week treatment period with changes in clinical measures of the disease, patient and physician measures of disease activity and pain. We hypothesized that WLQ measures have constructs different from but related to those of physical and clinical assessments; hence, statistically significant correlation coefficients of 0.2 to 0.7 demonstrated construct validity.
Results: In ACCLAIM, 99 of 127 patients (78%) were employed and are included in the analysis. Mean age was 47 years, 42% were female, mean psoriasis and PsA duration were respectively 20.4 years and 10.8 years. Cronbach's alpha estimates of WLQ scales were 0.851 (baseline), 0.847 (12 weeks), and 0.614 (change from baseline to 12 weeks) (all $p<0.001$). Regression analyses demonstrated significant linear relationships between change in clinical measures and WLQ Index.
Conclusions: The WLQ is a reliable and valid instrument in PsA patients, providing valuable information beyond clinical and physical assessments. As early as 12 weeks, adalimumab was associated with significant presenteeism improvements.

Keywords: *Psoriatic arthritis, Work Limitations Questionnaire (WLQ)*

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Impact of prior authorization on the use of health services: a retrospective cohort study

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Background: A payment authorization process for asthma medications combining inhaled corticosteroids (ICSs) and long-acting bronchodilators (LABDs) was introduced in Québec in October, 2003. The objective of this study was to evaluate the impact of this measure on asthma-related emergency department visits and hospitalizations.
Methods: A retrospective cohort study was conducted using administrative data banks kept by the Régie de l'assurance maladie du Québec (RAMQ). The data concerned the two-year periods preceding and following introduction of the process. Four groups were created based on time of asthma diagnosis (pre-process or post-process period) and type of prescription drug insurance (private or public). All health insurance beneficiaries aged 6 to 44 years newly diagnosed with asthma during the periods concerned were included. Cox regression was used to assess, for each group, the relative risk of an asthma-related first hospitalization or emergency department visit between the two periods. The interaction between group and period was evaluated to verify whether the risks observed differed by insurance group (publicly or privately insured).
Results: The risk of an asthma-related first hospitalization or emergency department visit remained unchanged after the introduction of the process among both the 47,579 publicly insured persons and the 93,177 privately insured persons. In addition, the difference in the change in risk from the pre-process period to the post-process period between the two groups was not statistically significant.
Conclusions: The results indicate that the introduction of the special authorization process had no major impact on the health of people with asthma.
Keywords: *Cohort study; asthma; reimbursement mechanism*

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Incidence and cost of cardiovascular co-morbidities in diabetic patients

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Background: Diabetes is associated with multiple co-morbidities including hypertension and dyslipidemia. The objective of this study is to compare the incidence and cost associated with the development of cardiovascular co-morbidities for diabetic patients versus non-diabetic patients.
Methods: Using longitudinal claims level data from private drug plans in Canada, patients were identified as diabetic or non-diabetic based on their prescription drug use in 2000. The diabetic group included patients who were new to diabetes therapies only, and those who developed diabetes between 2001 and 2007 were excluded from the study. Each group's claim history was subsequently examined to identify patients who developed hypertension or dyslipidemia. The incidence rate and treatment costs associated with each condition were then established by age for each patient cohort.
Results: The incidence rate for both cardiovascular co-morbidities was found to be significantly higher in diabetic patients in all age groups. By 2007, 86% of diabetic patients were treated for dyslipidemia while 83% were treated for hypertension. This compared to only 21% and 27% of non-diabetic patients, respectively. Treatment regimens associated with the development of these secondary conditions were almost two times more costly for diabetic patients than for non-diabetic patients. In addition, a demographic analysis revealed that diabetic patients aged less than 45 were 5 to 10 times more likely to develop cardiovascular co-morbidities than non-diabetic patients.
Conclusions: Not only are diabetic patients more likely to develop cardiovascular co-morbidities than non-diabetic patients, but they also require more intensive and costly therapies.
Keywords: *Longitudinal study, cardiovascular co-morbidities, diabetes*

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Interventions to improve medication reconciliation in primary care: a systematic review

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Background: Inaccuracies in medication records are common in primary care. Although medication reconciliation has been implemented in some hospitals, little is known about its efficacy in primary care. Objective: To systematically review all primary care intervention studies designed to implement medication reconciliation for effects on medication discrepancies,

clinical outcomes and patient knowledge of their medications.
Methods: Design: Systematic review of prospective intervention studies. Data sources: Medline (1988-2008), Healthstar (1966-2008), CINAHL (1982-2008), Embase (1980-2008), CENTRAL, and unpublished material. No language restrictions were applied. Studies reviewed: Studies that examined the effect of various interventions on medication discrepancies either in ambulatory settings or at hospital discharge were included. Two reviewers independently assessed studies to determine inclusion. Level of agreement between the reviewers was good with unweighted Cohen's κ of 0.71. Two of three independent reviewers abstracted data and evaluated validity from included studies.
Results: Four trials met inclusion criteria. Two before and after studies (n = 275) in ambulatory care examining systematic medication reconciliation at each visit produced mixed results. One showed a reduction in the prevalence of medication discrepancies from 98.2% to 84% after three months ($p<0.05$); the other showed no benefit. One RCT and one before and after study (n = 202) evaluated pharmacist medication review at hospital discharge. Neither showed a benefit. Heterogeneity precluded pooling of studies. All included studies had significant design flaws.
Conclusions: There is no convincing evidence of the effectiveness of medication reconciliation in primary care, primarily because of the lack of well-designed studies.
Keywords: *Medication errors, medical history taking, primary health care*

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Large scale anonymized longitudinal patient data and its role in better understanding health care provider response to advisories

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Background: The power of large scale anonymized patient level information can efficiently be harnessed to examine the disease treatment of Canadians, by mono and concomitant therapy use. Longitudinal prescription data (LRx) were examined to obtain a better understanding of therapeutic treatment choices in hypertension.
Methods: On January 16th 2009, the Heart and Stroke Foundation and Canadian Hypertension Education Program issued an advisory about a potential drug combination problem regarding two blood pressure medications. To demonstrate the value of LRx information, over 17 million lives were analysed cross-sectionally to develop relevant treated-prevalence estimates, for mono and concomitant treatment of hypertension across ACE and ARB therapies. A further longitudinal analysis of ACE/ARB patients before and after the advisory reveals how patient treatment has changed.
Results: The analysis shows treated prevalence for hypertension (by ACE and ARBs only) varies regionally from 4 to 10% across the country. New patients tended to be started on a 60/40 split of ACEs/ARBs. As a result, approximately 70% of patients moving to concomitant treatments were being treated with ACEs. More than half of these patients had ARBs added to their existing ACE therapy, prior to the advisory being issued.
Conclusions: Although the focus of this work has been on one particular advisory, the power of such databases can be leveraged against almost any medication risk (or benefit) advisory affecting Canadians. LRx Information is a powerful tool for governments, pharmaceutical manufacturers, medical researchers, and other healthcare professionals.
Keywords: *Longitudinal patient, risk advisory, LRX analysis*

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New measures of patients' adherence and prescribing patterns: the case of adult patients with symptomatic persistent asthma

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Background: Several measures of adherence to prescribed medications derived from administrative databases reflect both patients and physicians behaviour, even if they are often interpreted as being solely patient's adherence. Adherence has been shown to be low among asthmatic patients.
Methods: We developed a measure of prescription patterns defined as the total days' supply prescribed (including new prescriptions and allowed refills) and a new measure of patients' adherence defined as the ratio of the total days' supply dispensed to the total days' supply prescribed (PPDC) over 1 year. The PPDC is a modification of an existing adherence measure called the proportion days covered (PDC). The PPDC and PDC for inhaled corticosteroids (ICS), a controller therapy that should be prescribed for chronic daily use to patients with persistent asthma, were compared

within a cohort of 4190 ICS naive patients aged 18-45 years. This cohort was selected from administrative databases of Québec. We estimated the mean and 95% CI of the total number of supplies and days' supply prescribed the PPDC and the PDC over 1 year.
Results: Patients had on average 6.0 supplies prescribed (95% CI: 5.8-6.1) (1.6 new prescriptions and 4.3 allowed refills) of ICS corresponding to 161 days' supply prescribed (95% CI: 157-165) over 1 year. The average PDC and PPDC were 19.1% (95% CI: 18.6-19.6) and 57.7 % (95% CI: 56.7-58.7), respectively.
Conclusions: Forty-eight percent of non-adherence attributed to patients when measured with the PDC can, in fact, be attributed to physicians' failure to prescribe ICS for chronic daily use.
Keywords: *Treatment adherence, prescription patterns, asthma*

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Pharmaceutical disposal programs for the public: a Canadian perspective

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Background: The presence of pharmaceuticals in the environment has become an environmental issue. Although human excretion has been identified as the main factor, improper disposal practices can also contribute to this problem. This paper identifies and assesses safe pharmaceutical disposal programs for the public.
Methods: Each Canadian jurisdiction (national, provincial/territorial, and municipal) are reviewed. In addition, Canadian programs are compared with international programs. All information is gathered via Internet searches, personal communications, and scientific journal reviews.
Results: The main findings are: 1) Canada does not have a nation-wide pharmaceutical disposal program but a variety of programs are established at provincial, municipal, and community levels; 2) across the Canadian province-wide programs, Alberta seems to divert the most quantity, in absolute terms, of pharmaceutical waste from household wastes and sewer systems but Saskatchewan demonstrates a better performance per capita; and finally 3) outside of Canada, nation-wide pharmaceutical disposal programs exist in some countries.
Conclusions: Programs have seen increasing volumes of pharmaceutical waste collected in the past few years. However, in order to improve proper disposal of pharmaceuticals, it is important to increase public awareness and understanding of the risks associated with pharmaceutical products in the environment and the benefits of safe disposal methods. Finally, it is important that safe disposal management systems exist for all stakeholders.
Keywords: *Pharmaceuticals, take-back, disposal*

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Pharmacists' perspectives and initial experience with the MedsCheck pharmacist medication review in Ontario

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Background: Community pharmacists in Ontario are now compensated for providing a Medication Review Service (MedsCheck) to Ontarians taking three or more chronic medications. The objectives of this study were to identify barriers and facilitators to implementation of MedsCheck and identify factors predicting the number of MedsCheck reviews completed.
Methods: A sequential explanatory mixed methods study design was used, consisting of administration of a semi-structured mailed survey followed by an in depth telephone interview using open-ended questions with a random sample of community pharmacists across all regions of Ontario. Regression was conducted to determine the factors predicting the number of MedsCheck reviews completed.
Results: Completed surveys were received by 217 pharmacists. Twelve pharmacists were interviewed. The majority (98.6%) of pharmacists had completed at least 1 MedsCheck review. The average time to complete a review was 50.9 (SD, 22.2) minutes. Key facilitators to implementation included scheduling reviews by appointment and during slower times or when pharmacist coverage was available, reducing documentation, having a private counselling room, maximizing use of technicians, and motivating patients regarding the value of the service. Factors predicting an increase in MedsCheck reviews reported were having a target number of MedsChecks at the store, not reimbursing individual pharmacists for MedsChecks, using computers, being from northern Ontario, and a longer time since pharmacy graduation.
Conclusions: MedsCheck was well received by pharmacists in Ontario. Practical suggestions to improve the delivery of MedsCheck or similar services were identified. Further research can assess uptake of the program as well as the effectiveness (and cost-effectiveness of the program).

Keywords: *MedsCheck, community pharmacist, medication review*

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Restricted access to drugs is associated with less optimal mineral metabolism control in hemodialysis patients

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Background: Abnormalities in mineral metabolism (MM) are associated with increased morbidity and mortality in patients with Chronic Kidney Disease (CKD). PhotoGraphTM software allows dialysis centres to track MM and assess treatment efficacy. Recent Canadian studies in other patient populations have suggested that restricted access to medications in the Canadian healthcare setting was associated with poorer patient outcomes. This study aimed to compare MM management among dialysis patients living in provinces with more open vs. more restricted access to new drugs.
Methods: A sample of 50 Canadian dialysis centres which used PhotoGraphTM were selected. Phosphorus (P), calcium (Ca), intact parathyroid hormone (iPTH) and calcium-phosphate product (CaXP) were measured and compared between provinces with open and restricted access.
Results: MM targets were more likely to be reached by patients residing in provinces with formularies allowing more open access to non-calcium based phosphate binders (non-CBBs): P: 61.6% vs. 54.9%; Ca: 59% vs. 44.8%; iPTH: 31.1% vs. 27.3%; CaXP: 85.4% vs. 76.9%. Patients residing in provinces with more restrictive formularies were more likely to receive doses of calcium that exceed the maximum recommended in treatment guidelines (i.e., >1.5 g/day) than those with more open listings (62% vs. 15%). Patients residing in provinces with restricted access to sevelamer were less likely to receive this drug (16.2% vs. 42%).
Conclusions: MM was better managed among patients in settings with more open access to non-CBBs. There is a reasonable expectation that this may translate to better outcomes and reduced mortality among hemodialysis patients.
Keywords: *Hemodialysis, mineral metabolism, drug access*

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Rheumatoid arthritis, its treatments, and the risk of tuberculosis in Quebec, Canada

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Background: To determine the risk of tuberculosis (TB) among a cohort of patients with rheumatoid arthritis (RA) in Quebec and assess whether this risk is associated with exposure to nonbiologic disease-modifying antirheumatic drugs (DMARDs).
Methods: We studied a cohort of patients with RA identified from the Quebec provincial physician billing and hospitalization databases for 1980–2003. TB incidence rates were determined for the period 1992–2003 and compared with the general population, standardized for age and sex using the standardized incidence ratio (SIR). Conditional logistic regression was used in a nested case–control analysis to estimate the rate ratio (RR) of TB related to nonbiologic DMARD exposure during the year before the index date.
Results: Of the 24,282 patients with RA in the cohort, 50 cases of TB were identified. The standardized incidence rate was 45.8 cases per 100,000 person-years compared with 4.2 cases per 100,000 person-years in the general population of Quebec (SIR 10.9, 95% confidence interval [95% CI] 7.9 –15.0). The adjusted RR of TB was 2.4 (95% CI 1.1–5.4) with corticosteroid use and 3.0 (95% CI 1.6 –5.8) with nonbiologic DMARD use.
Conclusion: The age- and sex-standardized incidence rate of TB in RA patients is 10 times that of the general population. At least some of this risk may be related to nonbiologic DMARD and corticosteroid therapies. Our data support the role of TB screening before initiation of any immunosuppressive therapy.
Keywords: *Tuberculosis, antirheumatic drugs, corticosteroid*

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Schizophrenia modeling: factors associated with the risk of being in a specific disease state

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Background: Aim: As a first step to model schizophrenia, we are proposing a research project aimed at better understanding the factors associated with specific disease states associated with schizophrenia. Objectives: To evaluate the factors associated with the risk of being in a specific disease state of schizophrenia.

Methods: The model was based on data from RAMQ and Med-Echo databases. A total of 12,754 newly diagnosed patients with schizophrenia patients were identified between 1998 and 2006, aged between 0 and 60. Six discrete disease states were defined within the model (first episode – FE, low dependency state – LDS, high dependency state – HDS, Stable, Well and Death) and patients' movements between these disease states enabled 17 risks to be identified. To evaluate factors associated to the risk of being in each disease state, we constructed 6 risk functions based on Cox proportional hazard analysis for competing risks. The risk factors were modeled including age, gender, social assistance status, severity of schizophrenia, depression, anxiolytic drugs use and other mental disorders.

Results: After the FE of schizophrenia, 69.8% of patients transitioned to LDS, 11.2% to HDS, 1% to the death state and 18% into the Well state. Being male (HR: 0.93, 95% CI: 0.89-0.97) or older (HR: 0.94, 95% CI: 0.91-0.96) was associated with a decreasing risk of moving to LDS after being FE. In contrast, being on social assistance, depressed, using anxiolytic drugs or being diagnosed with other mental disorders were associated with an increased risk of being in a LDS after a FE, ranging from 1.11 to 1.55 folds. The factors associated with the risk of being in HDS or Death state after a FE were also estimated and similarly, the results of the other 5 risk functions were also obtained.

Conclusion: Some of our results are consistent with those obtained from the published literature. Based on these risk functions we estimate individual transition probabilities that will be used in the first Canadian model of schizophrenia incorporating transition probabilities adjusted for individual risk factors profiles using Canadian data.

Keywords: *Schizophrenia, risk factors, modelisation*

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Schizophrenia modeling: Markov model with Monte-Carlo microsimulation

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Funding Source: Genome Quebec, Genome Canada

Background: Aim: Pharmacological strategies for schizophrenia have received increasing attention due to the development of new and costly drug therapies. Evaluating their relative costs and benefits in Canada requires modeling the natural course of schizophrenia. Objectives: To develop a Markov model with 1st-order Monte-Carlo simulations to simulate the natural course of newly diagnosed schizophrenic patients.

Methods: Six discrete disease states defined the Markov model: 1): first episode - FE; 2) low dependency state - LDS; 3) high dependency state - HDS; 4) Stable; 5) Well; and 6) Death. Patients' movements between these disease states defined 17 probability transitions to be estimated. The model was based on data from the Régie de l'assurance maladie du Québec and Med-Echo databases, which were linked. All individuals aged 0-60 years with a diagnosis of schizophrenia between 1998 to 2000 were first identified by ICD-9 codes. Those without diagnostic of psychoses in the two years prior to entry date were considered newly schizophrenic diagnosed patients. Each individual was followed for a maximum of 8 years. Using this data, Cox proportional hazard models for competing risks were used to estimate the 17 probabilities of transition. Validation was conducted by comparing the model's probability transitions' predictions with the published literature.

Results: A total of 12,754 individuals were identified as newly diagnosed patients with schizophrenia. After the FE of schizophrenia, 69.8% of patients passed in LDS, 11.2% in HDS, 1% in death state and 18% in Well state. The mean transition probabilities after one year of follow-up were: FE to Well at 0.28 (± SD=0.10), FE to HDS at 0.11 (±0.05), FE to LDS at 0.60 (±0.08) and respectively FE to Death at 0.01 (±0.01). The corresponding values were similar to those obtained from other published models (i.e. 0.24, 0.15, and 0.61 with a mortality rate of 0.008 per year). The results for the other 5 transition probabilities were similar with those obtained from literature.

Conclusion: This model is the first Canadian model incorporating transition probabilities adjusted for individual risk factors profiles using Canadian data. Future applications will include pricing and cost-effectiveness of new therapies for schizophrenia.

Keywords: *Schizophrenia, Markov model, modelisation*

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Socioeconomic status of women obtaining emergency contraceptives from pharmacists in British Columbia

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Background: Emergency contraceptives (ECs) can reduce the risk of pregnancy after unprotected intercourse. A cohort of women who received a total of 8266 Yuzpe (YZP) or levonorgestrel (LNG) regimens of ECs from pharmacists were compared for post-treatment pregnancy rates. Initial analysis showed that unadjusted pregnancy rates were not significantly different between the two groups. Because the study was not randomized, and the costs of the two regimens were differential for most women who accessed them through pharmacies, we evaluated the socioeconomic characteristics of women in the two groups based on geographical units of residence.
Methods: Mean population income within geographical units was derived from census data and linked to postal codes of women in the cohort. Income of women in the two groups was compared at the forward sortation area (FSA) level and at the dissemination area (DA) level.
Results: At the FSA level, mean (SD) income was $29327.78 (5896.70) and $30783.76 (7432.29) for the YZP and LNG groups, respectively, $p<0.001$. At the DA level, mean (SD) income was $29268.34 (8817.53) and $31135.62 (11744.98), respectively, $p<0.001$. Among teenagers (26% of cohort), women 20-29 years (45%) and 40-49 years (6%), mean income was significantly lower in the YZP group than in the LNG group at both levels.
Conclusions: Socioeconomic status, as evaluated by geographical income analysis, was lower among women who received YZP than those who received LNG, irrespective of age. Observational studies of ECs should control for this potential threat to internal validity.
Keywords: *Emergency contraceptives, socioeconomic status, age-stratified analysis*

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The cost-effectiveness of a blood test for colorectal cancer screening

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Funding Source: GeneNews Ltd.
Background: Colorectal cancer (CRC) is the second leading cause of cancer death in Canada. Although regular screening with the fecal occult blood test (FOBT) can reduce CRC mortality, patient acceptance is poor. ColonSentryTM, a Canadian technology, is the first blood test for CRC screening. An initial cost-effectiveness analysis assessed the value of ColonSentry in screening for CRC.
Methods: A decision-analytic model was used to compare no screening to one cycle of screening with FOBT or ColonSentry in an average risk population aged 50 and over. The economic evaluation was conducted from the perspectives of the health care system, private payers, and society. The CRC detection rates for FOBT and ColonSentry were obtained from scientific sources. The healthcare system cost for CRC was obtained from a Statistics Canada model. Private payer costs were from the University of Toronto and Manulife. All costs were reported in 2008 Canadian dollars.
Results: ColonSentry detected more early stage CRC, saved lives, and lowered the costs associated with late stage CRC. From the healthcare perspective, ColonSentry was cost-effective versus no screening ($41,227/QALY) and FOBT ($47,699/QALY). For private payers, ColonSentry saved more lives and cost less than FOBT (-$40,124/QALY) or no screening (-$34,726/QALY). From the societal perspective, ColonSentry was also dominant.
Conclusions: This economic evaluation demonstrated that ColonSentry can be cost-effective for CRC screening.
Keywords: *Colorectal cancer, cancer screening, economic evaluation*

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The determinants of benzodiazepine (BZD) use among individuals with major depressive episodes (MDE) in Canada

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Background: Although Canadian clinical practice guidelines to manage major depression recommend antidepressants (ADs) alone for the pharmacotherapy of MDE, there is evidence of co-prescribing of BZDs to treat comorbid anxiety in individuals with major

depression. Objectives: to 1) determine the extent of co-prescribing, 2) explore the key determinants for co-prescribing, and 3) determine whether access to psychiatrists/general practitioners (GP's) influences co-prescribing.
Methods: Data from CCHS 1.2 was examined to measure co-prescribing rates of BZDs and ADs by analyzing the ratio (BZD/AD) in the use of the two drugs among Canadian's who have experienced MDE. Descriptive statistics measured the extent of co-prescribing while adjusted logistic regression models were employed to identify key predictors and test for the mediating effects of psychiatrists/GP's on co-prescribing. Appropriate sampling weights and bootstrap variance estimation procedures were used for all analyses.
Results: The overall prevalence of co-prescribing was 46.9% while key determinants were middle household income (OR=1.4), poor self perceived health (OR=2.3), age 15-35 years (OR=2.6), being a residents of Quebec (OR=1.8). Having been treated by a psychiatrist (OR=1.9) increased the odds of co-prescribing, while having been treated by a GP (OR=0.5) decreased co-prescribing.
Conclusions: A large proportion of the study population received co-prescribing that is inconsistent with clinical practice guidelines. Some individuals may be severe enough to necessitate co-prescribing while certain subpopulations may be adversely affected by co-prescribing. Both the patient and physician characteristics significantly influenced co-prescribing. Interventions to improve evidence informed prescribing and monitor outcomes from drug therapy regimens should be implemented.
Keywords: *MDE, co-prescribing, evidence informed prescribing*

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The effects of calcium-based vs. non calcium-based phosphate binders on outcomes among patients with chronic kidney disease: a meta-analysis

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Funding Source: Genzyme Canada Inc.
Background: Two-thirds of patients with Chronic Kidney Disease (CKD) will die of cardiovascular disease (CVD). Coronary artery calcification (CAC) is a major risk factor for CVD in CKD patients. Calcium-based phosphate binders (CBBs) may worsen CAC. The aim of this systematic review was to determine the effect of CBBs vs. non-CBBs on all-cause mortality and CAC among patients with CKD.
Methods: We conducted a detailed search of electronic databases (e.g., MEDLINE, EMBASE, CINHAL) using the following terms: kidney disease, phosphate binders, calcium dialysis, phosphate levels, CV events and mortality. Standard Cochrane methods for study selection and data abstraction were followed.
Results: Fifty-seven articles were retrieved for detailed evaluation. Sevelamer was the only non-CBB noted in the 9 trials which met the inclusion criteria. Sevelamer was associated with a trend towards a decrease in all-cause mortality (RR 0.81; 95% CI 0.65-1.02), p=0.07 vs. CBBs. Overall difference in change of CAC scores among those taking sevelamer vs. CBBs was -76.35 (95% CI -158.25 – 5.55), p=0.07.
Conclusions: Compared to CBBs, sevelamer is associated with a non-significant trend toward reduced all-cause mortality. This is concordant with the trend toward a modest reduction in CAC progression with sevelamer. Since CBBs are used frequently in CKD patients, this systematic review highlights the need to further evaluate the safety of CBBs in this high-risk population.
Keywords: *Chronic Kidney Disease, phosphate binders, mortality*

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The use of prescribed medications among residents of Quebec covered by a private drug insurance plan: results from the reMed pilot study

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Background: In order to circumvent the lack of computerized data on medications dispensed to people with private drug insurance in the province of Quebec, we developed a computerized registry called reMed. Objectives: To describe the pilot study that led to the construction of reMed and to compare medications data between reMed participants and Quebec residents with public and private drug insurance.
Methods: In 2007, community pharmacies were recruited in the Montreal area and persons aged 18-65 years with private drug insurance were recruited. Patient's identification, private drug plan information

and socio-demographic variables were gathered. Data related to prescriptions dispensed were transferred to reMed bi-monthly from the community pharmacies' computer services providers.
Results: Twelve (52%) pharmacies and 1153 (51%) subjects with private drug insurance accepted to participate. Participants were 44 years old on average, 34% were male, 21 % were current smokers and 32% were overweight. Smoking habits and obesity were found to be comparable between reMed and the general adult Quebec population. In 2007, statins were the most prevalent therapeutic class purchased by reMed participants (6.4% of all prescriptions) with an average cost of $68.99 per prescription. In 2007, ESI Canada reported similar estimates for statins among Quebec residents with private drug insurance (prevalence of 6.2%, average cost of $68.39). However, the corresponding cost estimate was only $56.36 for Quebec residents with public drug insurance.
Conclusions: The reMed database appears to be a valid research tool since it includes participants that are representative of Quebec residents with private drug insurance.
Keywords: *Database, private drug insurance*

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Trends in the use of potentially harmful medications among seniors prior the implementation of a pharmacy network

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Background: Pharmaceutical therapy is the most common form of medical intervention. However, when medications are used inappropriately they can put the patient at risk for harm. Seniors are at particular risk for inappropriate medication use because they experience age-related changes in their body's ability to handle medication. The purpose of this study was to profile inappropriate medication use among seniors prior to the implementation of a population-based pharmacy network in Newfoundland and Labrador.
Methods: Seniors were recruited using self-referral from advertisements and through random digit dialing. Pharmacists conducted in-home interviews with seniors to collect demographic information and compile a complete medication profile. A panel of pharmacists developed a list of inappropriate medications for the elderly building upon the Beer's Criteria, and used this to classify medications appropriateness. Duplicate therapy and drug-drug interactions were also examined.
Results: Preliminary findings show that nearly 45% of seniors are taking one or more medications that are deemed potentially inappropriate. Duplicate therapy and serious drug interactions were identified in 7.2% and 42.6% of seniors, respectively.
Conclusions: Inappropriate medication use among seniors is a prevalent problem and effective intervention strategies need to be developed to address the issue. Baseline data collected in this study will be used as a comparator in the post-implementation study that will be carried out approximately one year after the Pharmacy Network is implemented. Findings of the pre-/post-implementation study can then be used to support public health decision-making with respect to using a Pharmacy Network as a strategy to reduce inappropriate medication use among the elderly.
Keywords: *Inappropriate medication use, interviews*

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Using latent class analysis to model heterogeneity in patients' preferences for alternative routes of insulin delivery for diabetes management

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Background: Developed to offer diabetics alternative treatment options. The objective was to determine the patients' preferences for different routes and attributes of insulin administration using a discrete choice experiment (DCE), and to study the distribution of respondents preferences.
Methods: The DCE was designed to determine diabetic patients' preferences for route of insulin delivery and their association potential risks and benefits. The data were analyzed using a latent class model (LCM) to evaluate if heterogeneity in patients' preferences exists. Socio-demographic variables were investigated for inclusion in the final model.
Results: 284 respondents (mean age 57±13 years) completed the DCE. All attributes evaluated were statistically significant ($p<0.05$), and the LCM suggested that 5 classes exist. Class 1 (38% of respondents) viewed control as most important attribute, and tended to have low levels of HbA1c and a high household income. Class 2 (24%) deemed route of

administration most important and were more likely to be insulin näive and have moderate household income. Class 3 (15%) viewed cost as most important and tended to have moderate household income. Class 4 (13%) considered weight as most important and class 5 (10%) found hypoglycemia most important and tended to have high levels of HbA1c.

Conclusions: The identification of latent classes suggests the existence of heterogeneity in patient's preferences for different routes of insulin delivery and their associated risks and benefits. This underlines the importance of accounting for preference heterogeneity when analyzing data from DCEs to help inform treatment choices.

Keywords: *Latent class analysis, discrete choice experiment, diabetes management*

AUTHOR INDEX BY ABSTRACT